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Health Benefits of Dietary Protein throughout the Life Cycle

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Abstract

Dietary protein intake and the associated health benefits continue to be a subject of great debate. The quantity of protein consumed, the quality or source of protein consumed, and the timing of protein intake throughout the day all play a role in determining the health benefits of dietary protein. Research suggests that intake of dietary protein above the dietary recommendations has health benefits throughout the lifecycle. This book chapter describes the dietary recommendations for protein intake throughout pregnancy, childhood, and adulthood and the associated health benefits with protein intake above the dietary guidelines at each stage of life.

Keywords: dietary protein, dietary guidelines, children, adults, health benefits

1. Introduction

Proteins are chains of amino acids which are involved in nearly every process in the body. Proteins function as enzymes, transcription factors, binding proteins, transmembrane transporters and channels, hormones, receptors, structural proteins, and signaling proteins [1]. However, the primary role of protein in the diet is to provide amino acids required for the synthesis of new proteins. We especially rely on dietary protein to provide the nine essential amino acids, which cannot be synthesized in the body. Protein intake greater than the dietary recommendations may prevent sarcopenia [2], help maintain energy balance [3], improve bone health [4–7] and cardiovascular function [8–10], and aid in wound healing [11]. This chapter focuses on the role of dietary protein, and the associated health benefits, throughout the life cycle.

2. Dietary recommendations for protein intake

The current dietary recommendations for protein intake include the estimated average requirement (EAR) [12] and the recommended dietary allowance [12]. For daily protein intake, the EAR for dietary protein is $0.66 \text{ g kg}^{-1} \text{ day}^{-1}$, and the RDA is $0.8 \text{ g kg}^{-1} \text{ day}^{-1}$ for all adults over 18 years of age. This can become confusing when trying to make recommendations for individuals at different stages of life. Even the Food and Nutrition Board recognizes a difference between what is recommended in the RDA and the level of protein intake needed for optimal health [12]. Therefore, there is a third recommendation for protein called the acceptable daily

macronutrient range (ADMR) [13, 14]. The ADMR includes a recommendation for protein intakes ranging from 10 to 35% of daily energy (e.g., calorie intake), which makes the ADMR easier to use when developing dietary recommendations for protein [12].

3. Dietary protein intake in adults

A majority of the adult population in the United States exceeds the minimum recommendations for protein intake [15]. The current dietary protein intake in the United States is approximately 82 g d⁻¹ for men and 67 g d⁻¹ for women [16]. **Table 1** details the current protein intake as percent of energy intake in the United States based on sex and age. A majority of dietary protein comes from animal protein (46%), followed by plant protein (30%), dairy (16%), and mixed foods (8%) [16]. There is increasing evidence indicating that consuming dietary protein at levels above the current RDA (0.8 g dietary protein kg body weight⁻¹ day⁻¹) may be beneficial for children, adults, older adults, and physically active individuals [17]. For example, protein intake above the RDA may help reduce the risk of chronic diseases such as obesity, cardiovascular disease, type 2 diabetes, osteoporosis, and sarcopenia [13, 17]. However, high protein intake without a subsequent decrease in carbohydrates attenuates the beneficial effects of dietary protein [18].

Age	Total	Men	Women
Protein			
20–44 years	15.7	16.1	15.3
45–64 years	15.8	16.0	15.7
65–74 years	16.3	16.6	16.1
75 years and older	15.7	16.1	15.3

Table 1.
Percentage macronutrient intake in the United States by sex and age [19].

4. Dietary protein intake in children

Adequate dietary protein intake is essential to support cellular integrity, growth, and physical function. Although protein malnutrition is not prevalent in the United States, there is little research on optimal protein requirements for health benefits in children. Current EARs are based on the factorial method and the nitrogen balance technique. The factorial method incorporates the estimated nitrogen (protein) requirement plus the rate of protein deposition and an estimate of the efficiency of protein utilization [20] which is derived from adult dietary protein needs [12]. By using the indicator amino acid oxidation method in a group of healthy children 6–11 years old, it was found that the mean and population-safe (upper 95% CI) protein requirements were 1.3 and 1.55 g kg⁻¹ day⁻¹, respectively. This is higher than the 2005 DRI for protein (0.76 and 0.95 g kg⁻¹ day⁻¹, respectively) [12]. A similar study using the nitrogen balance technique also found that protein requirements in children in this age range are above current recommendations at 1.2 g kg⁻¹ day⁻¹ [21]. These higher estimated protein requirements in children seem to be in line with current protein consumption patterns in different pediatric age groups. For instance, children 2–3 years old are currently daily consuming ~3.6 g/kg of ideal body weight, children 4–8 years old are currently

consuming $\sim 2.6 \text{ g kg}^{-1}$ ideal body weight⁻¹, and children 9–13 years old are consuming $\sim 1.6 \text{ g kg}^{-1}$ ideal body weight⁻¹ [15]; however, the optimal protein intake for children is still under debate [22]. There are racial/ethnic differences in protein consumption in children (2–18 years old). For example, non-Hispanic black children eat about 5% below, non-Hispanic white children eat about 3% below, Hispanic children eat about 2% below, and Asian children eat less than 1% below the EAR for protein [15].

Although the currently established recommendations for protein intake in children may be lower than the requirements, the effect of diets higher in protein (e.g., 30% of total energy intake) in children is unclear [22]. Several studies have alluded to the potential benefit of higher protein intake dietary practices. For instance, diets higher in protein with a low glycemic index can be protective against obesity in children aged 5–18 years [23], and diets higher in protein can lead to smaller waist circumference, blood pressure, insulin, and serum cholesterol than lower-protein diets in children from the same age group. A recent cohort analysis found that protein intake in 8-year-olds is associated with higher fat-free mass [24], and an additional cohort analysis found that at ages 11, 15, and 22 years, protein intake is inversely associated with early adulthood BMI. However, protein intake at 2 years was positively associated with BMI and lean mass at age 22 [25], suggesting there are conflicting results regarding the benefits of increased dietary protein in children.

