

The Rise and Fall of Protein Malnutrition in Global Health

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Key Words

Amino acids · Children · Malnutrition · Micronutrients · Protein · Stunting

Abstract

Background: From the 1950s to the mid-1970s, United Nations (UN) agencies were focused on protein malnutrition as the major worldwide nutritional problem. The goal of this review is to examine this era of protein malnutrition, the reasons for its demise, and the aftermath. **Summary:** The UN Protein Advisory Group was established in 1955. International conferences were largely concerned about protein malnutrition in children. By the early 1970s, UN agencies were ringing the alarm about a 'protein gap'. In *The Lancet* in 1974, Donald McLaren branded these efforts as 'The Great Protein Fiasco', declaring that the 'protein gap' was a fallacy. The following year, John Waterlow, the scientist who led most of the efforts on protein malnutrition, admitted that a 'protein gap' did not exist and that young children in developing countries only needed sufficient energy intake. The emphasis on protein malnutrition waned. It is recently apparent that quality protein and essential amino acids are missing in the diet and may have adverse consequences for child growth and the reduction of child stunting. **Key Messages:** It may be time to re-include protein and return protein malnutrition in the global health agenda using a balanced approach that includes all protective nutrients.

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Introduction

The dominant idea in child malnutrition, originating from the 1950s, was that children in developing countries were not receiving enough quality protein. The programmatic activities of the United Nations (UN) agencies and international conferences were centered on protein malnutrition. As noted by Kenneth Carpenter (b. 1923), in the mid-1970s, protein malnutrition was 'suddenly discarded, amid some passionate debate and name calling' [1]. The goal of this review is to examine the era of protein malnutrition, the reasons for its demise, and the aftermath, which has had a lasting effect on programs and policy. A reevaluation of protein malnutrition may be timely, given recent developments in the field.

Micronutrient malnutrition is currently the main paradigm in maternal and child nutrition in developing countries and rose in prominence after the decline of interest in protein malnutrition. Over the last 4 decades, community-based nutritional interventions to improve the health and survival of young children in developing countries have focused on nutrient supplements like vitamin A, zinc, iron, and iodine [2, 3]. The micronutrient era began with the founding of the International Vitamin A Consultative Group (IVACG) and the International Nutritional Anemia Consultative Group (INACG) in 1975 and the International Council for the Control of Iodine Deficiency Disorders in 1985. At the World Summit for Children in 1990, world leaders assembled at the UN and set the goal

for the virtual elimination of iodine and vitamin A deficiency. The interests of IVACG and INACG were incorporated in the Micronutrient Forum in 2007.

Periodic high-dose vitamin A supplementation [4], oral zinc supplementation [5], and iodized salt [6] have improved the health and survival of millions of children in developing countries. However, micronutrients have little to no effect on linear growth in children [7–9]. Recent trials of lipid-based nutrient supplements in complementary feeding have also shown little to no effect upon linear growth [10, 11]. Other uncharacterized nutrients essential to growth are missing or insufficient in the diet, a point to which we will return at the end of this review.

The Evolution of Thought on Protein Malnutrition

In the 1930s, at a time when nutritional thinking was dominated by research on vitamins [12], the pediatrician Cicely Williams (1893–1992) described a syndrome in children in Africa characterized by peripheral edema, wasting, and diarrhea [13, 14]. The local term for the disease was ‘kwashiorkor’ [14]. The affected children were usually between the ages of 6 months and 4 years, often being breast-fed by a malnourished or pregnant mother, and being weaned only on maize porridge. The most effective treatment was a combination of cod-liver oil and milk. As to the etiology, Williams noted that ‘breast milk is probably deficient in some factors, which are at present uncertain. As maize was the only source of the supplementary food, some amino acid or protein deficiency cannot be excluded as a cause’ [13].

The Food and Agriculture Organization (FAO) of the UN and the World Health Organization (WHO) formed the Joint FAO/WHO Expert Committee on Nutrition in 1949. At their first session, they noted that kwashiorkor was widespread in developing countries and recommended an investigation. WHO sent John Fleming Brock (1905–1983) and FAO sent Marcel Autret (1909–2001) to conduct a survey in Africa [15]. Brock and Autret [15] noted kwashiorkor occurred in every part of Africa surveyed but was totally absent among the Masai and Batussi tribes that produce large quantities of cows’ milk. A subsequent survey conducted by Autret and Moisés Béhar (1922–2015) showed kwashiorkor was common in Central America [16]. John Conrad Waterlow (1916–2010) and Arturo Vergara also showed kwashiorkor was highly prevalent in Brazil [17].

