Nutritional Needs of the Micropreterm Infant

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We have used an expansive definition of a micropreterm infant as <30 weeks' gestation to provide a global perspective to a "high risk" group of preterm infants for which there are little published data to guide nutritional management. Consensus nutritional guidelines for preterm infants have been developed for infants >1000 g birth weight and >28 weeks' gestational age. Micropreterm infants have greater nutritional deficits at birth than more mature preterm infants and accumulate greater postnatal deficits. Nutritional guidelines based on the needs of preterm infants born >28 weeks' gestation are unlikely, on a theoretical basis, to meet nutritional requirements of micropreterm infants. Unfortunately, very few good quality studies have addressed the nutritional requirements of this group specifically; this makes it difficult to formulate solid, evidence-based nutritional recommendations for these neonates. Nutritional management of micropreterm infants is based on recommendations established for preterm infants, which are adjusted after considering an infant's gestational age, birth weight, and clinical status. Minimal enteral feeding should commence on the first or second day of life, with incremental advancement and fortification of human milk when 100 mL/kg is tolerated. Early use of parenteral nutrition is recommended, ideally initiated within the first hours of life and enteral feeds are being established; this will help prevent the accumulation of nutritional deficits and incidence of growth failure. Fortified human milk should be given in order to meet nutritional requirements. When human milk is not available in sufficient quantity, a preterm formula should be given. *(J Pediatr 2013;162:S72-80)*.

Although the more commonly accepted classifications of preterm infants are extremely low birth weight (ELBW) and extremely preterm (<28 weeks' gestation), we defined micropreterm as <30 weeks' gestation. A subset of this population is small for gestational age (GA); these infants weigh <10th percentile at birth at <30 weeks' gestation. This expanded definition was selected to gain a global perspective of a "high risk" group of preterm infants. We were unable to locate substantial information about this population. This discussion addresses the current state of knowledge and clinical practice on the nutritional requirements of the micropreterm infant.

Developmental Physiology and Biology

The composition of weight gained by the fetus changes with GA. The difference in body composition between a micropreterm and a more mature infant impact decisions about nutritional management. For example, body water as a percentage of body weight decreases rapidly during the last trimester. Water comprises about 80% of weight gained between 24 and 28 weeks of gestation but only 60% of weight gained between 36 and 40 weeks. The proportion of weight gained as fat increases markedly from 8% at 24-28 weeks to nearly 20% near term.[1]

The fetal intestine is capable of digesting and absorbing milk feeds by 25 weeks' gestation, but not as well as that of a more mature infant. Gastrointestinal motor activity develops later and may limit tolerance to enteral feeds. Motility is described as being "disorganized" between 25 and 30 weeks of gestation. This can cause nutrients to remain in the intestine, especially if digestion is suboptimal, and may increase the risk of necrotizing enterocolitis (NEC).[2] Antenatal steroids accelerate the maturation of the gut and reduce the incidence of NEC (relative risk: 0.46; 95% CI 0.29-0.74).[3]

Swallowing activity begins to develop during the second trimester, and enteral ingestion of amniotic fluid contributes to fetal nutrition and development of the gastrointestinal tract. Postnatally, ingestion of colostrum and milk plays an important role in stimulating gut maturation. Accompanying the development of the gastrointestinal tract, there is also progressive development of different enzymes throughout fetal life.[4] Gastric pepsin and brush-border enzymes, including sucrase, aminopeptidase, and lactase, develop in parallel and are present in low concentrations in infants born prematurely. Lactase activity remains low throughout fetal life but increases markedly with the first enteral feed, regardless of age. Shulman et al[5] initiated feeds on

BW	Birth weight
DBM	Donor breast milk
ELBW	Extremely low birth weight
GA	Gestational age
NEC	Necrotizing enterocolitis
P:E	Protein:energy
PDF	Post-discharge formula
PTF	Preterm formula

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Table I. Summary of theoretical concerns and available data from micropreterm infants for specific enteral nutrients