5. Dietary protein intake in pregnant women

Pregnancy is a period of rapid tissue growth during a short period of time. Maternal tissues, including breast, uterine, and adipose tissues, blood volume, and extracellular fluids, account for the largest amount of protein accretion during pregnancy at 60%. The remaining 40% of protein accretion occurs within the amniotic fluid, fetus, and placenta [26, 27]. In fact, protein needs to increase soon after conception to support tissue growth and development, maintenance of maternal homeostasis, and lactation preparation [27–29]. These alterations occur in an exponential way and only in response to adequate total energy intake. This means that protein deposition does not significantly change in the first trimester compared to pre-pregnancy, but increases during the second trimester and significantly increases to the highest levels of protein deposition in the third trimester. This variable period of growth makes it difficult to define recommendations regarding protein requirements. Thus, although current recommendations suggest constant protein intake throughout the duration of pregnancy, pregnancy may actually require an increase in protein intake throughout gestation to support adequate growth, although further research is needed. There are several benefits of protein intake during pregnancy including adequate maternal weight gain within recommendations, lower early pregnancy BMI, and decreased postpartum weight [30].

Although the benefits of increased protein intake during pregnancy are apparent as stated above, protein requirements during pregnancy are difficult to measure. This is due to the involved nature of some of the techniques used to measure protein requirements. Therefore, the current dietary protein recommendations during pregnancy are based on factorial estimates of recommendations for healthy, nonpregnant populations. Pregnancy protein needs have been derived from the EAR and RDA for healthy, nonpregnant populations and are set to $0.88 \text{ g kg}^{-1} \text{ day}^{-1}$ (EAR) and $1.1 \text{ g kg}^{-1} \text{ day}^{-1}$ (RDA) [12]. However, newer studies found protein needs to be $1.2 \text{ g kg}^{-1} \text{ day}^{-1}$ at 11–20 weeks, increasing to $1.52 \text{ g kg}^{-1} \text{ day}^{-1}$ at 30–38 weeks [31]. Both nonpregnant women of childbearing age (20–44 years)

and pregnant women consume at or above the current recommendations of protein intake [32, 33]. One study [31] found that pregnant women consume the same amount of protein in early pregnancy ($1.44 \pm 0.30 \text{ g kg}^{-1} \text{ day}^{-1}$) as they do in late pregnancy ($1.47 \pm 0.53 \text{ g kg}^{-1} \text{ day}^{-1}$), not taking fluid retention and changes in body composition into account. These findings support others that have noted little overall change in dietary protein patterns from early to late pregnancy [33]. Collectively, these findings demonstrate that pregnant women meet the recommendations for dietary protein intake. Improvements may potentially be made to increase dietary protein requirements as pregnancy progresses.

6. Protein quality versus protein quantity

An important factor to consider when incorporating protein into the diet is how the source of dietary protein (e.g., protein derived from animal or plant sources) affects nutrient intake, nutrient adequacy, and diet quality [13, 34, 35]. Proteins with differing amino acid profiles exhibit varied digestion and absorption rates [36–38], and amino acid profiles depend directly on the quality and quantity of the dietary protein [37]. For example, the digestion and absorption rates of fast- (e.g., whey) versus slow (e.g., casein)-digesting proteins need to be taken into consideration when developing protein recommendations. One study provided young, healthy subjects with either a whey protein meal (30 g) or a casein meal (43 g) (both contained the same amount of leucine [one of the BCAAs]) and measured whole-body protein synthesis. Researchers determined that the subjects consuming the whey (fast) protein meal had a high, rapid increase in plasma amino acids, while subjects consuming the casein (slow) protein meal had a prolonged plateau of EAA [39]. In addition, the chemical structure and the presence of anti-nutritional compounds such as phytic acid within the protein source can influence digestion and amino acid availability [40]. Compared to animal sources, plant proteins are shown to have a lower anabolic impact on muscle; however, the reduced ability to elicit anabolic effects can be overcome by increasing protein intake and increasing the content of leucine [41].

Whether or not the amino acid source is derived from the whole protein or a mixture of free amino acids can also influence the rate of muscle protein synthesis [42]. For example, when older subjects were given either an EAA mixture (15 g) or a whey protein supplement (13.6 g) after an overnight fast, subjects consuming the EAA mixture had higher mixed muscle fractional synthetic rate [42], which is often associated with increases in muscle mass. The differing response could be due to the differing leucine content between the supplements (EAA, 2.8 g leucine, and whey, 1.8 g leucine) or because the EAA supplement was composed of individual amino acids while the whey protein supplement was intact protein. These subtle differences could influence the rate of appearance of the amino acids into blood circulation and thus the protein synthetic response.

Another potential confounder of the protein synthetic response of various proteins is the form or texture of the protein itself, such as ground beef versus a beef steak [43]. When, older men consumed 135 g of protein as either ground beef or as a beef steak, the amino acids from the ground beef appeared more rapidly in the circulation than the amino acids from the beef steak. Whole-body protein balance was higher after consumption of the ground beef versus the beef steak. However, 6 h after the beef meals, muscle protein synthesis was not different [43]. Nonetheless, these data support that the form of the protein that is being consumed impacts digestion, absorption, and the rate of appearance of amino acids into circulation [35].

7. Timing of protein intake

The timing of dietary protein intake has received ample attention in the past several decades. Adults typically consume the majority of their protein intake at dinner (38 g) versus breakfast (13 g) [44]. However, recent research suggests that ingestion of more than 30 g of protein in a test meal does not further stimulate the effect of dietary protein on muscle protein synthesis [45]. This has led to discussion related to optimal timing of protein intake. For example, distributing protein intake throughout the day, timing of protein around nighttime eating, and protein eating at breakfast are all areas of increased interest. In general, research covering these topics is performed in young, healthy populations, or aging populations, and very few, if any, studies have been conducted in children and pregnant women.