In 1952, the Joint FAO/WHO Expert Committee on Nutrition held its third session in the Gambia, with the

meeting devoted to malnutrition in mothers, infants, and children, where the term ‘protein malnutrition’ was introduced. The following year, the first conference on protein malnutrition was held in Jamaica [18]. While the clinical and pathological features of kwashiorkor and marasmus were the main topics, Waterlow emphasized the importance of subclinical disease: ‘I realize very well that we are concerned not only with the very sick and the dying, but perhaps much more with mild or chronic, so-called ‘marginal’, states of malnutrition in infants and children...this is a far more important problem than acute kwashiorkor’ [18].

The second conference on protein malnutrition was held in Princeton, New Jersey in 1955 and was attended by 29 nutritionists, physicians, and scientists, including William Cumming Rose (1887–1985), the American biochemist who did seminal research on essential amino acids [19]. Rose noted: ‘You can’t build proteins unless you have all of the necessary building blocks. If you take out one of them, then the rest become largely useless’ [20]. The main conclusions of the conference were that the protein requirement of man was based upon the quality and quantity of protein. Milk was proposed as a reference protein to determine the amino acid requirements for infants and young children. To address protein needs, 2 strategies were proposed: a regional approach to encourage production and consumption of vegetable products or fish as a supplement to the local staple, and production of complementary protein-rich foods that are biologically effective, safe, inexpensive, easy to store, and acceptable [20].

During this period, many scientists began studying childhood malnutrition in research units around the world: John Hansen (1920–2011) at the University of Cape Town, Nevin Scrimshaw (1918–2013) at the Institute for Nutrition for Central America and Panama (INCAP), Colothur Gopalan (b. 1918) at the Nutrition Research Laboratories in Conoor, India, Robert Eugene Olson (b. 1919) in Thailand, Julio Meneghello (1911–2009) in Chile, Donald S. McLaren (b. 1924) in Beirut, Lebanon, Henri-Louis Vis (d. 2002) in Zaire, Federico Gómez Santos (1897–1980) in Mexico City, and John C. Waterlow in Jamaica [21]. These various sites facilitated many observations of child malnutrition. The pediatrician Derrick B. Jelliffe (1921–1992) emphasized that kwashiorkor was only the most full-blown manifestation of severe protein deficiency, and that within the category of protein deficiency there were many more young children who were short and suffering from subclinical protein malnutrition [22].

The UN Protein Advisory Group (PAG) was founded in 1955, following the recommendations made at the Princeton meeting for the formation of a group that would function autonomously and provide expertise on protein [23]. William J. Darby (1913–2001), was its first chair. Their role was to provide expert advice to WHO, FAO, and UNICEF regarding their ‘protein-rich food programs’ [23]. Members of the group included Benjamin Stanley Platt (1903–1969), L. Emmett Holt Jr. (1895–1974), Nevin Scrimshaw, and W. Henry Sebrell Jr. (1901–1992), Director of the National Institutes of Health.

The third conference on protein malnutrition was held in Cuernavaca, Mexico in 1960, with the idea of bringing in expertise in the social sciences in order to understand food habits in different cultures [24]. The term ‘protein-calorie malnutrition’ was used to describe the child malnutrition found ‘where diets are habitually poor in protein but provide calories in quantities that vary from gross inadequacy to excess’ [24]. The efforts to introduce protein-rich foods were expected to meet resistance in some communities because of cultural traditions and beliefs. Thus, the focus of this conference was on nutrition education, involvement of social scientists, methods of studying food habits, and finding ways to introduce new foods. Federico Gómez Santos proposed that growth failure, based on weight-for-age, be used to define the prevalence of protein-calorie malnutrition [24].

