Review Article



The Essential Role of Right Amount and Quality of Protein for Ensuring Child Growth and Maintenance of Bone and Muscle Mass

Shah Alam^{1,*} , Asma Ferdousi¹, Susmita Biswas¹, Ayesha Begum¹, Mitra Datta¹, Sunanda Shil¹, Fahim Hasan Reza², Mishu Talukdar²

¹Department of Paediatrics, Chattogram Medical College, Chattogram, Bangladesh ²Department of Paediatrics, Chattogram Maa Shishu O General Hospital, Chattogram, Bangladesh

Abstract

Protein is a vital macronutrient, essential for growth, tissue repair, and immune function. However, the impact of elevated protein intake during childhood and adolescence remains controversial. While high protein intake in older adults is often recommended for maintaining muscle mass and preventing frailty, excessive intake in younger populations has raised concerns about potential health risks, particularly related to obesity. This review aims to update current literature on the long-term effects of protein consumption in children and adolescents (ages 4-18) and to explore emerging methods for evaluating protein metabolism in this age group. The RDA for protein varies based on age, sex, and activity level. Generally, it is suggested that children consume about 0.95-1.3 grams of protein per kilogram of body weight per day, depending on age and specific requirements. In many developed countries, children and adolescents often consume protein at levels 2-3 times higher than the RDA, potentially leading to both positive and negative health outcomes. Protein is critical for normal growth and development during childhood and adolescence. Adequate intake supports muscle development, immune function, and the production of hormones. Studies suggest that elevated protein intake may be linked to increased Fat-Free Mass Index (FFMI), which is beneficial for muscle development and overall body composition. High protein diets have been associated with increased satiety, which can help in managing appetite and potentially reducing overall caloric intake, thus contributing to healthier weight maintenance. Some evidence suggests a correlation between high protein intake in infancy and childhood and increased risk of obesity later in life. This association may be due to the overactivation of growth pathways and increased insulin-like growth factor-1 (IGF-1) levels. Excessive protein intake has been hypothesized to strain kidney function, especially in individuals with pre-existing kidney conditions. However, current evidence in healthy children and adolescents is inconclusive. This narrative review emphasizes the need for a nuanced understanding of protein intake in children and adolescents, considering both the benefits and potential risks associated with high protein consumption. As research evolves, dietary guidelines may need to be adjusted to reflect the latest findings.

Keywords

Protein Intake, Children, Adolescent, Body Composition, BMI, FMI, FFMI, Right Amount and Quality of Protein, Protein for Bone and Muscle

*Corresponding author: shahalamk49@gmail.com (Shah Alam)

Received: 13 August 2024; Accepted: 3 September 2024; Published: 24 January 2025



Copyright: © The Author(s), 2025. Published by Science Publishing Group. This is an **Open Access** article, distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

1. Introduction

For children and adolescents to be healthy, operate properly, and develop to their full potential, nutrition is crucial [1]. Specifically, diet plays a major role in preventing disease, particularly chronic conditions like obesity and Type II Diabetes Mellitus (T2DM) [2-4]. The two initial years of life have been highlighted as a vital window that may influence health later in life [3, 5, 6]. Increased adipogenesis and a lifetime risk of obesity have been associated with high protein intake in infancy [3, 6]. In response to this issue, regulatory organizations lowered the protein levels in infant formula (IF) in an effort to better replicate human milk for infants who cannot be breastfed [7-9].

For both baby and Follow-On Formulas (FOF), the Commission Delegated Regulation (EU) 2016/127 [10] presently allows a minimum and maximum protein concentration of 1.80 g and 2.50 g per 100 kcal, respectively. The maximum levels of the previous rule (2006/141/EC) (3 g/100 kcal) are exceeded by these values.

For later life stages and groups, more protein consumption is recommended in order to promote good health benefits, whereas a reduced protein diet may be beneficial for infants [11-13]. 1.2 to 2.0 g/kg body weight per day is recommended by Dietitians of Canada (DC), the American College of Sports Medicine (ACSM), and the Academy of Nutrition and Dietetics (Academy) for physically active individuals in order to support metabolic adaption, repair, remodeling, and protein turnover. In comparison to the Recommended Dietary Allowance (RDA) of 0.8 g/kg bw/d for non-pediatric populations, this range suggests an increase of around 0.4-1.2 g/kg bw/d [14, 15]. For short periods of time during vigorous exercise or when reducing energy consumption, higher intakes may also be recommended [14]. In a similar vein, experts propose that increasing protein consumption to 1.2 to 2.0 g/kg bw per day or more-well above recommended levels-may be a useful nutritional strategy for older persons looking to avoid the detrimental effects of age-related muscle loss on their health [11, 16]. Increasing the amount of protein consumed by this demographic can help healthy older persons keep their independence and live better. This may promote cardiovascular function, avoid sarcopenia, preserve energy balance, aid control weight, and enhance muscular health [11, 16].

Despite the growing body of evidence and attempts to clarify optimal protein intake levels for specific populations, there is a lack of data available assessing optimal protein intake in pediatric populations older than infants (<1 year) and toddlers (1-3 years), according to the age group classification used by the European Food Safety Authority (EFSA) [17]. Hörnell et al. [18] reviewed scientific information on the short- and long-term health consequences of varied quantities of protein consumption from 0 to 18 years of age, and identified a total of 23 research that investigated the impact on growth and body composition. Six studies, however, solely

looked at the influence of protein consumption after the age of four and its impacts on later life (two interventional studies and four prospective cohorts); none looked at protein intake beyond the age of ten. However, given that the supplementation in both cases lasted for just seven days, it is interesting that the interventional studies may be categorized as short-term [19, 20].

Increased protein intakes may be helpful to support appropriate development after children and adolescents between the ages of 4 and 18 reach the current recommended intake, or conversely, they may raise the risk of disorders later in life. It has been suggested that there are some crucial windows for protein consumption, such as when switching to a family diet [21]. This stage is typically marked by a sharp rise in protein consumption, mostly from switching to cow's milk, which has a protein concentration of roughly 5.15 g/100 kcal, or roughly twice that of IF or FOF [22].

In Western Europe and the US, trends in protein intake among children and adolescents are typically two to three times higher than dietary recommendations [21, 23-25]. However, the factorial technique is used to compute these suggestions with information from nitrogen balance investigations [26, 27]. The literature has extensively examined nitrogen balance deficits, which arise from an inclination to overestimate nitrogen intake and underestimate excretion. This results in a positive net balance and could lead to an overestimation of one's actual needs [28, 29]. This raises the question of whether the current protein guidelines are appropriate or if they underestimate the true needs of kids and teenagers. Further study is needed to determine optimal protein consumption levels, potentially critical time windows, and if the current guidelines should be reassessed.

This narrative review is divided into four sections to address these issues. The present trends in protein intake in developed nations are outlined in the first part and are contrasted with dietary recommended intakes for every age group. The next section discusses the accuracy of existing protein guidelines, given that protein consumption is likely to exceed them.

