Minimum Protein Requirements in Infancy and Childhood: Insights from Patients with Protein-Restricted Diets

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Knowledge about the normal child’s requirements for protein and essential amino acids is still limited. Two approaches have been used to estimate protein requirements. The first involves estimating the protein intake of exclusively breastfed infants, which is supposed to represent the true requirement on an evolutionary basis. The second involves factorial analyses, based on the calculated amounts of protein required for growth, stool and skin losses, and obligatory catabolism. As infants get older, the requirement for protein and essential amino acids for growth decreases as growth rate declines, while protein loss from the body and obligatory catabolism maintenance account for an increasingly large proportion of the total requirement.

Genetic errors of enzyme function resulting in disturbed metabolism of proteins or essential amino acids provide opportunities for estimating the amounts of protein needed for normal growth and development. In theory, during such disorders the amount of specific protein or essential amino acid required for obligatory catabolism is nil. To meet this condition, the enzymatic block must be complete, without any residual enzymatic activity. In addition, the enzymatic block has to lack the ability to stimulate alternate pathways, and cannot be amenable to treatments that involve such pathways. In practice, the degree of residual enzyme activity is unknown and is evaluated \textit{a posteriori} on the basis of the individual tolerance for the controlled amino acid given in the diet. The lowest tolerances indicate complete block while higher tolerances suggest residual enzymatic activity. However, such diseases are useful tools only if the following conditions pertain: (a) the ability to make reliable metabolic assessments by accurate measurements of metabolites in plasma or urine, with a known range of safe values; (b) the availability of a satisfactory dietary treatment allowing normal nutritional status, growth, and development.

Only a few disorders meet these conditions and so can be studied in this way. The best examples are phenylketonuria (PKU), due to phenylalanine hydroxylase deficiency, and maple syrup urine disease (MSUD), due to branched chain decarboxylase
deficiency. Most of the other amino acid disorders have characteristics that make them inappropriate. For example, tyrosinemia type I, caused by fumarylacetoacetase deficiency, is treated with NTBC 2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanediyldiol, a molecule that blocks the second step of tyrosine catabolism. This model would have been ideal to compute the requirement for phenylalanine plus tyrosine. The therapeutic diet in these patients, however, results in high plasma tyrosine levels (=400 \mu M), which are obviously well outside the normal range (43 ± 16 \mu M). Methylmalonic aciduria and propionic aciduria are two other disorders that are treated with a protein-restricted or a valine-restricted diet. However, the site of the catabolic block in these conditions allows adjacent metabolic disturbances with accumulation of various additional organic acids. Except for general well-being, we have no clear criteria to assess metabolic control in these patients, and despite treatment, severely affected patients have poor growth and development. Urea cycle defects caused by various enzyme deficiencies in the urea cycle are responsible for hyperammonemia. Most patients with these conditions present in the neonatal period and die within a few days. Because of the presence of residual enzymatic activity, some patients have late-onset forms. These individuals can have normal growth and normal blood ammonia levels when on a protein-restricted diet and when given drugs such as sodium benzoate and sodium phenylbutyrate that permit nitrogen to be excreted in compounds other than urea.

Our first step in the study described in this chapter was to analyze the protein, phenylalanine, and leucine intakes in patients affected with PKU \((n = 34)\) and MSUD \((n = 12)\), using the dietary records at 3, 6, 9, 12, 24, and 36 months of age. These patients were obtained from cohorts diagnosed and treated during the last decade in the two main metabolic units in Paris. We compared our results with previously published data and with the results obtained by the two classic methods.

CLASSIC METHODS FOR COMPUTING PROTEIN AND ESSENTIAL AMINO ACID REQUIREMENTS

The Human Milk Model

Breastfeeding is the agreed reference of all international committees formed to assess nitrogen and amino acid needs during the first 6 months of life (1). Few data are available from 6 to 12 months of age and we use these for comparison (2). Requirements are derived from the average volume of milk absorbed by healthy breastfed infants and the mean bioavailable protein and amino acid content of mature human milk. These studies report a protein intake of 1.5 to 1.6 g/kg/d during the second month of life, decreasing gradually to about 1 g/kg/d between the third and 12th months (2–5).

