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EDITORIAL Adjustable fortification of human milk fed to preterm infants

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In adults, as protein intake increases, so does blood urea nitrogen (BUN), unless significant protein accretion is occurring and/or hepatic function; that is urea synthetic capacity, is compromised.

and SGA infant, (b) sex; that is, boys accrete more lean mass and grow faster than girls,¹⁵ (c) level of maturity; that is, protein:energy needs change with advancing gestation¹⁶ and (d) previous nutritional intake; that is, requirements for 'recovery' will vary.³ One formulation, therefore, is unlikely to meet the protein needs of all infants.



Figure 1 Relationship between BUN and nitrogen intake and nitrogen absorption.

When protein intake is low BUN is also low, unless renal or fluid status is compromised.¹ In children, BUN changes rapidly with protein intake, assuming adequate hydration.² Indeed, protein content of the diet can be directly related to the BUN; for example, if 8% of energy is protein then the BUN will be $\sim 8 \text{ mg/dl}$ in the otherwise normal infant.²

The situation has been less clear-cut in preterm infants. It takes time to establish adequate energy intakes during early life in sick immature infant,³ protein is catabolized and BUN increases, irrespective of protein intake or renal function. At the same time, urea synthetic capacity^{4,5} and/or renal excretory^{6–8} may be limited in the immature infant. Thus, early studies suggested BUN is not a valid measure of protein intake in preterm infants.^{4,9–11}

More recent studies, one by this group,¹² suggest otherwise in the clinically stable preterm infant.¹³ In the latter study, the relationship between nitrogen accretion and growth fed two levels of protein intake, 3.0 and 3.6 g/100 kcal, was assessed. Nitrogen intake varied widely but intake and absorption were linearly related to changes in BUN (see Figure 1).¹³ These data coupled with the findings in this study support the idea that, as in older children and adults, BUN is a valid measure protein intake in preterm infants.

The findings of this study, therefore, have important implications for feeding preterm infants. Protein requirements are not well established in preterm infants.¹⁴ Requirements will also vary depending upon (a) nutritional status at birth; that is, AGA

An additional consideration in this study is the wide variation in protein content of human milk^{17–20} that is rarely measured for individual mother—infant pairs. Irrespective of whether an infant is fed human milk or a preterm formula the idea that intake is 'tailored' to meet individual needs and is monitored to ensure efficacy, better growth and safety is a critical concept. The Arslanoglu *et al* paper in the current issue demonstrates that BUN determinations are an excellent index for adequacy of protein intake. This is a commonly overlooked, but important, message for day-to-day nutritional care in the neonatal intensive care setting.

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References

- Heimberger DC. Adulthood. In: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ (eds). *Modern Nutrition in Health and Disease*. Lippincott Williams & Wilkins, 2006, pp 830–842.
- 2 Fomon S. Protein. In: Fomon SJ (ed). Nutrition of Normal Infants. Mosby: St Louis, 1993, pp 121–139.

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- 3 Embleton NE, Pang N, Cooke RJ. Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? *Pediatrics* 2001; **107**: 270–273.
- 4 Boehm G, Muller DM, Beyreiss K, Raiha NC. Evidence for functional immaturity of the ornithine-urea cycle in very- low-birth-weight infants. *Biol Neonate* 1988; 54: 121–125.
- 5 Morris Jr SM. Regulation of enzymes of urea and arginine synthesis. *Ann Rev Nutr* 1992; **12**: 81–101.
- 6 Solhag MJ, Jose PA. Postnatal maturation of renal blood flow. In: Polin RA, Fox WW, Abman SH (eds). *Fetal and Neontal Physiology*. Saunders: Philadelphia, 2004, pp 1242–1249.
- 7 Guignard J-P. Postnatal development of glomerular filtration rate in neonates. In: Polin RA, Fox WW, Abman SH (eds). *Fetal and Neontal Physiology*. Saunders: Philadelphia, 2004, pp 1256–1266.
- 8 Feld LG, Corey HE. Renal transport of sodiumduring early development. In: Polin RA, Fox WW, Abman SH (eds). *Fetal and Neontal Physiology*. Saunders: Philadelphia, 2004, pp 1267–1278.
- 9 Boehm G, Teichmann B, Jung K. Development of urea-synthesizing capacity in preterm infants during the first weeks of life. *Biol Neonate* 1991; **59**: 1–4.
- 10 Boehm G, Gedlu E, Muller MD, Beyreiss K, Raiha NC. Postnatal development of urea- and ammonia-excretion in urine of very-low-birth-weight infants small for gestational age. *Acta Paediatrica Hungarica* 1991; **31**: 31–45.
- 11 Boehm G, Teichmann B, Jung K, Moro G. Postnatal development of urea synthesis capacity in preterm infants with intrauterine growth retardation. *Biol Neonate* 1998; 74: 1–6.

- 12 Moro GE, Minoli I, Ostrom M, Jacobs JR, Picone TA, Raiha NC, Ziegler EE. Fortification of human milk: evaluation of a novel fortification scheme and of a new fortifier. *J Pediatr Gastroenterol Nutr* 1995; 20: 162–172.
- 13 Cooke R, Embleton N, Rigo J, Carrie A, Haschke F, Ziegler E. High protein pre-term infant formula: effect on nutrient balance, metabolic status and growth. *Pediatr Res* 2006; **59**: 265–270.
- Klein CJ. Nutrient requirements for preterm infant formulas. J Nutr 2002;
 132: 1395S-1577S.
- 15 Cooke RJ, McCormick K, Griffin IJ, Embleton N, Faulkner K, Wells JC, Rawlings DC. Feeding preterm infants after hospital discharge: effect of diet on body composition. *Pediatr Res* 1999; **46**: 461–464.
- 16 Ziegler EE, Thureen PJ, Carlson SJ. Aggressive nutrition of the very low birthweight infant. *Clin Perinatol* 2002; **29**: 225–244.
- 17 Lemons J, Moye L, Hall D, Simmons M. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 1982; 16: 113–117.
- 18 Gross SJ, Geller J, Tomarelli RM. Composition of breast milk from mothers of preterm infants. *Pediatrics* 1981; 68: 490–493.
- 19 Anderson GH, Atkinson SA, Bryan MH. Energy and macronutrient content of human milk during early lactation from mothers giving birth prematurely and at term. *Am J Clin Nutr* 1981; **34**: 258–265.
- 20 Michaelsen KF, Skafte L, Badsberg JH, Jorgensen M. Variation in macronutrients in human bank milk: influencing factors and implications for human milk banking. *J Pediatr Gastroenterol Nutr* 1990; 11: 229–239.