Reply: Gut microbiota diversity and atopic disease: Does breast-feeding play a role?

Thomas Abrahamsson, Hedvig E. Jakobsson, Anders F. Andersson, Bengt Bjorksten, Lars Engstrand and Maria Jenmalm

N.B.: When citing this work, cite the original article.

Original Publication:
Thomas Abrahamsson, Hedvig E. Jakobsson, Anders F. Andersson, Bengt Bjorksten, Lars Engstrand and Maria Jenmalm, Reply: Gut microbiota diversity and atopic disease: Does breast-feeding play a role?, 2013, Journal of Allergy and Clinical Immunology, (131), 1, 248-249.  
http://dx.doi.org/10.1016/j.jaci.2012.10.045

Copyright: Elsevier  
http://www.elsevier.com/

Postprint available at: Linköping University Electronic Press  
http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-88363
Title: Reply

Thomas R Abrahamsson, MD, PhD

Hedvig E Jakobsson, MSc, PhD

Anders F Andersson, PhD

Bengt Björkstén, MD, PhD

Lars Engstrand, MD, PhD

Maria C Jenmalm, PhD

1. Department of Clinical and Experimental Medicine, Division of Pediatrics, Linköping University, Sweden
2. Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden
3. Science for Life Laboratory, School of Biotechnology, KTH Royal Institute of Technology, Stockholm, Sweden
4. Institute of Environmental Medicine, Karolinska Institutet, Stockholm, and School of Health and Medical Sciences, Örebro University Sweden
5. Department of Clinical and Experimental Medicine, Unit of Autoimmunity and Immune Regulation, Division of Clinical Immunology, Linköping University, Sweden
Correspondence to: Thomas Abrahamsson

Division of Paediatrics

Linköping University Hospital

SE-581 85 Linköping, Sweden

Phone: +46-(10)-1030000

Fax: +46-(13)-148265.

E-mail: thomas.abrahamsson@lio.se

Supported by grants from BioGaia AB, Stockholm, Sweden, the Ekhaga Foundation, the Heart and Lung foundation, the Research Council for the South-East Sweden (grant No. F2000-106), The Olle Engqvist Foundation, the Swedish Asthma and Allergy Association, the Swedish Research Council, the University Hospital of Linköping, the Söderberg Foundation, the Vårdal Foundation for Health Care Science and Allergy Research, Sweden.
To the Editor:

We thank Azad and colleagues for their important points regarding our article “Low diversity of the gut microbiota in infants with atopic eczema”. Admittedly, we were satisfied with the notion that all infants were breastfed until one month of age in the original paper. The absent increase in diversity from one week to one month of age also indicated that breastfeeding inhibited diversity development. However, we did not relate microbiota diversity to exclusive breastfeeding at one month of age. Reassessing the data, we identified three atopic and four healthy infants who were not exclusively breastfed at one month of age. As requested, we have analyzed whether exclusive breastfeeding was associated with lower gut microbiota diversity, and if this affected the comparison between the atopic and healthy infants.

As hypothesized, exclusive breastfeeding was associated with low diversity of the total microbiota in infant stool (Table 1). Interestingly, the results indicate that the difference was a consequence of low Firmicutes diversity in the exclusively breastfed infants. Thus, although the differences in Firmicutes diversity did not reach statistical significance and only seven partially breastfed infants were included in this analysis, formula introduction seems to favour the establishment of new Firmicutes strains. As expected, the relative abundance of bifidobacteria was higher in the exclusively than the partially breastfed infants (39% vs. 15%, p=0.04). The relative abundance of the other bacterial phyla and genera did not differ significantly (data not shown).

Our results are consistent with previous reports. However, most studies have compared breastfeeding with formula feeding, not with partial breastfeeding. What our findings and those of Azad et al add to the field is that the diversity is higher also among partially breastfed infants.
Secondly, we reassessed the diversity in the atopic and non-atopic infants, limiting the comparison to infants who were exclusively breastfed at one month of age. The differences in diversity of the total microbiota, Bacteroidetes and \textit{Bacteroides} between atopic and healthy infants in the original study\textsuperscript{2} remained (Table 1), and there were still no significant differences in relative abundance for any bacteria (data not shown).

There is poor evidence for an association between breastfeeding and allergy. Any allergy preventive effects seem to be at most marginal.\textsuperscript{5} Azad and colleagues argue that the exclusively breastfed infants in our study might run an increased risk for developing atopic disease since their mothers had allergic disease. The atopic eczema incidence was, however, similar between infants with maternal atopic heredity who were and were not exclusively breastfed at one months of age in the original allergy prevention study\textsuperscript{6}, 5/34 (15\%) vs. 10/116 (9\%), \textit{p} = 0.33.

In summary, exclusively breastfed infants subsequently developing atopic eczema had a lower diversity of the total microbiota, the phyla Bacteroidetes and the genus \textit{Bacteroides} than infants who remained healthy. Furthermore, exclusive breastfeeding was associated with less diversity. Other important sources of commensal bacteria than the nutrition seem to be responsible for the higher diversity among infants who remained healthy. Potential sources warrant further investigations.

\textit{Thomas R Abrahamsson, MD, PhD \textsuperscript{a}}

\textit{Hedvig E Jakobsson, MSc, PhD \textsuperscript{b}}

\textit{Anders F Andersson, PhD \textsuperscript{c}}
References


**TABLE.** Shannon diversity index of the total microbiota and dominant phyla and genera in stool samples obtained at one month of age in infants that were exclusively or partially breastfed, and exclusively breastfed infants that did or did not have atopic eczema during the first two years of life.

<table>
<thead>
<tr>
<th></th>
<th>Exclusive breastfeeding at one month</th>
<th>Atopic eczema (only exclusively breastfed incl.)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes median, (n=33) (iq range)</td>
<td>No median, (n=7) (iq range)</td>
</tr>
<tr>
<td>Total microbiota</td>
<td>1.57 (1.39-1.85)</td>
<td>1.93 (1.52-2.14)</td>
</tr>
<tr>
<td>Bacteroidetes</td>
<td>0.31 (0.00-0.53)</td>
<td>0.12 (0.00-0.56)</td>
</tr>
<tr>
<td><em>Bacteroides</em> species</td>
<td>0.12 (0.00-0.48)</td>
<td>0.12 (0.00-0.47)</td>
</tr>
<tr>
<td>Actinobacter</td>
<td>0.38 (0.22-0.56)</td>
<td>0.33 (0.09-0.46)</td>
</tr>
<tr>
<td><em>Bifidobacterium</em> species</td>
<td>0.35 (0.18-0.46)</td>
<td>0.32 (0.06-0.37)</td>
</tr>
<tr>
<td>Firmicutes</td>
<td>0.59 (0.35-0.87)</td>
<td>1.16 (0.43-1.80)</td>
</tr>
<tr>
<td>Proteobacteria</td>
<td>0.21 (0.09-0.35)</td>
<td>0.10 (0.06-0.42)</td>
</tr>
</tbody>
</table>

* only infants that were exclusively breastfed at one month of age were included in the analyses; ** Mann-Whitney U test