Vaginal seeding after a caesarean section provides benefits to newborn children AGAINST: Vaginal microbiome transfer - a medical procedure with clear risks and uncertain benefits

Maria Jenmalm

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Running Author: JENMALM

Re: 'Vaginal seeding' after a Caesarean section provides benefits to newborn children

AGAINST: Vaginal microbiome transfer—a medical procedure with clear risks and uncertain benefits

Maria C Jenmalm¹

Email maria.jenmalm@liu.se

AQ1

AQ2

¹ Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection, Linköping University, Linköping, Sweden

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Sir,

Limaye and Ratner argue in the *BJOG* Debate section that the unproven benefits of 'vaginal seeding' come with substantial risks to neonatal health and that use of the procedure should be confined to carefully monitored clinical trials.[1] While I fully agree that vaginal seeding should not be performed outside the context of an institutional review board-approved research protocol until adequate data regarding the safety and benefit of the process become available, I would like to clarify that their statement 'longitudinal data suggest that differences in the neonatal microbiome due to delivery mode are undetectable by 6 weeks of age (Chu et al. *Nat Med* 2017;23:314–26)' is contrary to findings of at least 21 independent cohorts.[2] Thus, we[3] and at least 20 other research groups,[2, 4] have found reduced faecal *Bacteroides* colonisation in caesarean section as compared with vaginally delivered infants during the first year of life. Furthermore, in the paper by Chu et al., claiming 'no discernible differences in community structure or function between infants delivered vaginally or by Caesarean surgery' at 6 weeks of age, reduced *Bacteroides* colonisation was indeed found in the caesarean section as compared with vaginally delivered infants, as shown in Supplementary Figure 12.[5] Thus, at 6 weeks of age, 20/28 stool samples from vaginally delivered infants have a relative abundance of *Bacteroides* >10%, as compared with 1/8 stool samples from caesarean section-delivered infants ($P = 0.0047$, Fisher's exact t -test, according to my calculation).

As the finding of reduced *Bacteroides* colonisation is in line with the results of so many studies from independent cohorts, I do believe it is important to clarify the limitations of the claim by Chu et al., which unfortunately has been stated as a fact in many scholarly articles, and also in the recent debate article by Limaye and Ratner. In the context of

vaginal seeding, is also important to note that the most likely source of the *Bacteroides* is the maternal stool.[3, 4] Thus, to better restore the neonatal microbiome, it may be crucial to transfer also maternal stool bacteria, in addition to maternal vaginal bacteria, as this approximates more closely the natural inoculum received by neonates during vaginal delivery, and the gut bacteria are more specialised to thrive in the gut. This needs to be evaluated in institutional review board-approved and carefully monitored clinical trials, with appropriate primary clinical outcomes, careful screening for maternal gut and vaginal pathogens, and detailed characterisation of the gut, oral, and skin microbiome development during infancy.

References

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