Suggestions in addition to fresh methods for evaluating kids' protein metabolism. The information that is now available on the effects of protein intake on later life in children and adolescents (ages 4 to 18) is thoroughly examined in the third section. Based on the main outcomes of the studies—body mass index, body composition, and insulin sensitivity—the findings have been arranged into three categories. Finally, a brief section that examines the function of protein in picky eaters—a complicated behavior marked by refusal to eat—has been added.

2. Recent Trends in Protein Intake

The majority of individuals in Western Europe and the

United States consume more protein than is advised in their diets, based on the evidence that is currently available [15, 26, 30]. Table 1 shows how the recommendations for protein consumption vary slightly depending on the health authority making them for the pediatric population (those under the age of 18). The two most often quoted recommendations are Dietary Reference Intakes (DRIs) from the US Institute of Medicine (IoM) [30] and Dietary Reference Values (DRVs) from the EFSA [26]. The most often mentioned recommendations are the RDA and the Population Reference Intake

(PRI), which denote the average daily dietary intake amount sufficient to fulfill nutritional needs and prevent deficiencies in almost all (97.5%) of the healthy individuals in a population, are the most frequently cited recommendations, despite the fact that they cover a variety of terms [15, 31].

However, beyond the dietary recommendations to prevent deficiency, there are no guidelines for an "optimal" protein intake in pediatric population for promoting healthy growth and development.

		EFSA ¹			DRI ²		
	AR (g/kg bw/d)	PRI (g/kg bw/d)	PRI (g/d)	EAR (g/kg bw/d)	RDA (g/kg bw/d)	RDA (g/d)	AMDR (%E) ³
4-8 years	0.72	0.89	19.30	0.76	0.95	19	10-30%
9-13 years	0.72	0.90	34.50	0.76	0.95	34	10-30%
14-17 years, boys	0.71	0.88	53.25	0.73	0.85	52	10-30%
14-17 years, girls	0.69	0.85	46.50	0.71	0.85	46	10-30%

Table 1. Current recommendations for protein requirements, estimated by age and sex, for children.

¹ From Ref. [26]. ² From Ref. [15]. ³ From Ref. [30]. AMDR, Acceptable Macronutrient Distribution Range; AR, Average Requirement; DRI, Dietary Reference Intakes; EAR, Estimated Average Requirements; EFSA, European Food Safety Authority; PRI, Population Reference Intake; RDA, Recommended Dietary Allowance.

Particularly in industrialized nations, trends in children's and adolescents' protein consumption are often two to three times higher than suggested, with the majority of these proteins coming from animal sources [21, 23-25]. Based on data from the National Diet and Nutrition Survey (NDNS) [25] (n \approx 1000; 500 adults and 500 children), which was performed in the United Kingdom (UK) between 2016 and 2017, it was determined that the mean protein intake was 52.9 and 64.5 g/d in the corresponding age groups of 4-10 years and 11-18 years. Protein consumption was 1.40 and 2.39 times greater for these ages in terms of PRI. The consumption of protein is significantly greater in other European nations.

The National Dietary Survey on the Child and Adolescent Population in Spain (ENALIA) [24], which included 1862 participants, found that average intakes ranged from 74.45 (4-8 years) to 93.6 g/d (14-17 years), with 3.88-1.88-fold higher values than PRI, respectively. It should be noted that the contribution of protein to total energy consumption for children aged 4-17 years was as high as 17.8%. Similar findings have been reported in the US, where the National Health and Nutrition Examination Survey 2001-2014 (NHANES) [23] (n = 15.829; 2-80 years) revealed average intakes that ranged from 59.7 g/d in those 4-8 years to 79.75 g/d in those 14-18 years. It is noteworthy that 0.96% of children aged 2-3 years had values above the specific.

Protein has an acceptable Macronutrient Distribution Range

(AMDR) of 10-30%E, however among Spanish children aged 1-3, this value was 12.1%. Although the maximum limit of AMDR (35% E) in adults has been linked to a risk for prediabetes and type 2 diabetes, AMDR expresses a range of protein intakes in the context of a complete diet [11, 15, 32]. AMDR should therefore be used with caution. Finally, original research extracted from cohorts, like the Generation R [33] or Dortmund Nutritional and Anthropometric Longitudinal Design (DON-ALD) study [21], revealed similar, greater protein consumption, in agreement with these national dietary surveys.

In conclusion, there are currently no recommendations for a "optimal" protein intake that exceeds these recommendations to support healthy growth and development, despite observational research consistently showing that children's average protein intake is two to three times higher than the dietary intakes that are recommended to prevent deficiency in 97.5% of the population.

3. Recommended Dietary Protein Intakes: A Conversation

The minimal consistent daily consumption required to avoid deficiencies is the definition of an adult's nutrient requirements [15]. However, this idea becomes much more crucial for youngsters, as proper growth and development should be supported by nutrients [34]. Using information from nitrogen balance studies, the factorial technique is used to determine the recommended protein consumption for kids and teens, taking into account their needs for both growth and maintenance [26, 27]. However, there are a number of methodological and data interpretation issues with the nitrogen balance technique that have been extensively covered elsewhere [29, 35] for estimating protein recommendations. In summary, this method tends to overestimate intake of nitrogen and underestimate excretion, which produces an excessively favorable net balance and, hence, an underestimating of needs. Furthermore, it takes a few days for the measuring procedure to adjust to the protein consumption amount that is tested, and more time is required for the related readings. To evaluate the zero balance, this procedure needs to be performed at least three times for protein intake levels [28, 29]. In addition, the limitations of data interpretation have been thoroughly investigated, leading to an independent reanalysis of nitrogen balance studies to establish alternative adult reference values [28]. However, this method remains the "gold standard" for figuring out protein needs [26, 30].

Emerging methods such as D3-Creatine, 5N End-Product, and Indicator Amino Acid Oxidation (IAAO) are being used to evaluate protein metabolism in children [29]. These three strategies, which include minimally invasive approaches for study participants in a free-living setting, can be used with vulnerable groups, including youth and young adults. In particular, Elango et al. [36] had previously examined the IAAO approach in children ages 6 to 10 years, and its findings are probably less prone to inaccuracy than those from nitrogen balance tests [28, 29, 36, 37].

Elango et al. [36] contend that school-age children (6-10 years old) in good health now have significantly underestimated protein requirements. Estimated Average Requirements (EAR) and RDA for protein were found to be 1.3 and 1.55 g/kg bw/d, respectively; these values are much higher than the DRI values for protein (71.0% and 63.2% higher, respectively). Furthermore, the authors used two distinct approaches to report identical findings in adults: the IAAO method and a reanalysis of the available nitrogen balance data using non-linear regression [28, 37].

The methodologies constitute a much-needed area of research and are a big step forward in assessing the life factors that influence protein intake [29]. On the basis of this data, new methods for evaluating protein metabolism in children underline the necessity of reassessing the advice that is now in place. These guidelines seem to be underestimating the amount of protein that youngsters need consume, and they also neglect to take into account other aspects of life.