The Food and Nutrition Board organized the Committee on Protein Malnutrition, a subgroup of the PAG, which was created to supervise a worldwide research program on high-protein foods, especially for growing children [25]. The Committee on Protein Malnutrition was supported by a grant of \$550,000 from the Rockefeller Foundation and \$300,000 from UNICEF. In 1960, the National Institutes of Health sponsored a meeting ‘Meeting Protein Needs of Infants and Children’ in Washington, D.C., USA [25]. Nearly 80 scientists from around the world attended this meeting, which highlighted protein-rich and protein quality foods that could be used to meet the protein and amino acid needs of children. The term ‘protein-calorie malnutrition’, as proposed by Jelliffe [22], came into frequent use and was officially adopted by FAO and WHO in 1961 [1].

Under the auspices of the 6th International Congress of Nutrition, an international symposium ‘How to Reach the Pre-School Child’ was held in Italy in 1963. One of the main conclusions was: ‘the present situation was so grave that it should be recognized as an emergency’ [26]. The following year, the International Conference on the Prevention of Malnutrition in the Pre-School Child was held

in Washington, DC, USA, organized by the Committee on Protein Malnutrition, The Committee on Child Nutrition, and the Food and Nutrition Board, National Academy of Sciences. Paul György (1893–1976) observed that ‘in many countries, pre-school children appear to be healthy, often with good proportional body build but greatly reduced height. The diet consumed by these children is often low, not only in proteins but also in calories...’ [27].

The American Chemical Society held a symposium ‘World Protein Resources’ in Atlantic City, New Jersey in September 1965, chaired by Aaron M. Altschul (1914–1994). Among the topics of the symposium were biochemical and technical perspectives on increasing the animal protein supply in developing countries, milk proteins, edible fish protein concentrates, seed protein concentrates, production of lysine and methionine, cottonseed protein, soybean flours, safflower protein, and production of better protein quality in maize [28]. Mortimer Louis Anson (1901–1968) highlighted the importance of providing limiting amino acids to children. A posthumous tribute was made at the conference to Maurice Pate (1894–1965), the director of UNICEF. Under his leadership, UNICEF had been strongly involved in efforts to provide skim milk powder to children in developing countries. In December 1965, UNICEF received the Nobel Peace Prize. The Nobel Lecture mentioned the ‘incomparable leadership’ of Pate, noting that UNICEF was intent on ensuring that children received adequate protein in their diets [29].

The ‘Protein Crisis’

By 1968, international organizations rang the alarm that the ‘protein gap’ or ‘crisis’ was a global emergency demanding immediate attention. The UN issued ‘International Action to Avert the Impending Protein Crisis’, (fig. 1) which outlined 7 policy objectives (table 1) [30]. Specific recommendations included adding essential amino acids to ordinary plant proteins so that all essential amino acids would be present in food and to ‘work on essential amino acid content and supplementation of diets’ [30]. The report recommended that the scope and function of the PAG for WHO, FAO, and UNICEF be expanded to disseminate new information and advise on project evaluation and feasibility studies [30].

FAO issued their own advisory ‘Lives in Peril: Protein and the Child’ in 1970 [31]. The report highlighted examples of protein food mixtures to address protein mal-

