Invited Commentary

Guts, germs and glucose: understanding the effects of prematurity on the interaction between bacteria and nutrient absorption across the intestine

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It is well known that necrotising enterocolitis (NEC) is one of the leading causes of death in preterm infants, and is by far the leading cause of long-term morbidity and mortality in infants from gastrointestinal causes(1). However, despite numerous theories that have been advanced in order to define the causes of NEC, the precise underpinnings of this disease remain incompletely understood(1–3). One consistent feature in infants who develop NEC is the observation that this devastating disease develops almost exclusively after feeds have been initiated and in the setting of microbial colonisation of the intestine, raising the distinct possibility that an underlying inability of the premature infant to tolerate bacterial products in the intestine, raising the distinct possibility that an underlying disease develops almost exclusively after feeds have been initiated and in the setting of microbial colonisation of the intestine, raising the distinct possibility that an underlying inability of the premature infant to tolerate bacterial products in the intestine, raising the distinct possibility that an underlying

In determining the individual steps which lead to the cascade of events that culminates in NEC, investigators have shown that the intestinal epithelium in the premature host is more apt to releasing pro-inflammatory cytokines when compared with post-natal intestine, while a causative role for an underdeveloped intestinal microcirculation that predisposes to impaired perfusion has also been proposed(15,16). Finally, we and others(17–19) have identified an important role for aberrant activation of the innate immune system of the intestinal epithelium in disease pathogenesis. It is therefore possible that each of these aetiological factors is influenced variably in the premature intestine by the presence of nutrients in the gut and by exposure to bacteria. Further studies along the lines of those that have been performed by Bering et al. will need to be completed in order to fully clarify how
each of these factors may act in concert in the steps that lead to NEC development.

It is noteworthy that the present study sought to evaluate a potential role for the lipopolysaccharide receptor, Toll-like receptor (TLR)-4, in the present model. Such a role may indeed have been predicted, given that the authors do demonstrate that bacteria and lipopolysaccharide affect intestinal function within the piglet intestine ex vivo. However, the authors did not demonstrate any differences in TLR-4 expression between premature and full-term piglets, despite observing an effect of bacterial exposure on nutrient absorption. These findings are difficult to reconcile in view of an abundance of studies showing the importance of TLR-4 signalling in the gut to the pathogenesis of NEC\cite{17,19–22}, as well as studies that have shown that TLR-4 expression is elevated in the premature intestine under conditions that lead to NEC in a variety of species including humans\cite{18,23}. It is possible therefore that the findings in the present study in which changes in TLR-4 expression between premature and postnatal piglet intestine were not detected may simply reflect differences between piglets and other species. Additional investigations in which the piglet intestine is examined from various regions of the bowel and at varying gestational ages may be required in order to fully determine the precise role – if any – of enterocyte TLR-4 in the steps by which bacteria may affect nutrient absorption using the present ex vivo system.

In summary, the present findings provide useful information regarding the role of prematurity and bacteria on nutritional absorption across the intestine. While the findings do not provide a definitive link between these factors in a model of NEC, they clearly offer an additional piece to the vast and complex puzzle that characterises the development of NEC.

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References