4. Impacts of Protein Intake in Healthy Children and Adolescents

Consumption of protein is essential for children's and ad-

olescents' healthy growth and development. Even though protein is necessary for good health overall, consuming too much or too little of it can have long-term consequences for their wellbeing. The following are some important details on how eating protein affects children and adolescents in good health over the long term:

- Development and Growth: Sufficient consumption of protein is essential for healthy growth and development in childhood and adolescence. The components of all tissues, including muscles, bones, skin, and organs, are proteins. Development might be delayed and growth can be hindered due to inadequate protein consumption.
- 2. Body Composition: Consuming protein modifies the amount of fat and muscle in the body. Lean muscle mass development is aided by a balanced protein intake and frequent exercise, both of which are critical for general strength and metabolic health. However, consuming too much protein, particularly from foods heavy in saturated fats, can lead to obesity and unhealthful weight gain.
- 3. Bone Health: The development and preservation of bones depend on protein. Sufficient amounts of calcium and vitamin D, in addition to an adequate protein consumption, promote bone health and lower the risk of osteoporosis and fractures in later life. But if it's not balanced with enough calcium intake, consuming too much protein—especially from animal sources—may raise calcium excretion and perhaps jeopardize bone health.
- 4. Metabolic Health: Protein helps to keep blood sugar levels in check and regulate metabolism. Consuming a balanced diet of proteins can help avoid insulin resistance and lower the chance of developing type 2 diabetes in later life. Excessive consumption of protein, particularly from processed or high-fat sources, has been linked to metabolic problems and insulin resistance.
- 5. Cardiovascular Health: The kind and origin of protein ingested can affect the state of cardiovascular health. Diets rich in plant-based proteins—like those found in nuts, seeds, and legumes—have been linked to a decreased risk of heart disease. On the other hand, due to their high cholesterol and saturated fat content, diets heavy in red and processed meats—sources of animal-based proteins—may raise the risk of cardiovascular disease.
- 6. Kidney Function: For healthy kidneys, a sufficient protein diet is generally safe. To lower the risk of future kidney damage, people with pre-existing kidney disorders may need to moderate their protein intake. Overindulgence in protein can strain the kidneys and eventually cause renal failure.
- Nutritional Imbalances: If one concentrates too much on protein consumption, other important nutrients may be overlooked, which can result in nutritional imbalances. Throughout childhood and adolescence, a well-balanced diet comprising a range of food groups is crucial for

fulfilling overall nutritional requirements.

In conclusion, although protein is essential for adolescent and child growth and development, it's critical to guarantee a balanced intake from a range of sources to promote long-term health and wellbeing. A customized nutrition plan that satisfies particular needs can be created by speaking with a healthcare professional or registered dietitian to ascertain an individual's protein requirements. (FMI).

5. Optimal Protein Consumption in Picky Eaters

Picky eating, often referred to as "fussy," "selective," or "choosy" eating, is a complicated behavior defined by the rejection of a significant portion of both recognized and novel foods, leading to the consumption of an inadequate variety or quantity of foods [83-85]. Picky eaters (PE) are difficult to define, quantify, and look into the true effects of because there isn't a single, widely agreed-upon definition. In spite of this, a number of research have recently [83-85] addressed the topic.

Picky eating is typically linked to far lower intakes of meats, fruits, and vegetables [84-88]. Energy and macronutrient intakes are comparable across PE and non-PE, as are dairy intakes [84, 85].

But in five out of ten studies, protein intakes were considerably lower in PE compared to non-PE, according to Samuel et al. [84]. Five out of seven studies [87-90] that focused mainly on children aged three or older revealed noticeably reduced protein consumption in PE. It might imply that as people age, this habit intensifies and results in a diet of low quality.

As a result, Taylor et al. [85] described the diets of children ages 10 and 13 in both a cross-sectional and longitudinal manner, indicating that children with chronic PE (beginning at age 3) displayed more noticeable variations at every age. In terms of protein intake, the group who continued PE ingested 10% less protein than the group that did not continue PE. Nonetheless, dietary protein intakes were frequently higher than the EFSA dietary recommendations in all age categories in the majority of studies [84, 85].

Causal inferences are hampered by the paucity of longitudinal research on the anthropometric traits and body composition of picky eater children [91-94]. In a recent research, the European Longitudinal Study of Pregnancy and Childhood (ELSPAC-CZ) cohort's 346 PE participants and 1722 non-PE participants were found. Grulichova et al. [92] published this analysis.

The modified models revealed negative correlations with height (PE were on average 0.8 cm shorter than non-PE) and weight (PE were on average 2.3 kg lighter than non-PE). These findings are consistent with those from the 7420 children in the Avon Longitudinal Study of Parents and Children (ALSPAC) [93]. PE were first detected at the age of three, and measurements of height and weight were taken seven times between the ages of seven and seventeen.

In this instance, the models projected that, at each age, males with chronic PE would weigh roughly 1.5-2.5 kg and females with persistent PE would weigh 1.0-1.5 kg less than non-PE. The findings indicated that height was negatively correlated with chronic PE in both females (1.0-1.5 cm shorter) and boys (1.5-2.0 cm shorter). On the other hand, DXA measured body composition five times between the ages of 9 and 17. The findings indicated that male children who were consistently picky had a lower lean mass index—by roughly 0.1 kg/m²—than non-picky children at all age groups starting at age 11. However, there was no correlation found between fussy eating and either sex's FMI or body fat percentage.

A study included in the Generation R prospective cohort (4191 children) provided data in support of this theory, indicating that 4 year olds who are fussy eaters may be more likely to be underweight at 6 years old and to have a lower fat-free mass. In particular, the fussy eating profile was associated with a reduced BMI-SDS, mostly because FFMI decreased rather than FMI [94].

The effects of oral nutritional supplements (ONS) have been investigated in this population as a way to enhance growth and nutritional status. Four randomized controlled trials (RCTs) with children who exhibited fussy eating patterns used dietary counseling (DC) in addition to ONS as an intervention; the results were compared to a control group that received DC only [95-98]. A metanalysis was conducted to demonstrate changes in growth parameters based on these RCTs [99]. Weight characteristics indicate that, in comparison to the group receiving DC alone, the intervention group in the four RCTs exhibits significantly higher weight increase, weight-for-age z-scores, and weight-for-height z-scores at 30, 60, and 90 days. On the other hand, the ONS + DC group showed a faster height rise in three of the four RCTs [99]. In particular, Sheng et al. [95] showed no significant difference between the intervention and control group.

There have also been reports of further advantages from obtaining ONS + DC. For example, the intervention group's appetite grew much more than the control group's [96]. According to Ghosh et al. and Alarcon et al., the ONS + DC group had a considerably reduced incidence of upper respiratory tract infections than the control group over the study period [96, 97]. Similarly, studies have evaluated the impact of a high-protein ONS diet on young, healthy individuals who are short and lean [100-102]. In a study conducted by Lebenthal et al. [100], 171 short and thin children between the ages of 3 and 9 years were given a high-protein ONS diet (24.5 g protein/serving) for six months. Height-SDS and weight-SDS considerably improved for "good" formula drinkers (intake of \geq 50% of the recommended dose of one serving/day), with no change in BMI-SDS compared with 'poor' consumers and the placebo group [100].

