



Functional Gastroenterology Bolus

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Early Life and GI Flora

Two early life history questions that I ask every new patient are the following:

- 1) Were you born vaginally or by Cesarean section?
 - 2) Were you fed formula or breastfed and if breastfed for how long?
- These factors have impact on the gut microbiota.

Transmission of Gastrointestinal Flora Through Birth Mode

Prenatal life is not sterile, and bacteria are found in meconium, amniotic fluid and the placenta.¹ Several studies have found *Escherichia*, *Leuconostoc*, *Enterococcus*, and *Lactococcus* in meconium.² During the birth process, microflora are initially passed from mother to child during passage through the vaginal canal followed by breastfeeding and skin to skin contact. In addition to bacteria and archaea there is evidence that parasites are a salutary factor in the health of human microbial flora.³ The human virome is just beginning to be studied and may turn out to be much larger than the bacterial flora.⁴ Additional changes to the flora occur with Cesarean birth and formula feeding.

The newborn acquires additional flora from vaginal and fecal flora. On the first day of life a full-term infant's flora includes *E. coli*, *Enterococci*, *Enterobacteria*, *Strep*, and *Staph*. Breastfeeding adds *Bifidobacteria*, which predominate by the end of the first week. A systematic review points to higher Firmicutes and lower numbers and diversity of Actinobacteria and Bacteroidetes in newborns born by Cesarean vs. vaginal routes.⁵ Cesarean delivery has significant effects on the viral makeup of the flora as well.⁴ Other studies fail to show a significant difference in flora based on mode of delivery.⁶

The first organisms to colonize the newborn gastrointestinal tract have profound effects on lifelong immunity. The flora create a two-way cross talk with the mucosa, influencing induction of gene expression which controls immunity and mucosal epithelial function.⁷⁻⁹ There are at least 100 times more bacterial genes than human genes and the combination of these is termed the "holobiome." It's unlikely that anyone in the developed world has the diverse, full spectrum of flora that humans have carried through evolutionary time. The average North American is treated with an average of seventeen courses of antibiotics by age 20 and thirty courses by age 40. Four generations have had exposure to potent broad-spectrum antibiotics. Women of childbearing age likely no longer have full diversified microbiota to pass on to their newborns, but it the best we have to offer.

Transmission of Flora and Immunity by Neonatal Feeding Mode

It is an understatement to say that breastfeeding provides the ideal nutrition for the newborn. The volume of the thymus in

exclusively breastfed infants is over twice that of formula-fed infants by four months of age.¹⁰ Human milk contains active macrophages and neutrophils, which phagocytize bacteria-IgA complexes and activated T cells.¹¹ Human whey protein contains lactoferrin, lysozyme and immunoglobulins IgA, IgE, IgG and IgM.^{12,13} Lactoferrin is one of the more important factors providing anti-inflammatory and anti-microbial activity.¹⁴ As mentioned above, human milk is the predominant source of *Bifidobacteria* for the infant, yet this essential micro-organism is also found in bottle-fed children, but in lower amounts.¹⁵ The prevalence is 3:1 in the breastfed neonate.¹⁶

The mode of delivery, birth weight and gestational age, home vs hospital birth and antibiotic use all affect the infant's flora. A Danish study using modern polymerase chain reaction-based assays determined that "term infants who were born vaginally at home and were breastfed exclusively seemed to have the most 'beneficial' gut microbiota (highest numbers of *Bifidobacteria* and lowest numbers of *C difficile* and *E coli*)."¹⁷

Knowing more about the origins of my patient's gut flora gives me a perspective about their constitutional state and prognosis for their gastrointestinal presenting diseases. I am more patient and expect treatment to be more complicated or lengthy if they were born by Cesarean and formula-fed. If things respond quickly and well, we have even more reason to rejoice, but if not – our expectations are tempered.

References

1. Chong CYL. Factors Affecting Gastrointestinal Microbiome Development in Neonates. *Nutrients*. 2018 Feb 28;10(3).
2. Koleva PT. Microbial programming of health and disease starts during fetal life. *Birth Defects Res C Embryo Today*. 2015 Dec;105(4):265-77.
3. Krogsgaard LR. Characteristics of the bacterial microbiome in association with common intestinal parasites in irritable bowel syndrome. *Clin Trans Gastroenterol*. 2018 Jun 19;9(6):161.
4. McCann A. Viromes of one year old infants reveal the impact of birth mode on microbiome diversity. *Peer J*. 2018 May 7;6:e4694.
5. Rutayisire E. The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review. *BMC Gastroenterol*. 2016 Jul 30;16(1):86.
6. Chu DM. Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery. *Nat Med*. 2017 Mar;23(3):314-326.
7. Hooper LV. Commensal host-bacterial relationships in the gut. *Science*. 2001 May 11;292(5519):1115-8.
8. Sonnenburg JL. Getting a grip on things: how do communities of bacterial symbionts become established in our intestine? *Nat Immunol*. 2004 Jun;5(6):569-73.
9. Xu J. Honor thy symbionts. *Proc Natl Acad Sci U S A*. 2003 Sep 2;100(18):10452-9.
10. Hasselbalch H. Decreased thymus size in formula-fed infants compared with breastfed infants. *Acta Paediatr*. 1996 Sep;85(9):1029-32.
11. Field CJ. The immunological components of human milk and their effect on immune development in infants. *J Nutr*. 2005 Jan;135(1):1-4.
12. Magrone T. Antimicrobial Peptides: Phylogenetic Sources and Biological Activities. First of Two Parts. *Curr Pharm Des*. 2018;24(10):1043-1053.
13. Smith-Norowitz TA. Detection of IgE anti-parvovirus antibodies in human breast milk. *Ann Clin Lab Sci*. 2008 Spring;38(2):168-73.
14. Raouf NA. Comparison of lactoferrin activity in fresh and stored human milk. *J Perinatol*. 2016 Mar;36(3):207-9.
15. Benno Y. The intestinal microflora of infants: composition of fecal flora in breast-fed and bottle-fed infants. *Microbiol Immunol*. 1984;28(9):975-86.
16. Ruvalcabello FF. Intestinal flora in breast- and bottle-fed infants. *J Perinat Med*. 1998;26(3):186-91.
17. Penders J. Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics*. 2006 Aug;118(2):511-21.