Assuming a birth weight of 3.5 kg and a normally growing infant, protein intakes average 6 to 7 g/d. Based upon estimated energy requirements (5) and the average body weight according to references for the French population (6), the daily protein requirement expressed in terms of energy intake averages 1 g per 100 kcal from the third to 12th months of life, while being higher in the first month (1.6 g/100 kcal) and in the second month (1.4 g/100 kcal) (Table 1).
TABLE 1. Estimates of the daily bioavailable protein and amino acid requirements, based upon the human milk model and factorial analysis

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>0–1</th>
<th>1–2</th>
<th>2–3</th>
<th>3–4</th>
<th>4–5</th>
<th>5–6</th>
<th>6–9</th>
<th>9–12</th>
<th>12–24</th>
<th>24–36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean body weight (kg)</td>
<td>3.55</td>
<td>4.35</td>
<td>5.125</td>
<td>5.875</td>
<td>6.625</td>
<td>7.1</td>
<td>8.1</td>
<td>9.05</td>
<td>10.75</td>
<td>13.75</td>
</tr>
<tr>
<td>Mean energy intake (kcal/d)</td>
<td>430</td>
<td>480</td>
<td>520</td>
<td>560</td>
<td>600</td>
<td>640</td>
<td>730</td>
<td>820</td>
<td>1000</td>
<td>1250</td>
</tr>
<tr>
<td>Protein requirement (HM/FA)</td>
<td>g/day</td>
<td>6.9/7.6</td>
<td>6.8/7.8</td>
<td>6/8</td>
<td>6.3/8</td>
<td>6.6/8.5</td>
<td>7.3/8.6</td>
<td>7.2/10.5</td>
<td>-/13.4</td>
<td>-/14.6</td>
</tr>
<tr>
<td>g/100 Kcal</td>
<td>1.6/1.8</td>
<td>1.4/1.6</td>
<td>1.1/1.5</td>
<td>1/1.4</td>
<td>1/1.3</td>
<td>1/1.4</td>
<td>1/1.2</td>
<td>0.9/1.3</td>
<td>-/1.3</td>
<td>-/1.2</td>
</tr>
<tr>
<td>PA requirement (HM/FA)</td>
<td>mg/day</td>
<td>180/300</td>
<td>180/310</td>
<td>224/320</td>
<td>228/320</td>
<td>239/320</td>
<td>277/340</td>
<td>277/340</td>
<td>275/420</td>
<td>-/540</td>
</tr>
<tr>
<td>mg/100 Kcal</td>
<td>42/70</td>
<td>70/38</td>
<td>43/60</td>
<td>41/57</td>
<td>40/53</td>
<td>39/53</td>
<td>38/46</td>
<td>33/51</td>
<td>-/54</td>
<td>-/48</td>
</tr>
<tr>
<td>Leu requirement (HM/FA)</td>
<td>mg/day</td>
<td>620/540</td>
<td>570/550</td>
<td>550/570</td>
<td>560/547</td>
<td>590/570</td>
<td>610/600</td>
<td>675/745</td>
<td>675/745</td>
<td>-/950</td>
</tr>
<tr>
<td>mg/100 Kcal</td>
<td>144/125</td>
<td>119/114</td>
<td>106/109</td>
<td>100/98</td>
<td>98/97</td>
<td>95/94</td>
<td>82/91</td>
<td>82/91</td>
<td>-/95</td>
<td>-/83</td>
</tr>
</tbody>
</table>

Leu, leucine; PA, phenylalanine; HM, human milk model; FA, factorial analysis.
The estimated minimum daily requirement for individual amino acids is obtained by multiplying the total daily protein consumption by a composite estimate of the lowest amino acid content of human milk reported by the Food and Agriculture Organization (FAO) (7). The study by Janas and Picciano (3) evaluated human milk consumption for the first 2 months of life in parallel with measurement of its amino acid content at 2, 4, and 8 weeks of age. This study gives an accurate estimate of the daily intakes of amino acids. The data obtained from these studies show that the daily intakes of phenylalanine could be as low as 180 mg/d in the first 2 months of life, increasing to 225 and 275 mg/d over the following 10 months. Intakes of leucine average 600 to 675 mg/d during the first and after the fourth months of life. Intakes are lower (550–570 mg/d) between the ages of 1 and 4 months. Expressed in terms of energy intake, the phenylalanine intake averages 40 mg/100 kcal and the leucine intake averages 100 mg/100 kcal, except for the first 2 months of life, during which it is estimated to be 145 and 120 mg/kcal, respectively.