Similar findings were found in the follow-up trial by Yackbovitch-Gavan et al. [101], indicating that a high-protein

ONS diet for a year was an effective intervention to promote the linear development of these children without affecting their BMI. On the other hand, a similar technique in prepubertal boys (10-14.5 y) who were short and slim revealed a shift in their body composition [102]. The intervention involved two phases: a double-blinded intervention with a high-protein ONS (36 g protein/serving) diet or placebo for 6 months, and later, an open-label, extended 6-month diet including ONS, for all the participants. When compared to "poor" formula users and the placebo group, "good" formula users demonstrated noticeably higher weight-SDS, BMI-SDS, fat-free mass, and muscular mass [102].

Nevertheless, it should be mentioned that while the body composition described by the authors could be relevant to with PE children, the presence of picky eating or any other behavior related to the refusal to eat adequately was not assessed [100-102].

The evidence that is now available has some flaws. First, there are very few RCTs (four papers found) evaluating ONS

in PE. Since protein makes up 12% to 15% of the total energy in the ONS, which is a well-balanced blend of macro and micronutrients, it's possible that the collection of nutrients—rather than simply the protein—is responsible for the health advantages. Finally, because only anthropometric parameter changes—not body composition, or FMI and FFMI—were evaluated, it is impossible to determine whether the changes are primarily attributable to alterations in either measure.

Overall, poorer intake of fruits and vegetables and higher intake of free sugar are indicators of a poor diet, even while PE children appear to have adequate protein intakes [85-88]. According to the most recent data, PE tend to be shorter and have less lean mass than their colleagues who aren't picky [91-94]. This suggests that in order to support healthy growth and development, PE may benefit from early identification and intervention. Well-designed RCTs are necessary to determine whether they might gain from consuming more protein as a dietary intervention.



Figure 1. Impacts of Dietary Macronutrients and Protein Impact in Children and Adolescent [103].

6. Protein Is Essential for Child Growth and the Maintenance of Bone and Muscle Mass

The Right Amount And Quality Of Protein Are Crucial For Ensuring Proper Development And Health, Here's a general guideline:

6.1. Amount of Protein

1. Infants (0-12 months): Infants require about 1.5 grams of

protein per kilogram of body weight per day.

- 2. Children (1-3 years): Children in this age group need approximately 1.1 grams of protein per kilogram of body weight per day.
- 3. Children (4-13 years): Protein needs slightly decrease to about 0.95 grams of protein per kilogram of body weight per day during this period.
- 4. Adolescents (14-18 years): Adolescents have higher protein needs due to growth spurts. They generally require around 0.85 to 0.9 grams of protein per kilogram of body weight per day.

6.2. Quality of Protein

The quality of protein is determined by its amino acid composition and digestibility. Proteins from animal sources are considered high-quality proteins as they contain all essential amino acids in adequate amounts. Examples include meat, poultry, fish, eggs, and dairy products. Plant-based protein sources, such as beans, lentils, nuts, seeds, and whole grains, can also provide adequate protein when consumed in combination to ensure all essential amino acids are obtained.

6.3. Tips for Ensuring Adequate Protein Intake

1. Include Protein-Rich Foods in Meals: Incorporate sources of protein in each meal and snack. This could include lean meats, poultry, fish, eggs, dairy products, legumes, nuts, and seeds.

- 2. Offer Variety: Provide a variety of protein sources to ensure a diverse intake of essential amino acids.
- 3. Consider Timing: Distribute protein intake evenly throughout the day rather than consuming large amounts in one meal.
- Monitor Growth and Adjust Intake: Keep track of your child's growth and consult with a pediatrician or dietitian if there are concerns about growth or nutritional adequacy.
- Encourage Healthy Eating Habits: Promote a balanced diet that includes a variety of nutrient-rich foods, not just focusing solely on protein.

It's important to note that individual protein needs may vary based on factors such as activity level, growth rate, and overall health status. Consulting with a healthcare provider or a registered dietitian can provide personalized recommendations tailored to a child's specific needs.



Figure 2. Right Amount And Quality Of Protein Are Crucial For Ensuring Proper Development [104].

7. Conclusions

In summary, the evidence on protein consumption and its effects on later life in healthy children and adolescents between the ages of 4 and 18 is comprehensively summarized in this narrative review. The principal conclusions are: Research employing observational data has consistently demonstrated that children eat, on average, two to three times as much protein as is recommended in the diet. There are currently no standards for a "optimal" protein intake that promotes healthy growth and development in the pediatric population, other from the intakes required to prevent deficiencies. There is a need for a reassessment since new techniques for assessing children's protein metabolism suggest that current protein requirements may be exaggerated. When the protein level rises beyond 15-20% E, the research advises exercising caution. This stage of life may benefit from high protein intake in the following ways: • There appears to be a positive correla-

tion between high protein intake and increased BMI, which is mainly explained by an increase in FFMI rather than FMI; • Protein intake may modulate the GH-IGF-I axis, increasing IGF-I levels during puberty and early adolescence, which may promote the development of bone and lean mass; and • In children who have fussy eating habits, higher nutrient intake, including protein, is linked to positive changes in weight and height parameters.

Author Contributions

Shah Alam: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Asma Ferdousi: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Susmita Biswas: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Ayesha Begum: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Mitra Datta: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Sunanda Shil: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Fahim Hasan Reza: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Mishu Talukdar: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Visualization

Conflicts of Interest

The authors declare no Conflicts of Interest.

References

- Das, J. K.; Lassi, Z. S.; Hoodbhoy, Z.; Salam, R. A. Nutrition for the Next Generation: Older Children and Adolescents. *Ann. Nutr. Metab.* 2018, *72* (Suppl. 3), 56-64.
- [2] Scaglioni, S.; Agostoni, C.; Notaris, R. D.; Radaelli, G.; Radice, N.; Valenti, M.; Giovannini, M.; Riva, E. Early macronutrient intake and overweight at five years of age. *Int. J. Obes. Relat. Metab. Disord.* 2000, 24, 777-781.
- [3] Luque, V.; Closa-Monasterolo, R.; Escribano, J.; Ferre, N. Early Programming by Protein Intake: The Effect of Protein on Adiposity Development and the Growth and Functionality of Vital Organs. *Nutr. Metab. Insights* 2015, *8*, 49-56.