7.1 Protein intake at breakfast

Breakfast is often recognized as the most important meal of the day [46–48]. However, there is debate as to what defines the ideal breakfast meal [47], in addition to a lack of strong evidence to define which nutrients should be represented at breakfast [47]. A recent commentary published by the American Academy of Nutrition and Dietetics suggests that protein-containing foods (e.g., eggs, lean meat, and low-fat dairy products) should be included in breakfast meals [47]. Literature supports diets higher in protein aid in the treatment of chronic, metabolic diseases such as obesity, type 2 diabetes, and heart disease and have been shown to increase EE, improve satiety, regulate glycemic control, and improve body composition (reviewed in [13, 14, 34, 49]).

7.2 Protein intake in the evening

Eating protein at night and immediately before bedtime has received substantial attention in the past decade. Although past common knowledge would claim that eating before bed precipitates negative effects on health and body composition, more recent studies show that there may be many metabolic, health, and body composition-related benefits [50]. Much of the previous research claiming the negative effects of nighttime eating was performed in shift workers [51], populations with night eating syndrome, who consume $\geq 50\%$ of daily calories after dinner [52], and epidemiological data [53]. Although some of the negative effects of nighttime eating in these populations may include high BMI and abdominal obesity [54]; increased triglyceride concentration, dyslipidemia, and impaired glucose tolerance [55]; impaired kidney function [56]; and increased carbohydrate oxidation and decreased fat oxidation [57], many other factors need to be taken into consideration. For example, these populations are awake during abnormal hours and report sleep disturbances [58, 59]. In fact, the duration of sleep is inversely related to BMI [60, 61]. These populations also consume significantly more carbohydrate, protein, and fat throughout the day. Nonetheless, it is clear that eating large amounts of energy in the evening hours, in particular when the energy is carbohydrate- and fat-laden, may not be beneficial for health and body composition outcomes.

However, much more evidence has shown that eating a small protein snack (~200 kcal) before bed may elicit significant benefits. Improved muscle protein recovery, muscle mass, and strength gains mediated by enhanced overnight and next-morning muscle protein synthesis have been shown to be enhanced with 40 g of casein protein supplementation in elderly [62] and recreationally active men [63]. These effects are particularly enhanced when this dietary practice is added to the practice of resistance exercise [63]. In addition, reported hunger is lower and

satiety is higher, and resting energy expenditure is higher the following morning after a small protein snack compared to a noncaloric placebo [50, 62]. Chronically (4 weeks) there are also reports of decreased blood pressure, decreased arterial stiffness [64], and a greater decrease in body fat in overweight and obese women when consuming nighttime protein [65, 66]. Importantly, these benefits are accompanied by no significant alterations in overnight or next-morning lipolysis, fat oxidation, substrate utilization, or any blood markers in obese men or resistance-trained young women [67].

7.3 Distribution of protein intake throughout the day

Current research demonstrates that even distribution of protein intake throughout the day is more effective at stimulating a 24-h protein synthesis compared to an uneven distribution [68, 69]. This is supported by data from a longitudinal study on nutrition and aging, which found that even distribution of daily protein intake across meals is independently associated with greater muscle strength and higher muscle mass in older adult, but is not associated with loss in muscle mass [70] or mobility [71] over 2–3 years. However, there are some studies that fail to confirm the importance of spreading protein intake out over the course of the day [71, 72]. Additional studies have compared pulse feeding (72% of daily protein at lunch) versus protein being evenly distributed over four daily meals in hospitalized older patients for 6 weeks [73, 74]. These studies found that pulse feeding of protein increased postprandial amino acid bioavailability [75] and increased lean mass [74] compared to spreading protein intake throughout the day. Taken together, the optimal timing and distribution of protein intake still need to be determined.

8. Dietary protein and health

8.1 Dietary protein and obesity

Obesity is a major public health concern [76] and is associated with the development of metabolic diseases such as cardiovascular disease, nonalcoholic fatty liver disease, and type 2 diabetes mellitus in both children and adults [77, 78]. Obesity is defined as having a body mass index (BMI) (weight in kilograms divided by height in centimeters squared) greater than or equal to 30.0. In 2015–2016, the prevalence of obesity (**Table 2**) in the United States was 39.6 for adults and 18.4% for youth [76]. Obesity also impacts racial and ethnic groups differently. For example, non-Hispanic black and Hispanic adults and youth have higher rates of obesity compared to non-Hispanic white and Asian populations [79].

A primary factor in controlling and preventing obesity and associated chronic diseases is through diet, for example, diets higher in protein [13, 14, 80, 81]. Diets higher in protein (>30% of energy intake) have been shown to improve body composition [82], improve glycemic response [81, 83–85], increase satiety [85–87], and increase postprandial energy metabolism [88, 89], which are all mediating factors of weight loss.

8.2 Dietary protein and sarcopenia

Sarcopenia is the term for age-associated loss of muscle mass and function [35]. The loss of muscle function associated with sarcopenia is often referred to as dynapenia [90]. A loss or reduction in skeletal muscle function often leads to increased morbidity and mortality either directly, or indirectly, via the development of

Age group (years)	Total (percent)	Boys or men (percent)	Girls or women (percent)
Youth, 2–19	18.5	19.1	17.8
Young children, 2–5	13.9	14.3	13.5
Youth, 6–11	18.4 [§]	20.4 [§]	16.3
Adolescents, 12–19	20.6 [§]	20.2	20.9 [§]
Adults, 20+	39.6	37.9	41.1
Young adults, 20–39	35.7	34.8	36.5
Middle-aged adults, 40–59	42.8 [*]	40.8 [*]	44.7 [*]
Older adults, 60+	41.0	38.5	43.1

[§]Significantly different from young children.