Factorial Analysis

Estimation of the protein requirements by the factorial method is highly controversial. This method implies that maintenance needs are known precisely and that there is agreement on the way to assess the needs for growth. However, based upon Fomon’s calculations for infants aged 0 to 12 months and by applying the method for 24- and 36-month-old children, protein requirements amount to 1.98 g/kg/d for the first month, and decrease to 1.14 g/kg/d from the second to the 12th month, with a further decrease to 1.1 g/kg/d during the second and third years of life (5). An estimate of minimum amino acid requirements can be derived from this factorial approach using the amino acid content in the whole body protein (8) and assuming that there is no difference between the amino acid profiles for maintenance and growth.

The results expressed as gram per 100 kcal for protein and milligram per 100 kcal for phenylalanine and leucine are summarized in Table 1. Except for the first 3 months of life, phenylalanine and leucine requirements are constant and average 50 and 90 mg/100 kcal, respectively. These results are in good agreement with the data previously obtained by the human milk method. During the first 3 months, the estimated leucine requirement is higher, averaging 100 to 125 mg/100 kcal. In comparison with the human milk model, the factorial analysis could underestimate the leucine requirement.

INBORN ERRORS OF METABOLISM AS A MODEL

Owing to the defective phenylalanine and branched chain amino acid catabolism, the treatment of patients with PKU and MSUD relies on diets restricted in phenylalanine and leucine, respectively. To prevent acute or chronic neurologic deterioration, the aim of the diet is to keep blood phenylalanine and leucine levels below 5 mg/dl. The desired amounts of phenylalanine and leucine are given, using quantified amounts of
milk in infancy and, progressively, quantified amounts of milk, cereals, vegetable, and fruits in childhood. In parallel, to allow normal growth and development, the diet is supplemented with specific mixtures that contain all the amino acids except for the harmful phenylalanine in PKU and the branched chain amino acids in MSUD. The proportions of the amino acids given in these mixtures are close to those in human milk, except that the PKU mixtures are enriched with tyrosine. In addition, the mixtures contain all the minerals, vitamins, and trace elements in concentrations proportional to the protein content. The prescription of daily amounts is calculated to cover the recommended protein requirements for age (1.5–2.0 g/kg/d), while appropriate daily energy is supplied by additional carbohydrate and lipid. In summary, these patients receive a normal diet for age except that they have a minimal intake of phenylalanine or leucine and thus minimal intakes of natural protein.

The PKU Model

During the first year, the distinction between typical PKU (without residual phenylalanine hydroxylase activity) and atypical PKU (with some residual enzyme activity) is imperfect. The ability to define phenylalanine tolerance (that is, the maximum quantity of phenylalanine that a child can ingest during a period of normal growth without an increase in blood phenylalanine level beyond what is considered ideal) is most often attained between the second and third years of treatment. During this period, some children (four of the 34 in our cohort) have phenylalanine intakes close to, or even greater than, the lowest estimated requirement. These patients obviously have atypical PKU, and their protein and phenylalanine intakes are not informative for estimating the minimum requirement. Conversely, patients whose intakes are lower than the estimated requirements have typical PKU (unless no attempt was made to increase their phenylalanine intake above their minimum needs).