- [4] Rolland-Cachera, M. F.; Deheeger, M.; Akrout, M.; Bellisle, F. Influence of macronutrients on adiposity development: A follow up study of nutrition and growth from 10 months to 8 years of age. *Int. J. Obes. Relat. Metab. Disord.* 1995, *19*, 573-578.
- [5] Zheng, M.; Lamb, K. E.; Grimes, C.; Laws, R.; Bolton, K.; Ong, K. K.; Campbell, K. Rapid weight gain during infancy and subsequent adiposity: A systematic review and meta-analysis of evidence. *Obes. Rev. Off. J. Int. Assoc. Study Obes.* 2018, 19, 321-332.
- [6] Camier, A.; Davisse-Paturet, C.; Scherdel, P.; Lioret, S.; Heude, B.; Charles, M. A.; de Lauzon-Guillain, B. Early growth according to protein content of infant formula: Results from the EDEN and ELFE birth cohorts. *Pediatr. Obes.* 2021, *16*, e12803.
- [7] EFSA NDA Panel. Scientific Opinion on the essential composition of infant and follow-on formulae. *EFSA J.* 2014, *12*, 3760.
- [8] Kouwenhoven, S. M. P.; Muts, J.; Finken, M. J. J.; Goudoever, J. B. V. Low-Protein Infant Formula and Obesity Risk. *Nutri*ents 2022, 14, 2728.
- [9] Wargo, W. F. The History of Infant Formula: Quality, Safety, and Standard Methods. J. AOAC Int. 2016, 99, 7-11.
- [10] Commission, E. Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding. *Off. J. Eur. Union (OJL)* 2016, 25, 1-29.
- [11] Baum, J. I.; Kim, I. Y.; Wolfe, R. R. Protein Consumption and the Elderly: What Is the Optimal Level of Intake? *Nutrients* 2016, 8, 359.
- [12] Lonnie, M.; Hooker, E.; Brunstrom, J. M.; Corfe, B. M.; Green, M. A.; Watson, A. W.; Williams, E. A.; Stevenson, E. J.; Penson, S.; Johnstone, A. M. Protein for Life: Review of Optimal Protein Intake, Sustainable Dietary Sources and the Effect on Appetite in Ageing Adults. *Nutrients* 2018, *10*, 360.
- [13] Volpi, E.; Campbell, W. W.; Dwyer, J. T.; Johnson, M. A.; Jensen, G. L.; Morley, J. E.; Wolfe, R. R. Is the optimal level of protein intake for older adults greater than the recommended dietary allowance? *J. Gerontol. A Biol. Sci. Med. Sci.* 2013, 68, 677-681.
- [14] Thomas, D. T.; Erdman, K. A.; Burke, L. M. Position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine: Nutrition and Athletic Performance. J. Acad. Nutr. Diet. 2016, 116, 501-528.
- [15] Trumbo, P.; Schlicker, S.; Yates, A. A.; Poos, M. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids. J. Am. Diet. Assoc. 2002, 102, 1621-1630.
- [16] Morais, J. A.; Chevalier, S.; Gougeon, R. Protein turnover and requirements in the healthy and frail elderly. J. Nutr. Health Aging 2006, 10, 272-283.

- [17] Authority, E. F. S. General principles for the collection of national food consumption data in the view of a pan-European dietary survey. *EFSA J.* 2009, 7, 1435.
- [18] 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 Nutr. Res.* 2013, *57*, 21083.
- [19] Hoppe, C.; Molgaard, C.; Dalum, C.; Vaag, A.; Michaelsen, K.
 F. Differential effects of casein versus whey on fasting plasma levels of insulin, IGF-1 and IGF-1/IGFBP-3: Results from a randomized 7-day supplementation study in prepubertal boys. *Eur. J. Clin. Nutr.* 2009, *63*, 1076-1083.
- [20] Hoppe, C.; Mølgaard, C.; Juul, A.; Michaelsen, K. F. High intakes of skimmed milk, but not meat, increase serum IGF-I and IGFBP-3 in eight-year-old boys. *Eur. J. Clin. Nutr.* 2004, 58, 1211-1216.
- [21] Günther, A. L.; Remer, T.; Kroke, A.; Buyken, A. E. Early protein intake and later obesity risk: Which protein sources at which time points throughout infancy and childhood are important for body mass index and body fat percentage at 7 y of age? *Am. J. Clin. Nutr.* 2007, *86*, 1765-1772.
- [22] Singhal, S.; Baker, R. D.; Baker, S. S. A Comparison of the Nutritional Value of Cow's Milk and Nondairy Beverages. J. Pediatr. Gastroenterol. Nutr. 2017, 64, 799-805.
- [23] Berryman, C. E.; Lieberman, H. R.; Fulgoni, V. L., III; Pasiakos, S. M. 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. *Am. J. Clin. Nutr.* 2018, *108*, 405-413.
- [24] Lopez-Sobaler, A. M.; Aparicio, A.; Rubio, J.; Marcos, V.; Sanchidrian, R.; Santos, S.; Perez-Farinos, N.; Dal-Re, M. A.; Villar-Villalba, C.; Yusta-Boyo, M. J.; et al. Adequacy of usual macronutrient intake and macronutrient distribution in children and adolescents in Spain: A National Dietary Survey on the Child and Adolescent Population, ENALIA 2013-2014. *Eur. J. Nutr.* 2019, *58*, 705-719.
- [25] National Institute of Health Research Cambridge Biomedical Research Centre (NIHR BRC). National Diet and Nutrition Survey Rolling Programme Years 9 to 11 (2016/2017 to 2018/2019); National Institute of Health Research Cambridge Biomedical Research Centre (NIHR BRC): Cambridge, UK, 2020.
- [26] EFSA NDA Panel. Scientific Opinion on Dietary Reference Values for protein. *EFSA J.* 2012, *10*, 2557.
- [27] Joint World Health Organisation; Food and Agriculture Organization; UNU Expert Consultation. Protein and amino acid requirements in human nutrition. World Health Organ. Tech. Rep. Ser. 2007, 935, 1-265.
- [28] Elango, R.; Humayun, M. A.; Ball, R. O.; Pencharz, P. B. Evidence that protein requirements have been significantly underestimated. *Curr. Opin. Clin. Nutr. Metab. Care* 2010, *13*, 52-57.
- [29] Hudson, J. L.; Baum, J. I.; Diaz, E. C.; Borsheim, E. Dietary Protein Requirements in Children: Methods for Consideration.

Nutrients 2021, 13, 1554.