^{*}Significantly different from young adults.

Table 2.
 Prevalence of obesity in the United States by age group and sex [76].

secondary diseases such as diabetes, obesity, and cardiovascular disease [91]. The causes of sarcopenia include poor nutrition, diminished responsiveness to anabolic hormones and/or nutrients, and a sedentary lifestyle.

The loss in muscle mass observed with aging is often accompanied by an increase in fat mass [92], which can happen even in the absence of changes in BMI [35]. The loss in muscle mass results in a decrease in basal metabolic rate (BMR) or the amount of caloric energy we use while at rest [93]. The loss of muscle mass induces a 2–3% decrease in BMR per decade after the age of 20 and a 4% decline in BMR per decade after the age of 50 [93, 94]. Muscle loss and subsequent reduction in metabolic rate contribute to obesity that accompanies the aging process.

Several studies identify protein as a key nutrient for aging adults [2, 95]. Low protein intake is linked to a decrease in physical ability in aging adults [96]. However, protein intake greater than the dietary guidelines may prevent sarcopenia [96], help maintain BMR [3], improve bone health [4–7], and improve cardiovascular function [8–10]. These benefits of increasing protein in the diet may improve function and quality of life in healthy older adults, as well as improve the ability of older patients to recover from disease and trauma [91].

Currently, the dietary recommendations for protein intake are the same for all healthy adults above the age of 19. However, experts in the field of protein and aging recommend a protein intake between 1.2 and 2.0 g kg⁻¹ day⁻¹ or higher for elderly adults [91, 95, 97]. The RDA of 0.8 g kg⁻¹ day⁻¹ is well below these recommendations and reflects a value at the lowest end of the AMDR. It is estimated that 38% of adult men and 41% of adult women have dietary protein intakes below the RDA [16, 44].

Both protein amount and source are important to consider when recommending protein intake to older adults [34, 35]. There are three important aspects to take into consideration when recommending a protein source: (1) the characteristics of the specific protein, such as the amount of essential amino acids (EAA); (2) the food matrix in which the protein is consumed, for example, as part of a beverage or a complete meal; and (3) the characteristics of the individuals consuming the food, including health status, physiological status, and energy balance [34]. In addition, the difference in digestibility and bioavailability of a protein can impact the quantity of protein that needs to be ingested to meet metabolic needs; this is especially important in older adults since gastric motility and nutrient absorption decrease with age. The speed of protein digestion and absorption of amino acids

from the gut can influence whole-body protein building [36]. Proteins with differing amino acid profiles exhibit different digestion and absorption rates [36, 38, 98]. Amino acid availability depends directly on both the quality and quantity of the dietary protein [98].

8.3 Dietary protein and gut health

Over the past 15 years, the gut microbiome has received increased attention regarding its role in impacting overall health [99]. Interestingly, it has been shown to influence diseases associated with metabolic health [100]. The intestinal mucosa houses nearly a trillion microorganisms, and the plasticity of this environment is highly reactive to changes in diet [101]. For instance, the gut becomes an active site for protein and amino acid metabolism prior to absorption. Following enzymatic denaturation by intestinal proteases, amino acids can become fermented into various metabolites which include short-chain fatty acids and ammonia [102]. The acute microbial response and long-term adaptation associated with dietary habits have become an important area of research.

As gut assay methodologies improve, researchers have identified associations between microbial populations and their metabolite concentrations in response to dietary patterns. For instance, in vitro and human models demonstrate a potential negative link between animal protein intake and protein fermentation end products such as ammonia and trimethylamine-N-oxide [103, 104]. However, favorable outcomes associated with animal- and plant-based protein sources have been observed. For example, ingestion of both whey [105] and pea protein [106] has been shown to increase favorable gut bacterial species such as *Bifidobacterium*. In addition, supplementation with pea protein intake has been shown to increase the production of short-chain fatty acids, an important energy substrate utilized by enterocytes [106].

9. Conclusions

There is sufficient evidence that protein intake higher than the current dietary recommendations is beneficial for most healthy individuals throughout the life cycle. However, benefits of dietary protein depend on the quality, the quantity, and the timing of protein intake. Although health benefits of dietary protein have been well-established for older adults, more research is needed to determine the health benefits of increased dietary protein intake through each state of life.

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Conflict of interest

The authors have no conflicts of interest to declare.