From our results, sufficient phenylalanine intakes could be estimated to be around 25 to 35 mg/100 kcal (250 mg/d) on average during the first 3 years of life. This is substantially less than the estimated requirements for normal children, but very close to the lower range of phenylalanine intakes of breastfed infants in the age range of 3 to 12 months (Table 2). These results are not in conflict with those obtained by others (7,9–12). In particular, our lower intakes are in good agreement with the American collaborative study (9), which showed that phenylalanine needs vary between 55 ± 16 mg/kg/d (46 ± 13 mg/100 kcal) during the first trimester and 27 ± 8 mg/kg/d during the fourth trimester in a group of children for whom the objective of treatment was to maintain blood phenylalanine levels between 1.0 and 5.4 mg/dl. Similarly, by computing the amount of natural protein intakes in our patients affected by typical PKU, the average intakes decrease progressively from 0.76 to 0.54 g/100 kcal, which means a progressive increase in the daily intake from 5 ± 1 to 7 ± 1 g/d. These amounts are about 45% to 50% of the recommended requirement and the minimum requirement, deduced from the factorial analysis and from the human milk model.
TABLE 2. Natural protein, phenylalanine and leucine intakes in patients affected with phenylketonuria and maple syrup urine disease

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>24</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKU patients (n = 34)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean body weight (kg)</td>
<td>5.920 ± 0.70</td>
<td>7.470 ± 0.85</td>
<td>8.680 ± 0.95</td>
<td>9.980 ± 0.95</td>
<td>12.430 ± 1.35</td>
<td>14.330 ± 1.50</td>
</tr>
<tr>
<td>Energy intakes (Kcal)</td>
<td>655 ± 70</td>
<td>785 ± 85</td>
<td>890 ± 105</td>
<td>965 ± 100</td>
<td>1120 ± 105</td>
<td>1300 ± 155</td>
</tr>
<tr>
<td>Natural protein intakes g/day</td>
<td>4.7 ± 0.8</td>
<td>5.6 ± 1.1</td>
<td>6.3 ± 1.3</td>
<td>6.5 ± 1.3</td>
<td>6.9 ± 1.1</td>
<td>7 ± 1.2</td>
</tr>
<tr>
<td>g/100 Kcal</td>
<td>0.72</td>
<td>0.71</td>
<td>0.71</td>
<td>0.67</td>
<td>0.62</td>
<td>0.54</td>
</tr>
<tr>
<td>PA intakes mg/day</td>
<td>235 ± 40</td>
<td>245 ± 47</td>
<td>246 ± 45</td>
<td>250 ± 51</td>
<td>264 ± 43</td>
<td>266 ± 44</td>
</tr>
<tr>
<td>mg/100 Kcal</td>
<td>36</td>
<td>31</td>
<td>27</td>
<td>26</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>MSUD patients (n = 12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean body weight (kg)</td>
<td>5.2 ± 0.5</td>
<td>7 ± 0.5</td>
<td>7.960 ± 0.85</td>
<td>8.710 ± 1.01</td>
<td>11.100 ± 1.50</td>
<td>13.820 ± 1.85</td>
</tr>
<tr>
<td>Energy intakes (Kcal)</td>
<td>600 ± 90</td>
<td>800 ± 85</td>
<td>870 ± 66</td>
<td>970 ± 66</td>
<td>1200 ± 117</td>
<td>1350 ± 81</td>
</tr>
<tr>
<td>Natural protein intakes g/day</td>
<td>3.7 ± 0.88</td>
<td>4.3 ± 1</td>
<td>5.3 ± 1</td>
<td>5.9 ± 1.4</td>
<td>6.5 ± 1.4</td>
<td>7.6 ± 1.5</td>
</tr>
<tr>
<td>g/100 Kcal</td>
<td>0.62</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>0.55</td>
<td>0.55</td>
</tr>
<tr>
<td>Leu intakes mg/day</td>
<td>340 ± 80</td>
<td>340 ± 80</td>
<td>370 ± 85</td>
<td>370 ± 85</td>
<td>400 ± 90</td>
<td>470 ± 95</td>
</tr>
<tr>
<td>mg/100 Kcal</td>
<td>57</td>
<td>42</td>
<td>42</td>
<td>38</td>
<td>33</td>
<td>35</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Leu, leucine; MSUD, maple syrup urine disease; PA, phenylalanine; PKU, phenylketonuria.

