New Hypothesis on Postnatal Infections and the Role of Group B Streptococci

An amazing field of research has opened with the new insights into the human microbiome. Communities of microbes (bacteria, fungi and other eukaryotic species) and viruses have been found to play a fundamental role in the function of the hosts immune system¹. The role of the human microbiome for the development of autoimmune diseases and its effects on mental health (brain-gut-axis) are objects of this research.

Neonates demonstrate complex microbial communities in the gut within the first week of life. Microbes from the mother and surrounding environment colonize the gastrointestinal tract of the infant until a dense, complex microbiome develops². But how is the neonate microbiome established?

Possible steps of inoculating the newborn with the maternal microbiome are³:

- intrauterine during pregnancy
- transvaginal during birth
- postnatal through breastfeeding

The reason for the inoculation with maternal microbes could be the preparation of the newborns immune system to the surrounding environmental microorganisms. The use of antibiotics in the sensitive perinatal phase when the

complex neonatal microbiom is established needs to be carefully reviewed.

Contrary to traditional assumption, latest publications show that placental tissue is not sterile but shows various physiologic and microbial

communities⁴. A publication by Aagaard and colleagues discussed changes of the vaginal microbiom during pregnancy and found that the overall diversity and richness of microbial species is reduced⁵ compared to non-pregnant women. Group B Streptococci belong to the physiologic human vaginal flora and are detected in 25% of pregnant women⁶.

The incidence of GBS related infection of the newborn is 0.24 cases per 1,000 live births (https://www.cdc.gov/groupbstrep/clinicians/clinical-overview.html).

The mismatch of GBS-positive mothers and rare GBS newborn infections could be due to antibiotic treatment of GBS-positive pregnant women.

But it is hypothesized by researchers that a certain gene defect could be the cause of severe postnatal infection. A mutation that effects key regulators of inflammatory and immune response was found in infants who suffer from severe, early onset infection⁷.

A recent publication by the CDC of a single case of late onset GBS infection discusses the transmission of GBS from the mother to the newborn through placenta consumption (http://dx.doi.org/10.15585/mmwr.mm6625a4).

The article gives no conclusion about the possible route of infection. The acidic environment of the stomach functions as a physiologic barrier for multiple microorganisms including streptococci. Further, no GBS was detected in maternal breastmilk.

The colonization of the mothers gut with GBS as a component of the maternal microbiome with an intrauterine inoculation of the fetus with GBS during pregnancy is probable.

Overall, with respect to new insight into the mammalian superorganism, the role of GBS in the development of newborn infection must be reviewed.

"Facing the microbes, the immune system does not react to combat evil, but merely shapes the microbial environment to allow the organism to live with the microbes. It is not a fight between good and evil, it is rather an equilibrium between microbes and host that generates a superorganism"⁸

1. Belkaid Y, Hand TW. Role of the Microbiota in Immunity and Inflammation. *Cell* 2014; **157**(1): 121-41.

2. Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. *The American journal of clinical nutrition* 1999; **69**(5): 1035S-45S.

3. Hildebrandt S. Das B-Streptokokken-Problem. Ein Update. *Hebammenforum* 2016; 17: 1088-1093.

4. Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. The placenta harbors a unique microbiome. *Science translational medicine* 2014; **6**(237): 237ra65. 5. Aagaard K, Riehle K, Ma J, et al. A metagenomic approach to characterization of the vaginal microbiome signature in pregnancy. *PLoS One* 2012; **7**(6): e36466.

6. Rocchetti TT, Marconi C, Rall VLM, Borges VTM, Corrente JE, da Silva MG. Group B streptococci colonization in pregnant women: risk factors and evaluation of the vaginal flora. *Arch Gynecol Obstet*2011; **283**(4): 717-21.

 Pannicke U, Baumann B, Fuchs S, et al. Deficiency of innate and acquired immunity caused by an IKBKB mutation. *N Engl J Med* 2013; **369**(26): 2504-14.
Eberl G. A new vision of immunity: homeostasis of the superorganism. *Mucosal Immunol* 2010; **3**(5): 450-60.