Nutrient	Theoretical concerns	Published data for micropreterm infants?	Current recommendations	New recommendations
Fluid	• Increased requirements due to immature skin • Vulnerable to fluid overload with worsening cardiovascular disease, patent ductus arteriosus	• No • Intakes of 150-180 mL/kg/d tolerated in enteral studies	• Range 135-200 mL/kg/d[12,13]	
Energy	• Low energy stores. Intake often inadequate due to concomitant illness restricting supply • Concern regarding NEC	• EE of 60-75 kcal/kg/d by indirect calorimetry and by doubly labeled water in stable ELBW infants[30,31] • Higher levels of EE of 88-96 kcal/kg/d by doubly labeled water method in infants with sepsis[31] and chronic lung disease[32]	• 130-150 kcal/kg/d[12]	• 120-140 kcal/kg/d
Protein	• Increased requirement for growth, especially if deficits accumulate • Greater risk of overload, metabolic acidosis, increased BUN and urea • Some amino acids conditionally essential	• ELBW infants (generally >750 g) included as subjects along with VLBW infants in enteral feeding studies defining protein requirements. • Factorial method[33] • ELBW infants randomized and treated for 7 days with IV amino acids starting at 0.5 g/kg/d and increased by 0.5-3.0 or starting 2 g/kg/d and increased by 1.0-4.0 daily; infants receiving higher amino acids in first week had lower NDI at 18 mo [not 2 y] and lower z-scores for weight, length, and head circumference at 2 y[34]	• Factorial approach[31]: 3.5-4.0 g/kg/d • Tsang et al[12]: 3.8-4.4 g/kg/d (26-30 wk PCA) • ESPGHAN[13]: 4.0-4.5 g/kg/d ELBW 3.8-4.4 g/kg/d VLBW	• 3.6-4.5 g/kg/d • Larger trials than Blanco, et al.[34] necessary to assess best IV amino acid advancement and dosage
P:E		• P:E 3.6 g/100 kcal with protein intake 4.6 g/kg/d tolerated for 1 wk[35] • P:E 3.6 g/100 kcal with protein intake 4.3 g/kg/d for longer periods reported some evidence of protein overload[36]	• Tsang et al[12]: 3.3-3.4 g/100 kcal • ESPGHAN[13]: 3.6-4.1 g/100 kcal	• 3.0-3.6 g/100 kcal
Carbohydrate	• Provides 40%-50% of calories • PTF has 23%-50% glucose polymers and some have Gos and Fos oligosaccharides as prebiotics	• 24-31 weeks GA infants (n=20): Formula supplementation with oligosaccharides reduced stool viscosity and accelerated GI transit[37]	• Tsang et al[12]: 9-20 g/kg/d for enteral feeding of growing ELBW infant	• 10.5-14 g/kg/d
Lipids	• May have increased requirements due to high energy needs and restricted fluid intake • Absorption may be reduced with resultant steatorrhoea • Provides 50% energy in human milk	• No	• Tsang et al[12]: 6.2-8.4 g/kg/d for enteral feeding of growing ELBW infant, or 4.1-6.5 g fat/100 kcal	• 5-7 g/kg/d for enteral feeding of growing micropreterm, or 4.4-6.0 g fat/100 kcal
LCPUFA	• Greater deficit at birth. LCPUFA oxidized if energy supply insufficient	• In a multicenter trial of infants <33 weeks maternal diet high in DHA and infant DHA dose of 1% total fatty acids increased MDI of females <1250 g[38] • For infants <1250 g, supplementation was associated with higher MDI in unadjusted, but not in adjusted, analyses • For males overall, and for all infants with bodyweight <1250 g the risk of BPD was lower in supplemented infants[39]	• DHA: 20-62 mg/kg/d • ARA: 30-36 mg/kg/d • EPA: ≤23 mg/kg/d	• Some evidence to suggest higher intake of DHA (1% of total fatty acids) might have particular benefits to micropreterm infants
Sodium	• High fractional excretion of sodium in first 10-14 d	• No		• 4-5 mmol/kg/d in first 10-14 d and • 2.5-3.0 mmol/kg/d thereafter
Calcium and phosphorus	• Greater mineral deficit at birth (majority of mineral accretion occurs in last trimester). Greater risk of metabolic bone disease. • Calcium absorption rate 50%-65%, phosphate absorption 90%	• No	• Tsang et al[12]: • Calcium 100-220 mg/kg/d • Phosphorus 60-140 mg/kg/d	• Calcium intake of 120-180 mg/kg/d • Phosphorus intake of 60-90 mg/kg/d; (maintain phosphorus levels ≥1.8 mmol/L)

(*continued*)