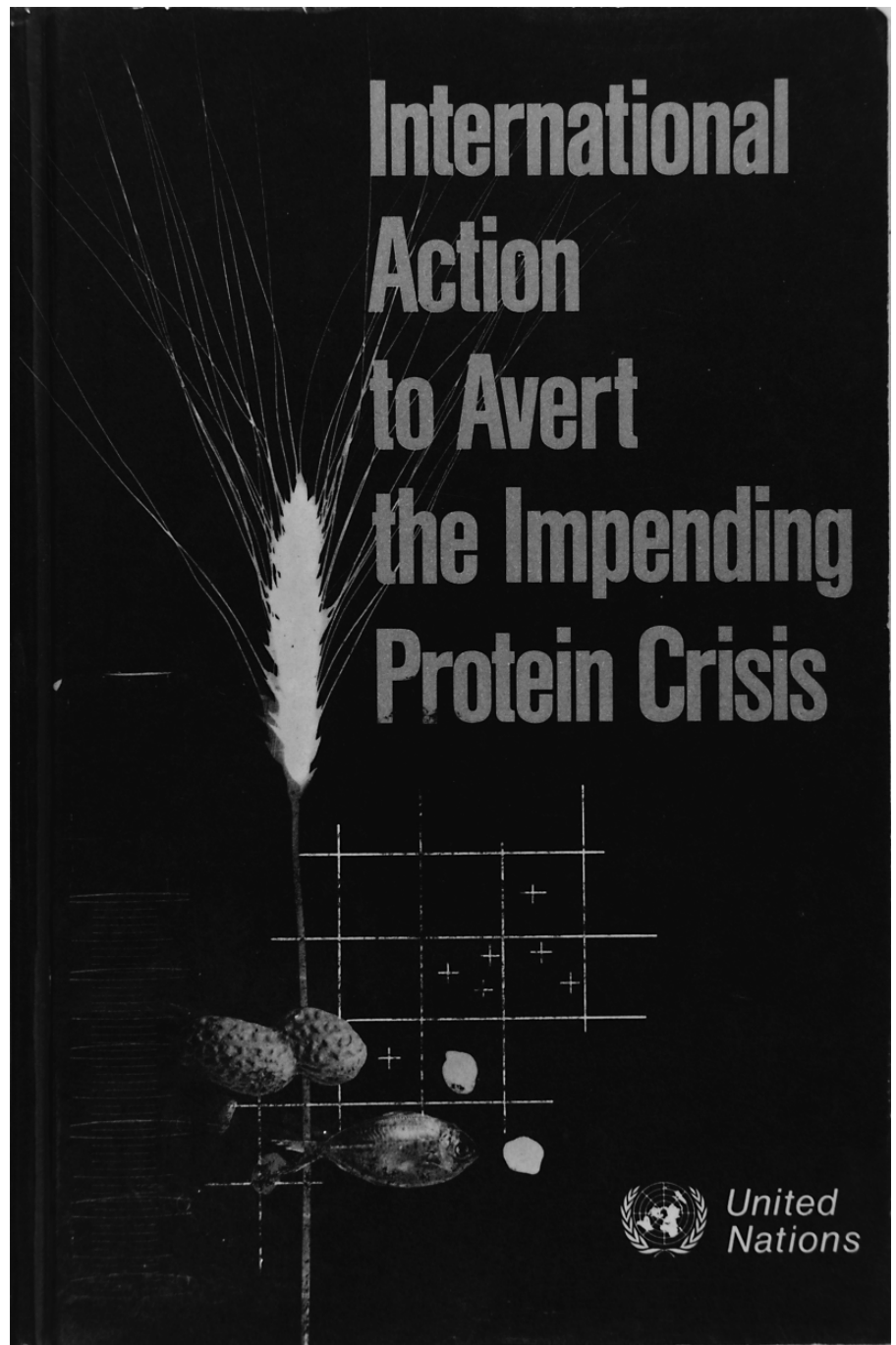


Fig. 1. Cover of UN report 'International Action to Avert the Impending Protein Crisis' (UN 1968) [30].

nutrition in children (table 2). Surveys indicated that severe protein-calorie malnutrition affected about 2–10% of children from 1 to 9 years in developing countries and in some areas, up to 50% of children aged 1–5 years were affected by less extreme protein-calorie malnutrition. In 1971, the UN issued a report of an expert panel on protein 'Strategy Statement on Action to Avert the Protein Crisis

in the Developing Countries' [32]. Protein malnutrition was recognized as 'an important cause of infant and young child mortality, stunted physical growth, low work output, premature aging and reduced life span in the developing world' [32].

During its early years, the PAG focused on developing protein-rich foods using soya, fish protein concentrate,

Table 1. UN policy objectives to avert the protein crisis (UN 1968) [30]

Number	Objective
1	Promotion of increased quantity and quality of conventional plant and animal protein sources suitable for direct human consumption
2	Improvement in the efficiency and scope of both marine and fresh-water fisheries operations
3	Prevention of unnecessary losses of proteinaceous foods in field, storage, transport and home
4	Increase in the direct food use of oil-seeds and oil-seed protein concentrates by the human population
5	Promotion of the production and use of fish-protein concentrates
6	Increase in the production and use of synthetic amino acids to improve the quality of protein in cereals and other vegetable sources, and the development of the use of other synthetic nutrients
7	Promotion of the development of single-cell protein for both animal feeding and direct utilization by man