The MSUD Model

The dietary tolerance of leucine in 12 children affected with the neonatal onset form of MSUD decreased from 57 to 35 mg/100 kcal during the first 3 years of treatment (340–470 mg/d) (Table 2). Whatever form of expression is used, these results are in the lower range of the intakes reported in previous studies (7,10,12). In previous studies, the aim of treatment was to maintain blood leucine levels between 5 and 10 mg/dl, whereas in the present study, blood leucine levels were maintained below 5 mg/dl. Similarly, by computing the amount of the natural protein intake in our patients with MSUD, intakes averaged 0.6 g/100 kcal, with daily intakes from 4.0 ± 0.9 to 7.5 ± 1.5 g/d. These amounts are somewhat lower than those recorded for children with PKU during the first year of life. The reason for this could be the risk of acute metabolic imbalance that makes clinicians more cautious about prescribing leucine in MSUD than they are with the treatment of PKU. As with the PKU model, the protein intakes in patients with MSUD are between 35% and 50% of both the recommended requirements and the minimum requirement, calculated by factorial analysis and from the human milk model.

COMMENT

The results of factorial analysis and the PKU or MSUD models are in good agreement over the daily amounts of protein and essential amino acids needed to meet the requirements for growth and non-urinary nitrogen losses (Fig. 1). In absence of catabolism of phenylalanine and leucine, patients with PKU and MSUD require 4.0 to 7.5 g/d (0.55–0.75 g/100 kcal) of protein to achieve normal growth and development. These intakes are between 35% and 50% lower than the minimum estimated requirement. This difference could represent the fraction of obligatory catabolism present in healthy infants fed on a normal diet (7). Whether these results can be applied
MINIMUM PROTEIN REQUIREMENTS IN CHILDHOOD

Protein g/100 Kcal

Estimated requirements

Protein requirements: factorial analysis

Protein intakes by BF infants

Protein intakes by PKU

Protein intakes by MSUD

FIG. 1. Natural protein intakes in 34 patients with PKU and 12 patients with MSUD compared with: (A) protein intakes in exclusively breastfed infants; (B) protein requirements estimated by factorial analysis; and (C) joint committee estimates. Exclusively breastfed infants drastically decrease their protein intakes from 1.8 to 0.8 g/100 kcal/d. Results of factorial analysis are in good agreement with the breastfed model during the first 2 or 3 months of life. Thereafter, the estimated requirements are 18% to 24% greater. These results have led Fomon et al to revise their recommended dietary intakes (5). If we consider the theoretical minimum protein requirements (needs for growth plus nonurinary nitrogen losses) represented by the lower part of the vertical bars, these are about 0.75 to 0.57 g/100 kcal from the third month of age up to the third year. Our PKU and MSUD patients have similar natural protein intakes.

to normal infants is unknown. Patients with PKU and MSUD have diets that provide large amounts of nitrogen and nonessential and essential amino acids, except for those that are controlled. Under such conditions, we do not know whether normal infants are able to cease their "obligatory" catabolism. However, this estimate of the fraction of obligatory catabolism suggests that a sufficient protein intake is around 1 g/100 kcal in normal children. This is well below the recommended dietary protein allowances. It is not unlikely that this estimate may also apply to normal adolescents and adults.

REFERENCES

DISCUSSION

**Dr. Pencharz:** I was a little confused by your presentation. At first you talked about intakes of protein in the younger age group of I think around 2 g/kg, and then it went down to about 0.5 g/kg, but in one of your slides towards the end you were talking about intakes of between 0.4 and 0.6 g/100 kcal. I'm not quite sure I understand the idea you were trying to put across.

**Dr. Ogier de Baulny:** I switched from g/kg/day to g/100 kcal/day because it's obviously not very satisfactory to go on expressing intake as g/kg/day with increasing age. In a 6 year old child, for example, you wouldn’t express intake as g/kg/day. Also, when you transform the requirement to g/100 kcal/day, the protein requirement becomes quite constant.

**Dr. Pencharz:** What you are talking about is protein intake as percentage of energy intake, which you say is constant through the life cycle of the child, but it isn’t—at least not in the FAO studies or in the North American process, and we’ve looked at this very closely in normal children. There is not a fixed relation between protein intake and energy intake, so I wouldn’t agree with your point of view.