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References

- [1] Stipanuk MH, Caudil MA. Protein and amino acid metabolism. In: Stipanuk MH, Caudil MA, editors. *Biochemical, Physiological, and Molecular Aspects of Human Nutrition*. 4th ed. St. Louis, Missouri: Elsevier; 2019. pp. 402-443
- [2] Morais JA, Chevalier S, Gougeon R. Protein turnover and requirements in the healthy and frail elderly. *The Journal of Nutrition, Health & Aging*. 2006;**10**:272-283
- [3] Wilson MM, Purushothaman R, Morley JE. Effect of liquid dietary supplements on energy intake in the elderly. *The American Journal of Clinical Nutrition*. 2002;**75**:944-947
- [4] Dawson-Hughes B. Calcium and protein in bone health. *The Proceedings of the Nutrition Society*. 2003;**62**:505-509
- [5] Dawson-Hughes B. Interaction of dietary calcium and protein in bone health in humans. *The Journal of Nutrition*. 2003;**133**:852S-854S
- [6] Thorpe MP, Jacobson EH, Layman DK, He X, Kris-Etherton PM, Evans EM. A diet high in protein, dairy, and calcium attenuates bone loss over twelve months of weight loss and maintenance relative to a conventional high-carbohydrate diet in adults. *The Journal of Nutrition*. 2008;**138**:1096-1100
- [7] Heaney RP, Layman DK. Amount and type of protein influences bone health. *The American Journal of Clinical Nutrition*. 2008;**87**:1567S-1570S
- [8] Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Speizer FE, et al. Dietary protein and risk of ischemic heart disease in women. *The American Journal of Clinical Nutrition*. 1999;**70**:221-227
- [9] Obarzanek E, Velletri PA, Cutler JA. Dietary protein and blood pressure. *JAMA*. 1996;**275**:1598-1603
- [10] Stamler J, Elliott P, Kesteloot H, Nichols R, Claeys G, Dyer AR, et al. Inverse relation of dietary protein markers with blood pressure. Findings for 10,020 men and women in the INTERSALT study. INTERSALT Cooperative Research Group. INTERNATIONAL study of SALT and blood pressure. *Circulation*. 1996;**94**:1629-1634
- [11] Stratton RJ, Ek AC, Engfer M, Moore Z, Rigby P, Wolfe R, et al. Enteral nutritional support in prevention and treatment of pressure ulcers: A systematic review and meta-analysis. *Ageing Research Reviews*. 2005;**4**:422-450
- [12] Institute of Medicine. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press; 2005
- [13] Layman DK, Anthony TG, Rasmussen BB, Adams SH, Lynch CJ, Brinkworth GD, et al. Defining meal requirements for protein to optimize metabolic roles of amino acids. *The American Journal of Clinical Nutrition*. 2015;**101**:1330S-1338S
- [14] Layman DK, Baum JI. Dietary protein impact on glycemic control during weight loss. *The Journal of Nutrition*. 2004;**134**:968S-973S
- [15] Berryman CE, Lieberman HR, Fulgoni VL 3rd, Pasiakos SM. Protein intake trends and conformity with the dietary reference intakes in the United States: Analysis of the National Health and nutrition examination survey, 2001-2014. *The American Journal of Clinical Nutrition*. 2018;**108**:405-413

- [16] Pasiakos SM, Agarwal S, Lieberman HR, Fulgoni VL 3rd. Sources and amounts of animal, dairy, and plant protein intake of US adults in 2007-2010. *Nutrients*. 2015;7:7058-7069
- [17] Phillips SM, Fulgoni VL 3rd, Heaney RP, Nicklas TA, Slavin JL, Weaver CM. Commonly consumed protein foods contribute to nutrient intake, diet quality, and nutrient adequacy. *The American Journal of Clinical Nutrition*. 2015;101:1346S-1352S
- [18] Mittendorfer B, Klein S, Fontana L. A word of caution against excessive protein intake. *Nature Reviews. Endocrinology*. 2020;16:59-66
- [19] Table 56. Mean macronutrient intake among adults aged 20 and over, by sex and age: United States, selected years 1988-1994 through 2011-2014. Health. 2017. Available from: <https://www.cdc.gov/nchs/data/hus/2017/056.pdf> [Accessed: 25 November 2019]; Trend tables
- [20] Elango R, Humayun MA, Ball RO, Pencharz PB. Protein requirement of healthy school-age children determined by the indicator amino acid oxidation method. *The American Journal of Clinical Nutrition*. 2011;94:1545-1552
- [21] Gattas V, Barrera GA, Riumallo JS, Uauy R. Protein-energy requirements of prepubertal school-age boys determined by using the nitrogen-balance response to a mixed-protein diet. *The American Journal of Clinical Nutrition*. 1990;52:1037-1042
- [22] Hornell A, Lagstrom H, Lande B, Thorsdottir I. Protein intake from 0 to 18 years of age and its relation to health: A systematic literature review for the 5th Nordic nutrition recommendations. *Food & Nutrition Research*. 2013;57:1-42
- [23] Papadaki A, Linardakis M, Larsen TM, van Baak MA, Lindroos AK, Pfeiffer AF, et al. The effect of protein and glycemic index on children's body composition: The DiOGenes randomized study. *Pediatrics*. 2010;126:e1143-e1152
- [24] Jen V, Karagounis LG, Jaddoe VVW, Franco OH, Voortman T. Dietary protein intake in school-age children and detailed measures of body composition: The Generation R Study. *International Journal of Obesity*. 2018;42:1715-1723
- [25] Wright M, Sotres-Alvarez D, Mendez MA, Adair L. The association of trajectories of protein intake and age-specific protein intakes from 2 to 22 years with BMI in early adulthood. *The British Journal of Nutrition*. 2017;117:750-758
- [26] Hytten FE. *Weight Gain in Pregnancy*. Blackwell Scientific: Oxford, United Kingdom; 1991
- [27] King JC. *Physiology of pregnancy and nutrient metabolism*. *The American Journal of Clinical Nutrition*. 2000;71:1218S-1225S
- [28] Butte NF. Energy requirements during pregnancy and consequences of deviations from requirement on fetal outcome. *Nestle Nutrition Workshop Series. Pediatr Programme*. 2005;55:49-67; discussion –71
- [29] Butte NF, King JC. Energy requirements during pregnancy and lactation. *Public Health Nutrition*. 2005;8:1010-1027
- [30] Kramer MS. *Balanced protein/energy supplementation in pregnancy*. *Cochrane Database of Systematic Reviews*. 2000:CD000032
- [31] Stephens TV, Payne M, Ball RO, Pencharz PB, Elango R. Protein requirements of healthy pregnant women during early and late gestation are higher than current

recommendations. *The Journal of Nutrition*. 2015;**145**:73-78

[32] Stephens TV, Woo H, Innis SM, Elango R. Healthy pregnant women in Canada are consuming more dietary protein at 16- and 36-week gestation than currently recommended by the dietary reference intakes, primarily from dairy food sources. *Nutrition Research*. 2014;**34**:569-576

[33] Crozier SR, Robinson SM, Godfrey KM, Cooper C, Inskip HM. Women's dietary patterns change little from before to during pregnancy. *The Journal of Nutrition*. 2009;**139**:1956-1963

[34] Millward DJ, Layman DK, Tome D, Schaafsma G. Protein quality assessment: Impact of expanding understanding of protein and amino acid needs for optimal health. *The American Journal of Clinical Nutrition*. 2008;**87**:1576S-1581S

