Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer


Introduction:

- Vaginally delivered infants harbor bacterial communities resembling those of the maternal vagina, whereas C-section-delivered infants are enriched in skin microbiota.
- The microbiome that colonizes the body of newborns can have a determinant role in educating the immune system.
- Epidemiological studies have reported associations between C-section delivery and an increased risk of obesity, asthma, allergies and immune deficiencies.
- Rates of cesarean delivery are increasing worldwide and in some countries exceed 50% of total births.

Goal of the study:

- C-section-delivered infants were exposed to their maternal vaginal fluids at birth and longitudinally determined the composition of their microbiota to assess whether it developed more similarly to vaginally born babies.

Materials and methods:

- Infants born by C-section were swabbed with a gauze that was incubated in the maternal vagina 60 min before the C-section. The gauze was extracted before the procedure, kept in a sterile container and used to swab the newborn within the first 1–3 min after birth, starting with the mouth, then the face and the rest of the body.
- All mothers delivering by C-section received antibiotics (penicillin or cephalosporins) as part of standard-of-care treatment.
- 18 infants and their mothers:
  - 7 born vaginally and
  - 11 delivered by scheduled C-section—>
    - 4 exposure to the maternal vaginal fluids
    - 7 no exposure
- A total of 1519 samples were obtained from anal, oral and skin sites of infants and mothers at six time points during the first month of life: 1 (first 5 min after birth), 3, 7, 14, 21 and 30 days after birth.
- Microbiome composition was characterized by sequencing the V4 region of 16S rRNA gene as previously described and 1016 samples were used for analysis after quality filtering.

Results:

- Bacterial source tracking of the infant microbiome revealed that the microbiomes of the exposed infants resembled those of vaginally delivered infants particularly so in the first week of life.
- In anal samples from exposed infants and vaginally delivered infants there was an early enrichment of Lactobacillus followed by a bloom of Bacteroides from week 2, which was not observed in newborns that were not exposed to vaginal fluids.
- Neonatal bacterial diversity was highest at birth in the anal and oral sites
- Bacterial diversity was not lower in the vaginal microbiota of mothers who received antibiotics and no clear differences were observed in taxonomic composition either.
Discussion:

- The results suggest that exposing infants to the maternal vaginal microbiota, the bacterial communities of newborns delivered by C-section can be partially restored to resemble those of vaginally delivered babies.

- The partial microbiota restoration provided by the gauze might be due to:
  a) compounded effects of the antibiotic treatments that accompany the C-section
  b) suboptimal bacterial transfer from the vagina to the gauze and then to the baby (infants exposed a single time to vaginal fluids)

- Limitations of the study: limited sample size and sampling extended only through the first month after birth.

- Future perspectives:
  - determination of more effective approaches to transfer the maternal microbiota to newborns (multiple exposure to the gauze, enteral administration of key bacterial species etc.).
  - Establishing which keystone species newborn infants should acquire at birth.
  - Extended longitudinal analysis of larger cohorts is needed to determine whether this procedure has any effects on diseases in later life.

Discussion round (based on conclusions of Cunnington AJ et al., BMJ 2016 Feb 23;352:i227):

- 1. Newborns may develop severe infections from exposure to vaginal commensals and pathogens, which the mother may carry asymptomatically (e.g. GBS, herpes simplex virus, Chlamydia trachomatis, and Neisseria gonorrhoeae).

- 2. There is no evidence (yet) that vaginal seeding is beneficial to the infant. Indeed, such evidence will be difficult to gather, requiring large clinical trials with many years of follow-up.

- 3. In the absence of evidence of benefit, or of guidelines to ensure the procedure is safe, how should health professionals engage with the increasing demand for vaginal seeding?
  - We have advised staff at our hospitals not to perform vaginal seeding.
  - However, the simplicity of vaginal seeding means that mothers can easily do it themselves. Under these circumstances we should respect their autonomy but ensure that they are fully informed about the theoretical risks.
  - Parents should be advised to mention that they performed vaginal seeding if their baby becomes unwell because this may influence a clinician's assessment of the risk of serious infection.
  - Health professionals should be aware that vaginal seeding is increasingly common and ask about it when assessing neonates who may have an infection.
  - Encouraging breast feeding and avoiding unnecessary antibiotics may be much more important than worrying about transferring vaginal fluid on a swab.

VH, 14.11.2016