**Dr. Ogier de Baulny:** I think that when you are treating patients on a protein restricted diet, it is easier to find the correct level of protein intake when it is expressed in terms of energy intake.

**Dr. Pencharz:** Well, this is something we need to talk about later in more detail. Is it your practice to give as low an amount of protein as you can and then you look at growth as your outcome variable, or have you been looking at nitrogen balance? What outcome variables have you been using?

**Dr. Ogier de Baulny:** We don’t carry out balance studies. We use growth parameters and nutritional labels like albumin, prealbumin, and plasma amino acids. The patients we have studied with PKU and MSUD have all had normal growth and nutritional status throughout their lives. This is in contrast to patients with methylmalonic aciduria and propionic aciduria who have decreased linear growth velocity in spite of having the same protein and energy intake. I don’t know the reason for this unless it is related to the harmful effects of propionic acid or other organic acids.

**Dr. Superti-Furga:** Although our patient numbers are smaller, we have the same experience as Dr. Ogier. I would like to respond to what Dr. Pencharz just said. It’s not that we try to give as small an amount of protein as possible; in fact we try to give as much protein as possible,
but we have to draw the line when patients decompensate or in the case of PKU show high phenylalanine levels. In general, though, our experience is exactly the same, and if you look at recent trends it is clear that protein requirements and RDAs have been constantly corrected downwards. I think the "truth" may still be a bit lower.

**Dr. Böhles:** Wouldn't we learn more if we could relate the protein intake to the desirable growth rate—"desirable" meaning the optimal growth rate that can be achieved? I think it is rather too static a concept to relate protein intake only to body weight or to energy intake later on. I think we need to change our focus to what is desirable and what can be achieved. Would the recommended protein intakes be altered if we related them to growth rate rather than to attained weight or energy intake?

**Dr. Ogier de Baulny:** I don't know. I haven't looked at it in that way. But our patients with PKU and MSUD grew strictly normally until the age of 10 or more. We don't have complete data for adolescence, however. During that period growth velocity is similar to that between 9 months and 12 months of age, so it is very likely that an increased protein intake will be required.

**Dr. Bachmann:** Your approach stresses that with a total enzyme block in PKU and MSUD, you won't have any obligate oxidation. This is true, but you probably still need protein or nitrogen just for gluconeogenesis. Did you do similar calculations for patients with urea cycle disorders put on protein restriction plus essential amino acids?

**Dr. Ogier de Baulny:** Yes, we have some patients with urea cycle defects. However, most of these are late onset forms so they have some residual activity. Secondly, there is a great deal of subclassification among these disorders, so few of them are exactly the same. This means that for a particular condition we rarely have more than a few patients. Also, we treat our patients with urea cycle disorders with a protein-restricted diet and with sodium phenylbutyrate and benzoate supplementation but we don't give essential amino acids as a supplement. On this regimen we get a protein intake of around 1-1.3 g/100 kcal/day at 3 years of age. They receive about 150 mg/kg/day of phenylbutyrate.

**Dr. Bachmann:** What the organism needs is a sum of optimally balanced essential amino acids plus some non-essential nitrogen. In this discussion I think there has been some confusion about this issue. The main thing that is relevant for optimal metabolism of protein is its quality, and a lack of imbalance is what is important for achieving the lowest protein intake compatible with normal growth. Dr. Ogier's message mainly concerns two amino acids where we get a feel for the minimum quantities necessary, compared with the non-specific data available on most nutrient mixtures where we only have a sum of all the amino acids or the total protein content. I think in this discussion we should clearly distinguish between specific amino acids and total amino acids or total protein composition. Would you agree?

**Dr. Ogier de Baulny:** Yes, I do.

**Dr. Fowler:** Isn't the quality of protein equal in all these comparison studies?

**Dr. Ogier de Baulny:** No, it's not. Early on the patients receive high quality protein through human milk or infant formula, but then they are progressively switched to less efficient protein by 4 to 6 months of age. Even so they still grow well and their total protein intake remains much the same.

**Dr. Fowler:** We talk about minimum requirements, but what about optimal requirements? What is optimal and does it matter if we have too much protein or above the minimum? What do nutritionists say about this? Can anyone answer that?