[35] Baum JI, Wolfe RR. The link between dietary protein intake, skeletal muscle function and health in older adults. *Healthcare (Basel)*. 2015;**3**:529-543

[36] Boirie Y, Dangin M, Gachon P, Vasson MP, Maubois JL, Beaufrere B. Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proceedings of the National Academy of Sciences of the United States of America*. 1997;**94**:14930-14935

[37] Dangin M, Boirie Y, Garcia-Rodenas C, Gachon P, Fauquant J, Callier P, et al. The digestion rate of protein is an independent regulating factor of postprandial protein retention. *American Journal of Physiology. Endocrinology and Metabolism*. 2001;**280**:E340-E348

[38] Pennings B, Boirie Y, Senden JM, Gijsen AP, Kuipers H, van Loon LJ. Whey protein stimulates postprandial muscle

protein accretion more effectively than do casein and casein hydrolysate in older men. *The American Journal of Clinical Nutrition*. 2011;**93**:997-1005

[39] Boirie Y, Gachon P, Beaufrere B. Splanchnic and whole-body leucine kinetics in young and elderly men. *The American Journal of Clinical Nutrition*. 1997;**65**:489-495

[40] Berrazaga I, Micard V, Gueugneau M, Walrand S. The role of the anabolic properties of plant-versus animal-based protein sources in supporting muscle mass maintenance: A critical review. *Nutrients*. 2019;**7**:11

[41] van Vliet S, Burd NA, van Loon LJ. The skeletal muscle anabolic response to plant- versus animal-based protein consumption. *The Journal of Nutrition*. 2015;**145**:1981-1991

[42] Paddon-Jones D, Sheffield-Moore M, Katsanos CS, Zhang XJ, Wolfe RR. Differential stimulation of muscle protein synthesis in elderly humans following isocaloric ingestion of amino acids or whey protein. *Experimental Gerontology*. 2006;**41**:215-219

[43] Pennings B, Groen BB, van Dijk JW, de Lange A, Kiskini A, Kuklinski M, et al. Minced beef is more rapidly digested and absorbed than beef steak, resulting in greater postprandial protein retention in older men. *The American Journal of Clinical Nutrition*. 2013;**98**:121-128

[44] Fulgoni VL 3rd. Current protein intake in America: Analysis of the National Health and nutrition examination survey, 2003-2004. *The American Journal of Clinical Nutrition*. 2008;**87**:1554S-1557S

[45] Symons TB, Sheffield-Moore M, Wolfe RR, Paddon-Jones D. A moderate serving of high-quality protein maximally stimulates skeletal muscle protein synthesis in young

and elderly subjects. *Journal of the American Dietetic Association*. 2009;**109**:1582-1586

[46] Clayton DJ, James LJ. The effect of breakfast on appetite regulation, energy balance and exercise performance. *The Proceedings of the Nutrition Society*. 2015;**14**:1-9

[47] O'Neil CE, Byrd-Bredbenner C, Hayes D, Jana L, Klinger SE, Stephenson-Martin S. The role of breakfast in health: Definition and criteria for a quality breakfast. *Journal of the Academy of Nutrition and Dietetics*. 2014;**114**:S8-S26

[48] Baum JI, Gray M, Binns A. Breakfasts higher in protein increase postprandial energy expenditure, increase fat oxidation, and reduce hunger in overweight children from 8 to 12 years of age. *The Journal of Nutrition*. 2015;**145**:2229-2235

[49] Layman DK. Protein quantity and quality at levels above the RDA improves adult weight loss. *Journal of the American College of Nutrition*. 2004;**23**:631S-636S

[50] Kinsey AW, Ormsbee MJ. The health impact of nighttime eating: Old and new perspectives. *Nutrients*. 2015;**7**:2648-2662

[51] Costa G. The problem: Shiftwork. *Chronobiology International*. 1997;**14**:89-98

[52] de Zwaan M, Roerig DB, Crosby RD, Karaz S, Mitchell JE. Nighttime eating: A descriptive study. *The International Journal of Eating Disorders*. 2006;**39**:224-232

[53] Andersen GS, Stunkard AJ, Sorensen TI, Petersen L, Heitmann BL. Night eating and weight change in middle-aged men and women. *International Journal of Obesity*

and Related Metabolic Disorders. 2004;**28**:1338-1343

[54] Macagnan J, Pattussi MP, Canuto R, Henn RL, Fassa AG, Olinto MT. Impact of nightshift work on overweight and abdominal obesity among workers of a poultry processing plant in southern Brazil. *Chronobiology International*. 2012;**29**:336-343

[55] Di Lorenzo L, De Pergola G, Zocchetti C, L'Abbate N, Basso A, Pannacciulli N, et al. Effect of shift work on body mass index: Results of a study performed in 319 glucose-tolerant men working in a southern Italian industry. *International Journal of Obesity and Related Metabolic Disorders*. 2003;**27**:1353-1358

[56] Charles LE, Gu JK, Fekedulegn D, Andrew ME, Violanti JM, Burchfiel CM. Association between shiftwork and glomerular filtration rate in police officers. *Journal of Occupational and Environmental Medicine*. 2013;**55**:1323-1328

[57] Gluck ME, Venti CA, Salbe AD, Votruba SB, Krakoff J. Higher 24-h respiratory quotient and higher spontaneous physical activity in nighttime eaters. *Obesity (Silver Spring)*. 2011;**19**:319-323

[58] Allison KC, Ahima RS, O'Reardon JP, Dinges DF, Sharma V, Cummings DE, et al. Neuroendocrine profiles associated with energy intake, sleep, and stress in the night eating syndrome. *The Journal of Clinical Endocrinology and Metabolism*. 2005;**90**:6214-6217

