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REVIEW

Protein and energy requirements for 'optimal' catch-up growth

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Protein and energy requirements in childhood can be considered as being made up of components such as maintenance and growth (Panel on Macronutrients, 2002/2005; Report of a Joint FAO/WHO/UNU Expert Consultation, 2004; Report of a Joint WHO/FAO/UNU Expert Consultation, 2007). This approach can readily be applied to the question of catch-up growth (Report of a Joint WHO/FAO/UNU Expert Consultation, 2007). Enteral nutrition requirements depend on the efficiency of digestion and absorption of protein (amino acids) and non-protein energy (carbohydrate and fats; Panel on Macronutrients, 2002/2005).

The initial approach of catch-up growth depends on the degree and type of undernutrition, namely adapted (normal plasma albumin or marasmus) or disadapted (reduced plasma albumin or Kwashiorkor). In adapted undernutrition the gut mucosal function is relatively normal, so the child's intake can be progressively increased to high levels (>200 kcal/kg/day). In children with disadapted undernutrition, there are two aspects to consider. First, the gut mucosa is atrophied and gut function limited. Second, with hypoalbuminaemia there is intra-vascular volume contraction and whole-body depletion of K and P, which contribute to the so-called 're-feeding syndrome'. Hence, to avoid the re-feeding syndrome, initially children need to be fed at levels that are only 10–20% above the resting metabolic rate. Experience has shown that, once diuresis occurs, the gut mucosa and intestinal function recovers enough to progressively increase intakes up to the high levels used for adapted undernourished children.

Another consideration is that of wasting versus stunting. Typically the marasmic child is wasted, but may also be stunted. Kwashiorkor is generally more acute, so wasting and stunting may be minimal, and once diuresis occurs needs for catch-up are less than those of a child with marasmus.

The targets in catch-up growth depend on the depletions that exist in body composition (in terms of lean and fat mass) and the rate at which repletion is possible (Report of a Joint WHO/FAO/UNU Expert Consultation, 2007). A practical way of estimating the requirements of catch-up growth is to decide on the composition of the new tissue to be laid down during re-feeding. Using Atwater figures, 1 g of fat would require 9 kcal/g and 1 g protein 4 kcal/g; if it is assumed that lean tissue contained 25% protein, then lean tissue would require 1 kcal/g. Therefore, if the catch-up growth desired involved 40% fat and 60% lean mass, then the energy cost of the catch-up would be $(0.4 \times 9) + (0.6 \times 1) = 4.2$ kcal/g of catch-up growth. If the desired rate of catch-up growth is 20 g/kg/day, this would mean an additional $4.2 \times 20 = 84$ kcal/kg/day above normal daily energy requirements.

A similar approach can be taken to determine the protein that is needed to replete the depleted lean body mass (LBM). Once a rate of growth with a desired rate of protein deposition is decided upon, these figures can be used to decide on the amount of protein required. A deficit in body protein can be estimated based on the calculated deficit in LBM, as LBM contains 20–25% protein. For repletion of this deficit, one should consider the % efficiency of protein utilization in the body. The metabolic efficiency of dietary protein is around 70%; therefore, to deposit 1 g new lean tissue (which equals 0.25 g protein), $0.25/0.7 = 0.36$ g protein should be ingested. In a child in whom the target weight gain is 10 g/kg/day (with 60% lean and 40% fat tissue), $10 \times 0.6 = 6$ g lean tissue should be accreted per kg per day. This would require an additional protein intake of $6 \times 0.36 = 2.2$ g protein per kg per day, or a total protein intake of $1.5 + 2.2 = 3.7$ g/kg/day.

Recalling the factorial approach, it is important to mention advances in our understanding of maintenance

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requirements for energy, protein and amino acids. With regard to energy, the new findings relate to direct measurements of total daily energy expenditure using doubly labelled water ($^2H_2{}^{18}O$). To define total daily energy requirements, the requirements for growth still have to be added (Panel on Macronutrients, 2002/2005; Report of a Joint FAO/WHO/UNU Expert Consultation, 2004; Report of a Joint WHO/FAO/UNU Expert Consultation, 2007).

