Interventional Strategies to Promote Appropriate Growth

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Postnatal growth failure among premature infants is strongly associated with poor neurocognitive development and retinopathy of prematurity. Since growth failure is primarily, if not in its entirety, caused by inadequate nutrient intakes, efforts are concentrating on improving nutrient delivery to premature infants. Nutrient administration to premature infants is complex, involving both parenteral and enteral nutrition in variable proportions and fortification of human milk.

The main reason why nutrient intakes are often inadequate is that nutrient administration, rightly or wrongly, is believed to be hazardous. Other reasons include uncertainty about nutrient requirements and, importantly, the lack of appropriate tools such as fortifiers with appropriate nutrient levels. In the past, there was also the perception that growth failure is innocuous and that growth would simply have to be made up. That is no longer the case as the short-term and long-term adverse effects of inadequate nutrition have become widely recognized.

Safety concerns were in the past responsible for the withholding of both parenteral nutrition and enteral feedings. Parenteral nutrition was for the longest time considered dangerous in premature infants and was therefore withheld during the first few days after birth and then was introduced and advanced very cautiously. It has now been established that the initial withholding of parenteral nutrition has serious adverse effects on neurocognitive development. Also, parenteral nutrition started immediately at birth has now been demonstrated to be free of adverse effects. Today, parenteral nutrition is routinely used beginning within hours of birth. Lingering concerns about the safety of parenteral nutrition are probably responsible for the continued use of inadequate doses of amino acids and of intravenous lipids and for the premature termination of parenteral nutrition therapy. But parenteral nutrition is universally used in industrialized countries.

Enteral feedings were also withheld for many years because it was believed that the withholding of feedings decreased the risk of necrotizing
enterocolitis (NEC). After several decades of research, it is now clear that the immature intestinal tract of the premature infant is initially not capable of accepting and digesting food and is susceptible to NEC. But maturation of the immature gut can be induced with small quantities of feedings (gut priming), the very thing that in the past was withheld. After a few days of gut priming, feedings may be advanced using the maturation of gut motility (gastric residuals) for guidance. Human milk is far superior as a gut priming agent compared to other feedings because of its trophic effects on the gut. It is also safer than other feedings because of its immunoprotective components. Prompt initiation of gut priming is not only safe (no risk of NEC) but actually reduces the risk of NEC and of nosocomial infections. It also enhances the ability of the infant to handle enteral feedings and thereby reduces the need for parenteral nutrition.

An important and continuing cause of growth failure is inadequate nutrient fortification of human milk. Protein concentration of expressed human milk is highly variable. Because of the prevalent ‘fear of protein’, existing human milk fortifiers are designed with an overriding aim of avoiding unduly ‘high’ protein intakes. Consequently, since milk protein content is mostly low, protein intakes of infants fed fortified human milk are almost always too low. That is, unless additional protein is provided in one form or another. Of the several methods for increasing protein fortification, only one is supported by published evidence of efficacy and safety [1].

At the University of Iowa, we have been striving for many years to improve nutrient intakes of premature infants. We adopted early parenteral nutrition (within 36 h of birth) in 1999 and immediate parenteral nutrition (within 2 h of birth) in 2002. Around 1998, we adopted early gut priming within the first 2 days of life [2]. And we established the Mother’s Milk Bank of Iowa, which has enabled us to use human milk as a gut priming agent in all infants, including those whose mothers do not express milk. We have for many years used greater than standard amounts of fortifier in order to increase the protein intake of infants. More recently, we have adopted the use of protein supplements to boost the protein provided by commercial fortifiers.

Figure 1 summarizes the growth of infants born in 2010 with birth-weight <1,250 g, broken down into three groups, AGA infants born at <27 weeks gestation, AGA infants born at 27–31 weeks and SGA infants born between 26 and 34 weeks. Shown as reference are the 10th, 50th and 90th percentiles of the fetal growth standards of Fenton [3]. It is evident that in 2010, growth is approaching fetal growth. A certain downward shift of postnatal growth curves is presumed to be inevitable due to the perinatal contraction of body water spaces. While growth of our infants is believed
to be good by current standards, there certainly is room for improvement. In particular, it seems that we should pay more attention to the specially high nutrient needs of SGA infants.

References