[59] Birketvedt GS, Florholmen J, Sundsfjord J, Osterud B, Dinges D, Bilker W, et al. Behavioral and neuroendocrine characteristics of the night-eating syndrome. *Journal of the American Medical Association*. 1999;**282**:657-663

- [60] Ford ES, Li C, Wheaton AG, Chapman DP, Perry GS, Croft JB. Sleep duration and body mass index and waist circumference among U.S. adults. *Obesity*. 2014;**22**:598-607
- [61] Ford ES. Habitual sleep duration and predicted 10-year cardiovascular risk using the pooled cohort risk equations among US adults. *Journal of the American Heart Association*. 2014;**3**:e001454
- [62] Groen BB, Res PT, Pennings B, Hertle E, Senden JM, Saris WH, et al. Intra-gastric protein administration stimulates overnight muscle protein synthesis in elderly men. *American Journal of Physiology. Endocrinology and Metabolism*. 2012;**302**:E52-E60
- [63] Snijders T, Res PT, Smeets JS, van Vliet S, van Kranenburg J, Maase K, et al. Protein ingestion before sleep increases muscle mass and strength gains during prolonged resistance-type exercise training in healthy young men. *The Journal of Nutrition*. 2015;**145**:1178-1184
- [64] Figueroa A, Alvarez-Alvarado S, Ormsbee MJ, Madzima TA, Campbell JC, Wong A. Impact of L-citrulline supplementation and whole-body vibration training on arterial stiffness and leg muscle function in obese postmenopausal women with high blood pressure. *Experimental Gerontology*. 2015;**63**:35-40
- [65] Ormsbee MJ, Kinsey AW, Eddy WR, Madzima TA, Arciero PJ, Figueroa A, et al. Corrigendum: The influence of nighttime feeding of carbohydrate or protein combined with exercise training on appetite and cardiometabolic risk in young obese women. *Applied Physiology, Nutrition, and Metabolism*. 2019;**44**:228
- [66] Ormsbee MJ, Kinsey AW, Eddy WR, Madzima TA, Arciero PJ, Figueroa A, et al. The influence of nighttime feeding of carbohydrate or protein combined with exercise training on appetite and cardiometabolic risk in young obese women. *Applied Physiology, Nutrition, and Metabolism*. 2015;**40**:37-45
- [67] Res PT, Groen B, Pennings B, Beelen M, Wallis GA, Gijsen AP, et al. Protein ingestion before sleep improves postexercise overnight recovery. *Medicine and Science in Sports and Exercise*. 2012;**44**:1560-1569
- [68] Mamerow MM, Mettler JA, English KL, Casperson SL, Arentson-Lantz E, Sheffield-Moore M, et al. Dietary protein distribution positively influences 24-h muscle protein synthesis in healthy adults. *The Journal of Nutrition*. 2014;**144**:876-880
- [69] Murphy CH, Churchward-Venne TA, Mitchell CJ, Kolar NM, Kassis A, Karagounis LG, et al. Hypoenergetic diet-induced reductions in myofibrillar protein synthesis are restored with resistance training and balanced daily protein ingestion in older men. *American Journal of Physiology. Endocrinology and Metabolism*. 2015;**308**:E734-E743
- [70] Farsijani S, Morais JA, Payette H, Gaudreau P, Shatenstein B, Gray-Donald K, et al. Relation between mealtime distribution of protein intake and lean mass loss in free-living older adults of the NuAge study. *The American Journal of Clinical Nutrition*. 2016;**104**:694-703
- [71] Kim IY, Schutzler S, Schrader A, Spencer H, Kortebein P, Deutz NE, et al. Quantity of dietary protein intake, but not pattern of intake, affects net protein balance primarily through differences in protein synthesis in older adults. *American Journal of Physiology. Endocrinology and Metabolism*. 2015;**308**:E21-E28
- [72] Arnal MA, Mosoni L, Boirie Y, Houlier ML, Morin L, Verdier E, et al.

Protein pulse feeding improves protein retention in elderly women. *The American Journal of Clinical Nutrition*. 1999;**69**:1202-1208

[73] Bouillanne O, Melchior JC, Faure C, Paul M, Canoui-Poitrine F, Boirie Y, et al. Impact of 3-week citrulline supplementation on postprandial protein metabolism in malnourished older patients: The Ciproage randomized controlled trial. *Clinical Nutrition*. 2019;**38**:564-574

[74] Bouillanne O, Curis E, Hamon-Vilcot B, Nicolis I, Chretien P, Schauer N, et al. Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: A randomized controlled trial. *Clinical Nutrition*. 2013;**32**:186-192

[75] Bouillanne O, Neveux N, Nicolis I, Curis E, Cynober L, Aussel C. Long-lasting improved amino acid bioavailability associated with protein pulse feeding in hospitalized elderly patients: A randomized controlled trial. *Nutrition*. 2014;**30**:544-550

[76] Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007-2008 to 2015-2016. *Journal of the American Medical Association*. 2018;**319**:1723-1725

[77] Reaven GM. Insulin resistance: The link between obesity and cardiovascular disease. *The Medical Clinics of North America*. 2011;**95**:875-892

[78] Yaghootkar H, Scott RA, White CC, Zhang W, Speliotes E, Munroe PB, et al. Genetic evidence for a normal-weight “metabolically obese” phenotype linking insulin resistance, hypertension, coronary artery disease, and type 2 diabetes. *Diabetes*. 2014;**63**:4369-4377

[79] Hales CM, Fryar CD, Carroll MD, Freedman DS, Aoki Y, Ogden CL.