Table 2. Examples of protein food mixtures under development in 1970 (FAO of the UN 1970) [31]

Product	Country	Composition	Protein content, %
Incaparina	Guatemala	Maize, cottonseed flour, vitamin A, lysine, calcium carbonate	27.5
	Columbia	Same – plus defatted soybean flour	
	Mexico	Same – plus defatted soybean flour but without cottonseed flour	
Fortifex	Brazil	Maize, defatted soybean flour, vitamins, dl-methionine, calcium carbonate	30.0
Pronutro	South Africa	Maize, skim milk powder, groundnut, soybean, fish protein concentrate, yeast, wheat germ, vitamins, niacin, sugar, iodized salt	22.0
Protone	United Kingdom Congo	Maize, skim milk powder, yeast, vitamins, minerals	22.4
Arlac	Nigeria	Groundnut flour, skim milk powder, salts and vitamins	42.0
Lac-Tone	India	Groundnut flour, skim milk powder, wheat and barley flour, vitamins, calcium	26.0
Aliment de sevrage	Senegal	Millet flour, groundnut flour, skim milk powder, sugar, vitamins, calcium	20.0
CSM	United States	Maize (precooked), defatted soybean flour, skim milk powder, sugar, vitamins, calcium	20.0
Supro	East Africa	Maize or barley flour, torula yeast, skim milk powder, salt, condiments	24.0

peanut, sesame, sunflower and leaf meals, algal protein, and synthetic amino acids, but the products suffered serious setbacks because of the issues of cost, production, and acceptability [23]. Scrimshaw put the greatest effort into developing complementary foods. After a process was developed to remove a toxin from cottonseed flour, ‘Incaparina’ was developed by INCAP [23]. By the early 1970s, the senior staff of FAO, WHO, and UNICEF were filled with discontent that the PAG had not met much practical success [23]. There was also friction between the PAG

and FAO, which had nutrition experts within its own ranks [23]. In 1968, under an administrative reorganization, the FAO became the supervising agency of the PAG. Marcel Autret, now director of the nutrition division at FAO, asserted that FAO should take the leadership on protein issues, not the PAG [23]. E.J.R. ‘Dick’ Heyward (1914–2005), the Deputy Director of UNICEF, complained that the FAO was not giving the PAG any work to do [23]. The PAG attempted to gain greater leverage by expanding its terms of reference under the 1971 UN

Strategy Statement [32], which brought it into further conflict with FAO. The Director General of FAO, Addeke Hendrik Boerma (1912–1992) sought to limit the influence of the PAG; FAO began to waver in their support for the ‘protein gap’ [23]. As a consequence, the PAG began to lose influence within the UN agencies.

The Great Protein Fiasco

In July 1974, Donald S. McLaren issued a scathing indictment of activities directed toward alleviating protein malnutrition in ‘The Great Protein Fiasco’ published in *The Lancet* under the subheading ‘Dogma Disputed’ [33]. McLaren declared that there was no ‘protein gap’ worldwide, and that kwashiorkor due to protein deficiency was not the main form of child malnutrition in developing countries. He criticized the ‘the protein era’ as producing little worthwhile and noted that the experts had unwittingly closed the ‘protein gap’ by lowering the dietary requirements for protein. In comments aimed directly at Scrimshaw [23], the current head of the PAG, he noted that the committee ‘is now caught in a crossfire of criticism and is experiencing a crisis of identity. The underlying causes of this display of disarray may not be immediately evident. This is an account of what is seen to be a long and disastrous train of events which, once set in motion, led inexorably to the present crisis’. McLaren sarcastically suggested that instead of cost/benefit analysis, someone should calculate a cost/detriment analysis to determine how much money was wasted on research and development projects, scientific meetings, publications, and food-industry and public involvement centered on protein malnutrition [33].

Given their waning influence, the timing of McLaren’s attack could not have been worse for the PAG. The FAO organized the World Food Conference in Rome in November 1974. In the backdrop was an ongoing famine in Bangladesh that killed an estimated 1.5 million people. The PAG was not consulted for the conference and protein was conspicuously absent from the proceedings [23]. At this conference, Henry Kissinger (b. 1923) famously vowed thus: ‘Within a decade, no man, woman or child will go to bed hungry’. At the recommendation of the World Food Conference, the World Food Council was established in Rome in 1974. The mission of the World Food Council was to coordinate the work of concerned UN agencies relating to nutrition and food production, security, trade, and aid [34].