**Dr. Bier:** I'll try to answer the question if you can define optimum for me!

**Dr. Fowler:** Okay, what is maximal then? Too high is bad, is it not?

**Dr. Ogier de Baulny:** When you give too much protein to young infants, you get hyperaminoacidaemia and a high blood urea. This is not good for the kidney or the liver.
Dr. Fowler: We’re all aware, of course, that in the old days we used to see many cases of methioninemia and tyrosinemia caused by high protein intakes. I’m sure there is a maximum level that should be aimed for, and this might be close to the minimum level—which would be the optimal level too.

Dr. Endres: There are many studies showing that infants and toddlers receive too much protein. I will cite three. First, 10 years ago a study from Milan (1) showed that the protein intake was more than three times higher than that recommended by European and American nutrition societies. Second, 4 years ago a study from Denmark (2) showed that the intake was about two times higher than recommended. Third, a study from Germany carried out 3 years ago then found much the same (3). Thus I think the message Dr. Ogier gave us—that is, of values of about 0.6–0.8 g protein/100 kcal compared with the current range of 1.8–3 g/100 kcal for starter formulas and up to 4.5 g/100 kcal for follow on formula—shows there is a great discrepancy between what may be needed and what is actually given. To answer the question about possible harm caused by this high protein intake, it is evident that plasma urea nitrogen is much higher in infants receiving a formula containing 2.25 g of protein/100 kcal or more compared with breast-fed infants. I think this renal burden should be considered.

To return to Dr. Böhles’s comment, it is difficult to determine standards for protein intake after the breast-feeding age, though up to, say, 6 months, it is possible to use breast milk protein content as the standard. However, I think it is very helpful to look at plasma amino acids and urea nitrogen. My aim is to decrease the protein content in formulas—and we just launched one containing only 1.8 g protein/100 kcal—because we are convinced that in most formulas the protein content is too high. The practical point of Dr. Ogier’s presentation is that she showed that the requirement for protein is much lower than even that recommended by national nutritional bodies.

Dr. Pencharz: I can help answer the question about minimum and maximum protein because. This is something we’ve looked at in terms of dietary recommendations. The lower end is the RDA, and then there is also an upper limit. We regard the bottom end of the range as a safe intake. The reason I was having problems with the protein intake per 100 kcal is that it goes up through childhood. Thus even if you take the absolute obligatory minimum intake in healthy populations, which is around 0.7 g/100kcal by the time the child is 6 or 8, it goes up to 1.4 g/100 kcal. In North America at the moment we are saying there is a minimum for an individual, which is the average or the EAR, and then there is the minimum for a population, which is the RDA. We think in children the maximum is lower than it is in adults. For adults, we’re talking about 30% of energy intake; for children, we’re talking about 15% to 20% of energy intake.

Dr. Böhles: I would like to bring another point into the discussion that’s always forgotten when talking about protein requirements, and that is that there are no protein stores in the body. This means you only have the protein you need. If a child is sick in bed and doesn’t move about much, naturally that child has a smaller protein requirement than when normally active. If the entire population always ran instead of walking calmly, it would have a totally different protein requirement. This point is never emphasized in discussions on the subject. We should always define what activities are being done, which is especially important in childhood—children never walk about calmly! We should take these factors into consideration when discussing protein requirements.

Dr. Ogier de Baulny: Of course, I agree about that, but that is always going to be a problem with standards.

Dr. Borum: We need also to remember the old concept of “conditionally essential” nutrients, which was based on the idea that something occurring during development, or in old age,
or when there is altered organ function, such as renal disease, that may alter the nutrient requirements. We've spoken about using dietary components to respond to altered nucleotide sequences in DNA, but perhaps we should also think about how dietary components, or ratios of dietary components, might actually affect transcription and translation, and might thereby influence or control gene expression directly. Such influences may be acting in addition to what you describe as part of the inborn error of metabolism.

Dr. Ogier de Baulny: I agree, and probably this is one of the reasons why human milk has optimal nutrient quality, because besides amino acids there are many other proteins and non-protein nitrogen containing components that may have a role in growth. These are absent from infant formulas.

REFERENCES