- [30] Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids; The National Academies Press: Washington, DC, USA, 2005; p. 1358.
- [31] EFSA Panel on Dietetic Products, Nutrition, and Allergies. Scientific Opinion on principles for deriving and applying Dietary Reference Values. *EFSA J.* 2010, *8*, 1458.
- [32] Mittendorfer, B.; Klein, S.; Fontana, L. A word of caution against excessive protein intake. *Nat. Rev. Endocrinol.* 2020, 16, 59-66.
- [33] Jen, V.; Karagounis, L. G.; Jaddoe, V. W. V.; Franco, O. H.; Voortman, T. Dietary protein intake in school-age children and detailed measures of body composition: The Generation R Study. *Int. J. Obes.* 2018, *42*, 1715-1723.
- [34] Moore, D. R. Protein Metabolism in Active Youth: Not Just Little Adults. Exerc. Sport Sci. Rev. 2019, 47, 29-36.
- [35] Weiler, M.; Hertzler, S. R.; Dvoretskiy, S. Is It Time to Reconsider the U.S. Recommendations for Dietary Protein and Amino Acid Intake? *Nutrients* 2023, *15*, 838.
- [36] Elango, R.; Humayun, M. A.; Ball, R. O.; Pencharz, P. B. Protein requirement of healthy school-age children determined by the indicator amino acid oxidation method. *Am. J. Clin. Nutr.* 2011, *94*, 1545-1552.
- [37] Pencharz, P. B.; Elango, R.; Wolfe, R. R. Recent developments in understanding protein needs-How much and what kind should we eat? *Appl. Physiol. Nutr. Metab.* 2016, *41*, 577-580.
- [38] Gattas, V.; Barrera, G. A.; Riumallo, J. S.; Uauy, R. Protein-energy requirements of prepubertal school-age boys determined by using the nitrogen-balance response to a mixed-protein diet. *Am. J. Clin. Nutr.* 1990, *52*, 1037-1042.
- [39] Baxter-Jones, A. D.; Eisenmann, J. C.; Mirwald, R. L.; Faulkner, R. A.; Bailey, D. A. The influence of physical activity on lean mass accrual during adolescence: A longitudinal analysis. *J. Appl. Physiol.* 2008, *105*, 734-741.
- [40] Tobias, J. H.; Steer, C. D.; Mattocks, C. G.; Riddoch, C.; Ness, A. R. Habitual levels of physical activity influence bone mass in 11-year-old children from the United Kingdom: Findings from a large population-based cohort. J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 2007, 22, 101-109.
- [41] Boisseau, N.; Le Creff, C.; Loyens, M.; Poortmans, J. Protein intake and nitrogen balance in male non-active adolescents and soccer players. *Eur. J. Appl. Physiol.* 2002, *88*, 288-293.
- [42] Boisseau, N.; Persaud, C.; Jackson, A. A.; Poortmans, J. R. Training does not affect protein turnover in pre- and early pubertal female gymnasts. *Eur. J. Appl. Physiol.* 2005, 94, 262-267.
- [43] Burd, N. A.; McKenna, C. F.; Salvador, A. F.; Paulussen, K. J. M.; Moore, D. R. Dietary Protein Quantity, Quality, and Exercise Are Key to Healthy Living: A Muscle-Centric Perspective Across the Lifespan. *Front. Nutr.* 2019, *6*, 83.

- [44] Moore, D. R.; Volterman, K. A.; Obeid, J.; Offord, E. A.; Timmons, B. W. Postexercise protein ingestion increases whole body net protein balance in healthy children. *J. Appl. Physiol.* 2014, *117*, 1493-1501.
- [45] Pikosky, M.; Faigenbaum, A.; Westcott, W.; Rodriguez, N. Effects of resistance training on protein utilization in healthy children. *Med. Sci. Sports Exerc.* 2002, *34*, 820-827.
- [46] Volterman, K. A.; Moore, D. R.; Breithaupt, P.; Godin, J. P.; Karagounis, L. G.; Offord, E. A.; Timmons, B. W. Postexercise Dietary Protein Ingestion Increases Whole-Body Leucine Balance in a Dose-Dependent Manner in Healthy Children. J. Nutr. 2017, 147, 807-815.
- [47] Volterman, K. A.; Obeid, J.; Wilk, B.; Timmons, B. W. Effects of postexercise milk consumption on whole body protein balance in youth. J. Appl. Physiol. (1985) 2014, 117, 1165-1169.
- [48] Thams, L.; Stounbjerg, N. G.; Hvid, L. G.; Molgaard, C.; Hansen, M.; Damsgaard, C. T. Effects of high dairy protein intake and vitamin D supplementation on body composition and cardiometabolic markers in 6-8-y-old children-the D-pro trial. *Am. J. Clin. Nutr.* 2022, *115*, 1080-1091.
- [49] Hermanussen, M. Nutritional protein intake is associated with body mass index in young adolescents. *Georgian Med. News* 2008, 156, 84-88.
- [50] Assmann, K. E.; Joslowski, G.; Buyken, A. E.; Cheng, G.; Remer, T.; Kroke, A.; Günther, A. L. B. Prospective association of protein intake during puberty with body composition in young adulthood. *Obesity* 2013, *21*, E782-E789.
- [51] Joslowski, G.; Remer, T.; Assmann, K. E.; Krupp, D.; Cheng, G.; Garnett, S. P.; Kroke, A.; Wudy, S. A.; Gunther, A. L.; Buyken, A. E. Animal protein intakes during early life and adolescence differ in their relation to the growth hormone-insulin-like-growth-factor axis in young adulthood. *J. Nutr.* 2013, *143*, 1147-1154.
- [52] Magarey, A. M.; Daniels, L. A.; Boulton, T. J.; Cockington, R. A. Does fat intake predict adiposity in healthy children and adolescents aged 2-15 y? A longitudinal analysis. *Eur. J. Clin. Nutr.* 2001, *55*, 471-481.
- [53] Switkowski, K. M.; Jacques, P. F.; Must, A.; Fleisch, A.; Oken, E. Associations of protein intake in early childhood with body composition, height, and insulin-like growth factor I in mid-childhood and early adolescence. *Am. J. Clin. Nutr.* 2019, *109*, 1154-1163.
- [54] van Vught, A. J.; Heitmann, B. L.; Nieuwenhuizen, A. G.; Veldhorst, M. A.; Brummer, R. J.; Westerterp-Plantenga, M. S. Association between dietary protein and change in body composition among children (EYHS). *Clin. Nutr.* 2009, 28, 684-688.
- [55] van Vught, A. J.; Heitmann, B. L.; Nieuwenhuizen, A. G.; Veldhorst, M. A.; Andersen, L. B.; Hasselstrom, H.; Brummer, R. J.; Westerterp-Plantenga, M. S. Association between intake of dietary protein and 3-year-change in body growth among normal and overweight 6-year-old boys and girls (CoSCIS). *Public Health Nutr.* 2010, *13*, 647-653.

