Establishing a healthy gut microbiota in early life

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Role of gut microbiota

- Colonization resistance
- Scavenge energy
- Bioavailability of nutrients/minerals
- Stimulate epithelial development
- Maturation of the immune system
- Health of host
  - Short/long-term, acute/chronic
  - GI, immunological, psychological

Multifactorial development
Initial acquisition

- During birth and post-natally
- ??? Sterility of neonatal GI tract
  - Placenta and cord blood
  - Amniotic fluid
- Possible in utero exposure
- Early colonizers aerobes and facultative anaerobes
- Anaerobes colonize ~ d4-d7

In utero exposure

- LAB recovered from placenta, umbilical cord, amniotic fluid and meconium of neonates (Martin et al., 2004)
- Enterococcus faecium, Propionibacterium acnes, Staphylococcus epidermidis, Streptococcus sanguinis recovered from cord blood of CS infants (Jimenez et al., 2005)
- Prevalence and diversity of amniotic fluid microbiota associated with pre-term delivery and neonatal outcomes

Birth characteristics

- Delivery mode (Caesarian section)
- Gestational age (pre-term infants)
- Birth weight (low/extremely low birth weight infants)
- Therapeutics
  - delayed colonization
  - reduced diversity
  - delayed establishment of climax microbiota
Pre-term infants

- Species belonging to family Enterobacteriaceae
  - Especially E. coli and Klebsiella pneumoniae
- Enterococcus
- Streptococcus
- Staphylococcus
- NEC thought to have bacterial etiology
  - Significantly lower diversity and/or bacterial richness
  - Proteobacteria dominance (Wang et al., 2009)

Pre-term: microbial colonization

- Nutritional, microbiological and immunological dysfunctions all play a role in NEC disease progression
- No significant differences in gut microbiota between developing NEC and non-NEC infant
- "no gut, no NEC!"
- "Important differences were found in microorganisms who develop NEC:"

Diet: Mother’s milk vs formulae

"Breast is best!"
BF vs FF: first 20 days

(Harmsen et al., 2000; Pediatr Gastroenterol Nutr 30: 61-7)

BNF Taskforce Launch, May 2013

BF vs FF: longitudinal study

- Fourteen 4-week old infants recruited (7 BF, 7 FF)
- Polyphasic examination of the faecal microbiota: FISH and DGGE (community analysis), cultivation and Bif-specific DGGE (Bifidobacterium population)

(Roger & McCartney, 2010; Microbiology 156:3317-28)

BNF Taskforce Launch, May 2013

BF vs FF: FISH data

BNF Taskforce Launch, May 2013
BF vs FF: FISH data

BF vs FF: DGGE data

Weaning (Roger & McCartney, 2010; Microbiology 156:3317-28)
Human breast milk

"Bifidobacteria-optimised" primers

Proportions of DNA in each mixture

Proportions of 454 sequencing reads obtained using both primer sets

Sim et al., 2012 (PLoS ONE 7(3): e32543. doi:10.1371/journal.pone.0032543)

BF vs FF: Global view

- Bifidobacteria are predominant members of milk-fed infants' faecal microbiota
- Faecal microbiota of BF and FF infants are distinguishable
  - Higher prevalence of bifidobacteria in BF
  - Higher prevalence and levels of other bacterial groups in FF
- Gradual development of microbiota
- Weaning increased complexity (esp. BF)
- Convergence towards a climax community (adult-like) by 18-24 months
Human milk oligosaccharides

- > 200 different structures
- Composition and concentration differ during lactation
- Certain HMOs have common structural motifs with intestinal epithelial glycans
- Lewis blood group
  - Le (a+b+): (~70%): α1-2, α1-3 and α1-4-linked fucosyl residues
  - Le (a+b-): (~20%): lack α1-2-linked fucosyl residues
  - Le (a-b-): (~10%): lack α1-4-linked fucosyl residues

Chichlowski et al., 2011 (Annu Rev Food Sci Technol 2: 331-51)

Prebiotic supplemented formulae

- GOS:FOS mixture (9:1)
  - Most studied
  - Bifidogenic effect demonstrated
  - Faecal characteristics also improved
  - Recent work suggests decreased clostridia
- Generally lack diversity studies
  - Bifidobacterial species and/or strains may be important
Key points

- Human gut microbiota plays a role in host health and well-being, including energy harvest
- Multiple factors influence GI microbiota development
- Gut microbiota of breast-fed and formula-fed infants are distinctly different
- Initial weaning is associated with a transitional phase
- Infant gut microbiota converges towards adult-like microbiota between 1 and 2 years of age