Differences in obesity prevalence by demographic characteristics and urbanization level among adults in the United States, 2013-2016. *Journal of the American Medical Association*. 2018;**319**:2419-2429

[80] Wolfe RR, Baum JI, Starck C, Moughan PJ. Factors contributing to the selection of dietary protein food sources. *Clinical Nutrition*. 2018;**37**:130-138

[81] Layman DK, Evans EM, Erickson D, Seyler J, Weber J, Bagshaw D, et al. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *The Journal of Nutrition*. 2009;**139**:514-521

[82] Layman DK, Boileau RA, Erickson DJ, Painter JE, Shiue H, Sather C, et al. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. *The Journal of Nutrition*. 2003;**133**:411-417

[83] Lasker DA, Evans EM, Layman DK. Moderate carbohydrate, moderate protein weight loss diet reduces cardiovascular disease risk compared to high carbohydrate, low protein diet in obese adults: A randomized clinical trial. *Nutrition & Metabolism (London)*. 2008;**5**:30

[84] Pearce KL, Clifton PM, Noakes M. Egg consumption as part of an energy-restricted high-protein diet improves blood lipid and blood glucose profiles in individuals with type 2 diabetes. *The British Journal of Nutrition*. 2011;**105**:584-592

[85] Ratliff J, Leite JO, de Ogburn R, Puglisi MJ, VanHeest J, Fernandez ML. Consuming eggs for breakfast influences plasma glucose and ghrelin, while reducing energy intake during the

next 24 hours in adult men. *Nutrition Research*. 2010;**30**:96-103

[86] Tischmann L, Drummen M, Gatta-Cherifi B, Raben A, Fogelholm M, Hartmann B, et al. Effects of a high-protein/moderate-carbohydrate diet on appetite, gut peptides, and endocannabinoids—A preview study. *Nutrients*. 2019;**21**:11

[87] Veldhorst M, Smeets A, Soenen S, Hochstenbach-Waelen A, Hursel R, Diepvens K, et al. Protein-induced satiety: Effects and mechanisms of different proteins. *Physiology & Behavior*. 2008;**94**:300-307

[88] Drummen M, Tischmann L, Gatta-Cherifi B, Adam T, Westerterp-Plantenga M. Dietary protein and energy balance in relation to obesity and co-morbidities. *Frontiers in Endocrinology (Lausanne)*. 2018;**9**:443

[89] Westerterp-Plantenga MS, Lejeune MP, Smeets AJ, Luscombe-Marsh ND. Sex differences in energy homeostasis following a diet relatively high in protein exchanged with carbohydrate, assessed in a respiration chamber in humans. *Physiology & Behavior*. 2009;**97**:414-419

[90] Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: Evolution of modern measurement concepts in the context of sarcopenia. *The Proceedings of the Nutrition Society*. 2015;**74**:355-366

[91] Wolfe RR. The role of dietary protein in optimizing muscle mass, function and health outcomes in older individuals. *The British Journal of Nutrition*. 2012;**108**(Suppl 2):S88-S93

[92] Mathus-Vliegen L, Toouli J, Fried M, Khan AG, Garisch J, Hunt R, et al. World Gastroenterology Organisation global guidelines on obesity. *Journal of Clinical Gastroenterology*. 2012;**46**:555-561

[93] Buch A, Carmeli E, Boker LK, Marcus Y, Shefer G, Kis O, et al. Muscle function and fat content in relation to sarcopenia, obesity and frailty of old age—An overview. *Experimental Gerontology*. 2016;**76**:25-32

[94] Kim TN, Park MS, Ryu JY, Choi HY, Hong HC, Yoo HJ, et al. Impact of visceral fat on skeletal muscle mass and vice versa in a prospective cohort study: The Korean Sarcopenic Obesity Study (KSOS). *PLoS One*. 2014;**9**:e115407

[95] Wolfe RR, Miller SL, Miller KB. Optimal protein intake in the elderly. *Clinical Nutrition*. 2008;**27**:675-684

[96] Welch AA. Nutritional influences on age-related skeletal muscle loss. *The Proceedings of the Nutrition Society*. 2014;**73**:16-33

[97] Volpi E, Campbell WW, Dwyer JT, Johnson MA, Jensen GL, Morley JE, et al. Is the optimal level of protein intake for older adults greater than the recommended dietary allowance? *Journal of Gerontology Series A: Biological Sciences and Medical Sciences*. 2013;**68**:677-681

[98] Dangin M, Boirie Y, Guillet C, Beaufrere B. Influence of the protein digestion rate on protein turnover in young and elderly subjects. *The Journal of Nutrition*. 2002;**132**:3228S-3233S

[99] Cani PD. Human gut microbiome: Hopes, threats and promises. *Gut*. 2018;**67**:1716-1725

[100] Festi D, Schiumerini R, Eusebi LH, Marasco G, Taddia M, Colecchia A. Gut microbiota and metabolic syndrome. *World Journal of Gastroenterology*. 2014;**20**:16079-16094

[101] Singh RK, Chang HW, Yan D, Lee KM, Ucmak D, Wong K, et al. Influence of diet on the gut microbiome and implications for human health. *Journal of Translational Medicine*. 2017;**15**:73

[102] Zhao J, Zhang X, Liu H, Brown MA, Qiao S. Dietary protein and gut microbiota composition and function. *Current Protein & Peptide Science*. 2019;**20**:145-154

[103] Wang Z, Bergeron N, Levison BS, Li XS, Chiu S, Jia X, et al. Impact of chronic dietary red meat, white meat, or non-meat protein on trimethylamine N-oxide metabolism and renal excretion in healthy men and women. *European Heart Journal*. 2019;**40**:583-594

[104] Conlon MA, Bird AR. The impact of diet and lifestyle on gut microbiota and human health. *Nutrients*. 2014;**7**:17-44

[105] Swiatecka D, Zlotkowska D, Markiewicz LH, Szyc AM, Wroblewska B. Impact of whey proteins on the systemic and local intestinal level of mice with diet induced obesity. *Food & Function*. 2017;**8**:1708-1717

[106] Swiatecka D, Narbad A, Ridgway KP, Kostyra H. The study on the impact of glycated pea proteins on human intestinal bacteria. *International Journal of Food Microbiology*. 2011;**145**:267-272