- [56] Maffeis, C.; Talamini, G.; Tatò, L. Influence of diet, physical activity and parents' obesity on children's adiposity: A four-year longitudinal study. *Int. J. Obes. Relat. Metab. Disord.* 1998, 22, 758-764.
- [57] Skinner, J. D.; Bounds, W.; Carruth, B. R.; Morris, M.; Ziegler, P. Predictors of children's body mass index: A longitudinal study of diet and growth in children aged 2-8 y. *Int. J. Obes. Relat. Metab. Disord.* 2004, *28*, 476-482.
- [58] Durao, C.; Oliveira, A.; Santos, A. C.; Severo, M.; Guerra, A.; Barros, H.; Lopes, C. Protein intake and dietary glycemic load of 4-year-olds and association with adiposity and serum insulin at 7 years of age: Sex-nutrient and nutrient-nutrient interactions. *Int. J. Obes.* 2017, *41*, 533-541.
- [59] Wright, M.; Sotres-Alvarez, D.; Mendez, M. A.; Adair, L. The association of trajectories of protein intake and age-specific protein intakes from 2 to 22 years with BMI in early adulthood. *Br. J. Nutr.* 2017, *117*, 750-758.
- [60] Romero-Corral, A.; Somers, V. K.; Sierra-Johnson, J.; Thomas, R. J.; Collazo-Clavell, M. L.; Korinek, J.; Allison, T. G.; Batsis, J. A.; Sert-Kuniyoshi, F. H.; Lopez-Jimenez, F. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int. J. Obes.* 2008, *32*, 959-966.
- [61] Nuttall, F. Q. Body Mass Index: Obesity, BMI, and Health: A Critical Review. *Nutr. Today* 2015, 50, 117-128.
- [62] Cossio Bolaños, M. A.; Andruske, C. L.; de Arruda, M.; Sulla-Torres, J.; Urra-Albornoz, C.; Rivera-Portugal, M.; Luarte-Rocha, C.; Pacheco-Carrillo, J.; Gómez-Campos, R. Muscle Mass in Children and Adolescents: Proposed Equations and Reference Values for Assessment. *Front. Endocrinol.* 2019, 10, 583.
- [63] Koppes, L. L. J.; Boon, N.; Nooyens, A. C. J.; van Mechelen, W.; Saris, W. H. M. Macronutrient distribution over a period of 23 years in relation to energy intake and body fatness. *Br. J. Nutr.* 2008, *101*, 108-115.
- [64] van Vught, A. J.; Nieuwenhuizen, A. G.; Brummer, R. J.; Westerterp-Plantenga, M. S. Effects of oral ingestion of amino acids and proteins on the somatotropic axis. J. Clin. Endocrinol. Metab. 2008, 93, 584-590.
- [65] Isidori, A.; Lo Monaco, A.; Cappa, M. A study of growth hormone release in man after oral administration of amino acids. *Curr. Med. Res. Opin.* 1981, 7, 475-481.
- [66] Grenov, B.; Larnkjaer, A.; Ritz, C.; Michaelsen, K. F.; Damsgaard, C. T.; Molgaard, C. The effect of milk and rapeseed protein on growth factors in 7-8 year-old healthy children—A randomized controlled trial. *Growth Horm. IGF Res.* 2021, 60-61, 101418.
- [67] Rachdaoui, N. Insulin: The Friend and the Foe in the Development of Type 2 Diabetes Mellitus. *Int. J. Mol. Sci.* 2020, 21, 1770.
- [68] Juul, A. Determination of insulin-like growth factor I in children: Normal values and clinical use. *Horm. Res.* 2001, 55 (Suppl. 2), 94-99.

- [69] Koletzko, B.; Demmelmair, H.; Grote, V.; Totzauer, M. Optimized protein intakes in term infants support physiological growth and promote long-term health. *Semin. Perinatol.* 2019, 43, 151153.
- [70] Bidlingmaier, M.; Friedrich, N.; Emeny, R. T.; Spranger, J.; Wolthers, O. D.; Roswall, J.; Korner, A.; Obermayer-Pietsch, B.; Hubener, C.; Dahlgren, J.; et al. Reference intervals for insulin-like growth factor-1 (igf-i) from birth to senescence: Results from a multicenter study using a new automated chemiluminescence IGF-I immunoassay conforming to recent international recommendations. J. Clin. Endocrinol. Metab. 2014, 99, 1712-1721.
- [71] Smith, C. P.; Dunger, D. B.; Williams, A. J.; Taylor, A. M.; Perry, L. A.; Gale, E. A.; Preece, M. A.; Savage, M. O. Relationship between insulin, insulin-like growth factor I, and dehydroepiandrosterone sulfate concentrations during childhood, puberty, and adult life. *J. Clin. Endocrinol. Metab.* 1989, 68, 932-937.
- [72] Caprio, S.; Plewe, G.; Diamond, M. P.; Simonson, D. C.; Boulware, S. D.; Sherwin, R. S.; Tamborlane, W. V. Increased insulin secretion in puberty: A compensatory response to reductions in insulin sensitivity. *J. Pediatr.* 1989, *114*, 963-967.
- [73] Breen, M. E.; Laing, E. M.; Hall, D. B.; Hausman, D. B.; Taylor, R. G.; Isales, C. M.; Ding, K. H.; Pollock, N. K.; Hamrick, M. W.; Baile, C. A.; et al. 25-hydroxyvitamin D, insulin-like growth factor-I, and bone mineral accrual during growth. J. Clin. Endocrinol. Metab. 2011, 96, E89-E98.
- [74] Xu, L.; Wang, Q.; Wang, Q.; Lyytikäinen, A.; Mikkola, T.; Völgyi, E.; Cheng, S.; Wiklund, P.; Munukka, E.; Nicholson, P.; et al. Concerted actions of insulin-like growth factor 1, testosterone, and estradiol on peripubertal bone growth: A 7-year longitudinal study. J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 2011, 26, 2204-2211.
- [75] Matar, M.; Al-Shaar, L.; Maalouf, J.; Nabulsi, M.; Arabi, A.; Choucair, M.; Tamim, H.; El-Hajj Fuleihan, G. The Relationship Between Calciotropic Hormones, IGF-1, and Bone Mass Across Pubertal Stages. J. Clin. Endocrinol. Metab. 2016, 101, 4860-4870.
- [76] Levine, M. A. Assessing bone health in children and adolescents. *Indian J. Endocrinol. Metab.* 2012, *16*, S205-S212.
- [77] Moran, A.; Jacobs, D. R., Jr.; Steinberger, J.; Cohen, P.; Hong, C. P.; Prineas, R.; Sinaiko, A. R. Association between the insulin resistance of puberty and the insulin-like growth factor-I/growth hormone axis. *J. Clin. Endocrinol. Metab.* 2002, 87, 4817-4820.
- [78] Renehan, A. G.; Zwahlen, M.; Minder, C.; O'Dwyer, S. T.; Shalet, S. M.; Egger, M. Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: Systematic review and meta-regression analysis. *Lancet* 2004, *363*, 1346-1353.
- [79] Conti, E.; Carrozza, C.; Capoluongo, E.; Volpe, M.; Crea, F.; Zuppi, C.; Andreotti, F. Insulin-like growth factor-1 as a vascular protective factor. *Circulation* 2004, *110*, 2260-2265.
- [80] Yamaguchi, T.; Kanatani, M.; Yamauchi, M.; Kaji, H.; Sugishita, T.; Baylink, D. J.; Mohan, S.; Chihara, K.; Sugimoto, T. Serum levels of insulin-like growth factor (IGF); IGF-binding

proteins-3, -4, and -5; and their relationships to bone mineral density and the risk of vertebral fractures in postmenopausal women. *Calcif. Tissue Int.* 2006, 78, 18-24.