In a meeting of UN agency representatives in July 1975, Halfdan Mahler (b. 1923), the Director General of

WHO, expressed the view that the PAG had become useless and should be disbanded, and the other participants agreed [23]. The Advisory Committee on Coordination (ACC), responsible for coordinating UN efforts, recommended the formation of a Sub-Committee on Nutrition (SCN) of the ACC. An ACC preparatory committee met in October 1975 to determine why ‘despite overwhelming moral imperatives’ the UN and governments had not produced a strategy for elimination of hunger and malnutrition. The real problem was seen as the food supply, not protein. The problem was complex, since poverty was at the root of malnutrition. In addition, governments had not set national nutrition targets [23].

Waterlow, who led much of the effort focused on protein malnutrition, and Phillip Reid Payne (1928–2012) published ‘The Protein Gap’ in *Nature* in November 1975. They admitted that the concept of a worldwide protein gap was ‘no longer tenable’. According to current estimates of children’s protein and energy requirements, ‘the problem is mainly one of quantity rather than quality of food’ [35]. Waterlow and Payne [35] expressed concern that the pendulum did not swing too far in the opposite direction, noting:

‘One difficulty is that the controversy about the protein gap, which represents a genuine difference of scientific opinion, is accompanied by another controversy, potentially far more dangerous. This arises from the attitude that research on these nutritional problems is academic, irrelevant and a waste of time; that we know how to prevent malnutrition and therefore what matters is to use this knowledge. Malnutrition is an emotive subject; it is certainly true that there is much that can be done with existing knowledge, and that action cannot wait on the perfectionism of research. But perhaps the story of the protein gap shows the arrogance of supposing that we know the answers, and illustrates the need for a continuing critical examination of the premises on which action is based’.

With the planned establishment of the SCN, it became clear in 1976 that an advisory panel on nutrition would replace the PAG. At the annual meeting of the PAG in September 1976, Joaquin Cravioto (1922–1998) resigned from the committee, blaming the sponsoring agencies for not requesting advice from the group [23]. The PAG was dissolved the following year, replaced by an Advisory Group on Nutrition (AGN), as recommended by the ACC. The AGN would provide advice as requested from ACC’s SCN. The SCN held its first meeting in September 1977, with Heyward as its chair.

Looking Back at the Fiasco

Over 25 years later, in reflecting upon his 1974 paper in *The Lancet*, McLaren declared with satisfaction that ‘the protein-rich food mixtures and all the other trappings of the fiasco have long disappeared as evidence that that particular fallacy is long dead and gone’ [36]. He added that ‘it has been instructive for me to reminisce over the episode of the great protein fiasco that preoccupied my thoughts for years long ago. It was a battle and not a war, but it was a battle won that made possible a truer and saner approach thereafter to the problem of childhood malnutrition. The overturning of false paradigms is a painful and costly business and lacks the glamor of making new discoveries’ [36]. During an interview in 2011, McLaren recapitulated: ‘In my opinion, the belief in the ‘protein gap’ is one of the greatest errors committed in the name of nutrition science in the past half-century’ [37].

Establishing Protein and Amino Acid Requirements for Infants and Young Children

Although the international focus on the ‘protein gap’ faded away after the mid-1970s, FAO/WHO expert committees continued to address protein and amino acid requirements and protein quality evaluation in human nutrition. FAO/WHO issued reports in 1957 [38], 1965 [39], 1973 [40], 1985 [41], and 2007 [42] and an additional report on protein quality in 2013 [43]. The most recent estimates for protein and amino acid requirements for infants are based upon the assumption that human milk intake from a healthy, well-nourished mother provides optimal protein intake for an infant [42]. For children 12–59 months of age, estimates of dietary essential amino acid requirements are based upon a factorial computation because of a lack of direct experimental data. In the 2007 report, the committee did not see their report as ‘an endpoint, but an important step in the continuous quest for scientifically-based answers, and for understanding the implications of these answers in terms of improved nutrition and health’ [42].