Regarding protein requirements, recent isotope studies and reappraisal of nitrogen balance literature using nonlinear regression have suggested that the WHO 2007 (Report of a Joint WHO/FAO/UNU Expert Consultation, 2007) estimates of adult protein requirements are too low, by a factor of around 30% (Humayun *et al*., 2007). Hence it is likely that maintenance estimates in children are also low. Our recent work points towards a protein intake of 1.5 g/kg/day being a safe level (mean plus 2 s.d.) in healthy children.

However, this level may prove inadequate for some children with LBM depletion or metabolic stress. When determining the protein requirements of these children, one should account for the loss in LBM. Overall, an intake of 2.0 g/kg/day should meet the requirements of most cases of catch-up growth, with the exception of those children with more LBM depletion or in metabolically stressed conditions, for example, cystic fibrosis (a protein intake of 5 g/kg/day was found to improve protein synthesis in cystic fibrosis children; Geukers *et al*., 2005).

It may be advisable to aim for the upper limit of daily protein intake given that the overall protein deficit will take time to replete, in part due to less-efficient digestion and absorption initially in a malnourished infant or child.

One can also consider low birth weight infants as a model for catch-up growth. High-protein, nutrient-dense formulas for these infants have been shown to increase their linear growth as well as LBM.

Low birth weight formulas have considerably higher protein energy percent (PE%; 12%) than standard feeds (8%) or human milk (6%). These principles have been applied to the re-feeding of malnourished infants, and faster linear growth has been observed with a PE% of 11 versus 8 (Report of a Joint WHO/FAO/UNU Expert Consultation, 2007).

An issue that has not been extensively examined is the upper limit of protein intake. In low birth weight infants, high protein intakes (from 6 g/kg/day; albeit from casein-dominant formulas) were associated with a condition known as late metabolic acidosis (Goldman *et al*., 1969). In addition, the infants had elevated plasma Meth, Phe and Tyr levels. At follow-up, these infants showed worse development than those fed lower-protein foods (Goldman *et al*., 1971). Hence, the issue is not just the amount of protein but also the mix (casein to whey protein ratio) and the amino-acid balance.

This raises the question of whether disease alters amino-acid requirements. Clearly, this is so with inborn errors of amino-acid metabolism (Bross *et al*., 2000; Courtney-Martin *et al*., 2002; Riazi *et al*., 2004). Furthermore, liver disease increases the requirements for branched-chain amino acids (Mager *et al*., 2006). Recent work in children has shown that their maintenance amino-acid requirements are identical to those of adults (Elango *et al*., 2007, 2008a, b), and hence their dietary indispensable amino-acid requirements are maintenance and growth (Panel on Macronutrients, 2002/2005; Report of a Joint WHO/FAO/UNU Expert Consultation, 2007). This is an evolving field of active research and we have shown in our piglet model that the gut has a major effect on amino-acid metabolism (Brunton *et al*., 2000). We have since applied our novel technique of indicator amino-acid oxidation to directly determine the total sulphur amino-acid requirements of total parenteral nutrition-fed human neonates (Courtney-Martin *et al*., 2008). This approach can be applied to study amino-acid requirements in a wide variety of different diseases (Elango *et al*., 2008a, b).

It is well documented that diseases have an effect on energy expenditure, which is sometimes known as 'The Pathogenesis of Energy Balance in Disease' (Wilson and Pencharz, 1997), but less is known on protein. We have shown that surgery increases protein requirements by around 20%, although this is short lived (Duffy and Pencharz, 1986), while re-nourishing cystic fibrosis patients may require increased protein intakes (Geukers *et al*., 2005) and was found to increase the energy expenditure by around 25% (Vaisman *et al*., 1991).

Practical considerations

The 2007 WHO Protein and Amino acid report (Report of a Joint WHO/FAO/UNU Expert Consultation, 2007) shows a detailed calculation of protein and energy ratios for different rates of catch-up growth, with PE% ranging from 4.6 to 11.5% depending on the rate and composition of weight gain. North American tube feeds for children have a PE% of around 12%. On balance, provided that blood urea nitrogen and acid base are measured, most children requiring nutritional support can be managed safely with a PE% of around 12%.