- [81] Sandhu, M. S.; Heald, A. H.; Gibson, J. M.; Cruickshank, J. K.; Dunger, D. B.; Wareham, N. J. Circulating concentrations of insulinlike growth factor-I and development of glucose intolerance: A prospective observational study. *Lancet* 2002, 359, 1740-1745.
- [82] Hua, Y.; Remer, T. Adult Stature and Protein Intake during Childhood and Adolescence from 3 Years Onward. J. Clin. Endocrinol. Metab. 2022, 107, e2833-e2842.
- [83] Wolstenholme, H.; Kelly, C.; Hennessy, M.; Heary, C. Childhood fussy/picky eating behaviours: A systematic review and synthesis of qualitative studies. *Int. J. Behav. Nutr. Phys. Act.* 2020, 17, 2.
- [84] Samuel, T. M.; Musa-Veloso, K.; Ho, M.; Venditti, C.; Shahkhalili-Dulloo, Y. A Narrative Review of Childhood Picky Eating and Its Relationship to Food Intakes, Nutritional Status, and Growth. *Nutrients* 2018, *10*, 1992.
- [85] Taylor, C. M.; Hays, N. P.; Emmett, P. M. Diet at Age 10 and 13 Years in Children Identified as Picky Eaters at Age 3 Years and in Children Who Are Persistent Picky Eaters in a Longitudinal Birth Cohort Study. *Nutrients* 2019, *11*, 807.
- [86] Haszard, J. J.; Skidmore, P. M.; Williams, S. M.; Taylor, R. W. Associations between parental feeding practices, problem food behaviours and dietary intake in New Zealand overweight children aged 4-8 years. *Public Health Nutr.* 2015, 18, 1036-1043.
- [87] Taylor, C. M.; Northstone, K.; Wernimont, S. M.; Emmett, P. M. Macro- and micronutrient intakes in picky eaters: A cause for concern? *Am. J. Clin. Nutr.* 2016, *104*, 1647-1656.
- [88] Xue, Y.; Zhao, A.; Cai, L.; Yang, B.; Szeto, I. M.; Ma, D.; Zhang, Y.; Wang, P. Growth and development in Chinese pre-schoolers with picky eating behaviour: A cross-sectional study. *PLoS ONE* 2015, *10*, e0123664.
- [89] Dubois, L.; Farmer, A.; Girard, M.; Peterson, K.; Tatone-Tokuda, F. Problem eating behaviors related to social factors and body weight in preschool children: A longitudinal study. *Int. J. Behav. Nutr. Phys. Act.* 2007, *4*, 9.
- [90] Dubois, L.; Farmer, A. P.; Girard, M.; Peterson, K. Preschool children's eating behaviours are related to dietary adequacy and body weight. *Eur. J. Clin. Nutr.* 2007, *61*, 846-855.
- [91] Berger, P. K.; Hohman, E. E.; Marini, M. E.; Savage, J. S.; Birch, L. L. Girls' picky eating in childhood is associated with normal weight status from ages 5 to 15 y. *Am. J. Clin. Nutr.* 2016, *104*, 1577-1582.
- [92] Grulichova, M.; Kuruczova, D.; Svancara, J.; Pikhart, H.; Bienertova-Vasku, J. Association of Picky Eating with Weight and Height—The European Longitudinal Study of Pregnancy and Childhood (ELSPAC-CZ). *Nutrients* 2022, *14*, 444.
- [93] Taylor, C. M.; Steer, C. D.; Hays, N. P.; Emmett, P. M. Growth and body composition in children who are picky eaters: A longitudinal view. *Eur. J. Clin. Nutr.* 2019, *73*, 869-878.

- [94] de Barse, L. M.; Tiemeier, H.; Leermakers, E. T.; Voortman, T.; Jaddoe, V. W.; Edelson, L. R.; Franco, O. H.; Jansen, P. W. Longitudinal association between preschool fussy eating and body composition at 6 years of age: The Generation R Study. *Int. J. Behav. Nutr. Phys. Act.* 2015, *12*, 153.
- [95] Sheng, X.; Tong, M.; Zhao, D.; Leung, T. F.; Zhang, F.; Hays, N. P.; Ge, J.; Ho, W. M.; Northington, R.; Terry, D. L.; et al. Randomized controlled trial to compare growth parameters and nutrient adequacy in children with picky eating behaviors who received nutritional counseling with or without an oral nutritional supplement. *Nutr. Metab. Insights* 2014, 7, 85-94.
- [96] Ghosh, A. K.; Kishore, B.; Shaikh, I.; Satyavrat, V.; Kumar, A.; Shah, T.; Pote, P.; Shinde, S.; Berde, Y.; Low, Y. L.; et al. Effect of oral nutritional supplementation on growth and recurrent upper respiratory tract infections in picky eating children at nutritional risk: A randomized, controlled trial. *J. Int. Med. Res.* 2018, *46*, 2186-2201.
- [97] Alarcon, P. A.; Lin, L. H.; Noche, M., Jr.; Hernandez, V. C.; Cimafranca, L.; Lam, W.; Comer, G. M. Effect of oral supplementation on catch-up growth in picky eaters. *Clin. Pediatr.* 2003, *42*, 209-217.
- [98] Khanna, D.; Yalawar, M.; Saibaba, P. V.; Bhatnagar, S.; Ghosh, A.; Jog, P.; Khadilkar, A. V.; Kishore, B.; Paruchuri, A. K.; Pote, P. D.; et al. Oral Nutritional Supplementation Improves Growth in Children at Malnutrition Risk and with Picky Eating Behaviors. *Nutrients* 2021, *13*, 3590.
- [99] Zhang, Z.; Li, F.; Hannon, B. A.; Hustead, D. S.; Aw, M. M.; Liu, Z.; Chuah, K. A.; Low, Y. L.; Huynh, D. T. T. Effect of

Oral Nutritional Supplementation on Growth in Children with Undernutrition: A Systematic Review and Meta-Analysis. *Nutrients* 2021, *13*, 3036.

- [100] Lebenthal, Y.; Yackobovitch-Gavan, M.; Lazar, L.; Shalitin, S.; Tenenbaum, A.; Shamir, R.; Phillip, M. Effect of a nutritional supplement on growth in short and lean prepubertal children: A prospective, randomized, double-blind, placebo-controlled study. J. Pediatr. 2014, 165, 1190-1193. e1191.
- [101] Yackobovitch-Gavan, M.; Lebenthal, Y.; Lazar, L.; Shalitin, S.; Demol, S.; Tenenbaum, A.; Shamir, R.; Phillip, M. Effect of Nutritional Supplementation on Growth in Short and Lean Prepubertal Children after 1 Year of Intervention. *J. Pediatr.* 2016, *179*, 154-159. e151.
- [102] Fisch Shvalb, N.; Lazar, L.; Demol, S.; Mouler, M.; Rachmiel, M.; Hershkovitz, E.; Shamir, R.; Phillip, M.; Yackobovitch-Gavan, M. Effect of a nutritional supplementation on growth and body composition in short and lean preadolescent boys: A randomised, double-blind, placebo-controlled study. *Acta Paediatr.* 2022, *111*, 141-150.
- [103] Kim OY, Kim EM, Chung S. Impacts of Dietary Macronutrient Pattern on Adolescent Body Composition and Metabolic Risk: Current and Future Health Status—A Narrative Review. Nutrients. 2020; 12(12): 3722. https://doi.org/10.3390/nu12123722
- [104] Carbone JW, Pasiakos SM. Dietary Protein and Muscle Mass: Translating Science to Application and Health Benefit. Nutrients. 2019 May 22; 11(5): 1136. https://doi.org/10.3390/nu11051136