Protein-Energy Malnutrition and Its Consequences

Two important papers on protein-energy malnutrition in 1993 [44] and 1995 [45] attracted much attention but did not galvanize the scientists or policymakers to focus on providing protein to young children. The lack of action

may be related to the demise of protein malnutrition in the 1970s. Carpenter commented that the nutrition community seemed to reflect upon the earlier emphasis on protein malnutrition ‘as an embarrassment’ [1]. Using the WHO Global Database on Child Growth, de Onís et al. [44] showed that more than a third of the world’s children are affected by protein-energy malnutrition. Pelletier et al. [45] showed that low weight-for-age, used to represent protein-energy malnutrition, potentiated the effects of mortality due to infectious diseases. They concluded that protein-energy malnutrition accounted for ~56% of child deaths in developing countries.

Recent Studies on Protein Quality, Essential Amino Acids, and Stunting

Recent studies challenge the widespread assumption that young children in developing countries receive sufficient dietary protein. Using national data from 180 countries, Ghosh et al. [46] showed that protein quality, which takes into account essential amino acid composition, digestibility, energy deficit, and infections, was associated with the prevalence of stunting. Millions of children subsist on staple foods that are poor sources of essential amino acids, such as cassava and maize. Cassava is the main source of dietary protein in Africa for 250 million people [47, 48]. Maize provides the main source of energy intake in much of sub-Saharan Africa and is a poor source of tryptophan and lysine [49]. Stunted children in Malawi had serum concentrations of all 9 essential amino acids that were about 10–20% lower than non-stunted children [50]. In addition, stunted children had significantly lower serum concentrations of conditionally essential amino acids (arginine, glycine, glutamine), non-essential amino acids (asparagine, glutamate, serine), and 6 different sphingolipids compared with non-stunted children [50].

Over the last 2 decades, it has become clear that insufficient availability of amino acids will have adverse effects upon cell and organismal growth. The availability of amino acids is sensed via the master growth regulatory pathway of the cell, the mechanistic target of rapamycin complex 1 (mTORC1) [51, 52] and by a related amino acid sensing pathway, the general control nonderepressible 2 pathway [53]. mTORC1 integrates environmental cues such as nutrients, growth factors, oxygen, and energy to regulate growth and homeostasis. mTORC1 will repress protein and lipid synthesis and cell and organismal growth when amino acids are deficient [52].

Rethinking Protein

The protein and amino acid requirements for children in the first 3 years of life, or the first 1,000 days when children are most vulnerable to stunting, remain poorly understood [54]. It is not known how infectious diseases or conditions such as environmental enteric dysfunction affect protein and amino acid requirements among children in developing countries, and what the protein and amino acid requirements are during catch-up growth [54, 55]. A recent study using the indicator amino acid oxidation (IAAO) technique showed the lysine requirement increased by ~20% in children with intestinal parasitic infections [56]. Further work is needed using the IAAO technique under real-life circumstances to establish amino acid requirements for young children in developing countries and to collect new data on dietary protein quality using such approaches as the digestible indispensable amino-acid score [57].

There are some signs of renewed awareness of the importance of protein in complementary food supplements for young children [58–62]. In other words, the renewed emphasis upon what McLaren termed ‘the protein-rich food mixtures and all the other trappings of the fiasco’ [36] are a stark recognition that quality protein is important to child health and not a fallacy. Milk and animal source foods such as meat show a strong association with linear growth in children in developing countries [63–66]. Golden emphasizes there are no generally accepted Recommended Nutrient Intakes for children with moderate malnutrition, wasting, and stunting, who live in

poor environments [67]. Golden proposes that the diet should contain 24 g of protein with a quality of at least 70% of reference protein per 1,000 kcal with avoidance of proteins with low amino acid scores, and for supplementary foods, 26 g/1,000 kcal, with emphasis on proteins containing sulfur amino acids for children with stunting [67]. Currently, while there are dietary estimates, which continually evolve [42], there are no official policy recommendations from the WHO or UNICEF regarding dietary protein or amino acid intake in young children. New scientific knowledge on dietary protein and amino acids may help guide future policy. Four decades of relative neglect may be ending, as we return to the importance of protein, derived from the Greek adjective *πρωτειος* (proteios), meaning the first rank or primary [68].

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No conflicts of interest.

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