Conflict of interest

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References

Bross R, Ball RO, Clarke JTR, Pencharz PB (2000). Tyrosine requirements in children with classical PKU determined by indicator amino acid oxidation. *Am J Physiol* **278**, E195–E201.

Brunton JA, Ball RO, Pencharz PB (2000). Current total parenteral nutrition solutions for the neonate are inadequate. *Curr Opin Nutr Metab Care* **3**, 299–304.

Courtney-Martin G, Bross R, Rafii M, Clarke JT, Ball RO, Pencharz PB (2002). Phenylalanine requirement in children with classical

phenylketonuria determined by indicator amino acid oxidation. *Am J Physiol* **283**, E1249–E1256.
Courtney-Martin G, Chapman KP, Moore AM, Kim JH, Ball RO, Pencharz PB (2008). Total sulphur amino acid requirement and metabolism in the parenterally fed postsurgical human neonates. *Am J Clin Nutr* **88**, 115–124.
Duffy B, Pencharz P (1986). The effect of surgery on the nitrogen metabolism of parenterally fed human neonates. *Pediatr Res* **20**, 32–35.
Elango R, Ball RO, Pencharz PB (2008a). Indicator amino acid oxidation: concept and application. *J Nutr* **138**, 243–246.
Elango R, Ball RO, Pencharz PB (2008b). Individual amino acid requirements in humans: an update. *Curr Opin Nutr Metab Care* **11**, 34–39.
Elango R, Humayun MA, Ball RO, Pencharz PB (2007). Lysine requirement of healthy school-age children determined by indicator amino acid oxidation method. *Am J Clin Nutr* **86**, 360–365.
Geukers VGM, Oudshoorn JH, Taminiau JAJM, van der Ent CK, Schilte P, Ruiter AF *et al*. (2005). Short-term protein intake and stimulation of protein synthesis in stunted children with cystic fibrosis. *Am J Clin Nutr* **81**, 605–610.
Goldman HI, Freudenthal R, Hollan B, Karelitz S (1969). Clinical effects of two different levels of protein intake on low-birth-weight infants. *J Pediatr* **74**, 881–889.
Goldman HI, Liebman OB, Freudenthal R, Reuben R (1971). Effects of early dietary protein intake on low-birth-weight infants. Evaluation at 3 years of age. *J Pediatr* **78**, 126–129.
Humayun MA, Elango R, Ball RO, Pencharz PB (2007). A re-evaluation of protein requirement in young men using the indicator amino acid oxidation technique. *Am J Clin Nutr* **86**, 995–1002.
Mager DR, Wykes LJ, Roberts EA, Ball RO, Pencharz PB (2006). Branched chain amino acid requirements in children with mild-moderate chronic cholestatic liver disease. *J Nutr* **136**, 133–139.
Panel on Macronutrients (2002/2005). *Dietary Reference Intakes for Energy, Carbohydrate. Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids*. Institute of Medicine, National Academy of Sciences: Washington, DC.
Report of a Joint FAO/WHO/UNU Expert Consultation (2004). *Human Energy Requirements. Food and Nutrition Technical Report Series 1*. Food and Agriculture Organization (FAO): Rome.
Report of a Joint WHO/FAO/UNU Expert Consultation (2007). *Protein and Amino Acid Requirements in Human Nutrition. WHO Technical Report Series No. 935*. World Health Organization: Geneva.
Riazi R, Clarke J, Ball RO, Pencharz PB (2004). Total branched chain amino acid requirement in patients with maple syrup urine disease by use of indicator amino acid oxidation using L-[13C]phenylalanine. *Am J Physiol* **287**, E142–E149.
Vaisman N, Clarke R, Pencharz PB (1991). Nutritional rehabilitation increases resting energy expenditure without affecting protein turnover in patients with cystic fibrosis. *J Pediatr Gastroenterol Nutr* **13**, 383–390.
Wilson DC, Pencharz PB (1997). Nutritional care of the chronically ill. In: Tsang R (Editor-in-Chief). *Nutrition During Infancy: Birth to 2 Years*, vol. 3. Digital Educational Publishing Inc.: Cincinnati, OH. pp 37–56.