Re: ESPGHAN Commentary and Education That Probiotics Substantially Reduce All-cause Mortality and Necrotizing Enterocolitis in Preterm Infants

To the Editor: We congratulate Professor Goudoever and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition on their commentary published in the January 2010 issue (1). However, the committee only had access to articles published by early 2007 when the commentary was drafted.

Their conclusion that present data do not permit recommending the routine use of probiotics in preterm infants did not take into account (1) the Cochrane Review in 2008, which found that probiotics reduced all-cause mortality and necrotizing enterocolitis (NEC) by more than half (2), with no increase in sepsis, and recommended a change in practice with regard to starting probiotics in preterm infants >1000 g birth weight, or (2) subsequent randomized controlled trials (RCTs) (3–8).

A meta-analysis of 11 RCTs in 2032 preterm infants in April 2009 (3) showed that probiotics reduced all-cause mortality ($P < 0.00001$) and NEC ($P < 0.00001$) by more than half, confirming an earlier systematic review (4). We suggest that readers consider the evidence from 11 published RCTs (2–8), which suggest that probiotics substantially reduce all-cause mortality and NEC in preterm infants. Given that evidence, requiring that safety and efficacy be established in RCTs of each probiotic versus placebo would now be ethically problematic. A more appropriate strategy would be to undertake RCTs with multiple treatment arms of different probiotic regimens with no placebo. One commentator asks, ''Do we, knowing what we now know, have the right to deny parents the option of giving a probiotic if that is what they would like? (9)''.

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Authors' Response

To the Editor: We thank Professor Tarnow-Mordi for his letter on the important question of providing probiotics to preterm infants to reduce the risk of necrotizing enterocolitis (NEC) and mortality rates. Indeed, since the preparation of our manuscript, 9 additional studies have been published. Issues such as the number of infants studied per strain, dosage, timing of initiation, and long-term safety, however, necessitate more studies before a general conclusion on the use of various probiotics can be made, especially for European neonatal intensive care units, where the NEC incidence is frequently lower than in many of the reported studies. Furthermore, for any given probiotic microorganism there are rarely data from more than a single study. Feeding with milk from the infant's own mother, and especially when exclusively feeding with human milk, has been reported to reduce NEC and mortality rates in observational trials, and this seems to afford a greater degree of risk reduction than the addition of certain probiotics (1,2). Promoting the use of maternal milk, preferably fortified, should be a priority for all neonatologists.

The use of probiotics may be considered in units where the incidence of NEC is high. The choice of type of strain, dosage, timing of initiation, and duration of intervention should be based on data from the present literature. The most logical choice would be the strain that is most studied, with the highest effect size and with the best short- and long-term safety profile; however, the presently available evidence does not allow firm conclusions on these questions. Therefore, the steering committee of the comment on enteral nutrient supply to preterm infants (3) and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition reemphasize their position that at this time the routine use of probiotics in preterm infants is not recommended. We intend to continually reassess our position in the light of any additional new evidence, as this becomes available.

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