Allergy and Breast Feeding

CON (?)

Hugo Van Bever
Department of Pediatrics
NUHS
Singapore

WAC, Cancun, December 2011
As a pediatrician...

are you crazy?
Breast milk is the best!

1. Nutritional
2. Psychological
3. Immunological
4. Financial
Breast milk ➔ a living milk!

Maternal Milk:
- Antigen
  - Free
  - Complexed to IgA
  - Complexed to IgG
- Tolerogenic immune mediators
  - TGF-β, IL10, Vit A, ...
- Microbiota modulating factors
  - Prebiotics (oligosaccharides, glycoproteins)
  - Antimicrobial (lysozyme, lactoferrine, IgA, ...)
- Gut growth factors (EGF, TGF-β, ...)

Antigen transferred across gut barrier

Oral tolerance

Antigen handling by maternal digestive system

Food or environmental antigen
Better questions might be...

1. Is there any milk better than breast milk?
   (cow? goat? monkey? soy? elephant?)

2. Can we improve the quality of breast milk?
Studies on breast feeding

- Difficult (ethics) $\Rightarrow$ bias
- Results are controversial
Study design (breast feeding)

- Randomization process
- Breast feeding
  - Double-blind
  - Formula feeding

OUTCOME

AL provocation testing
Maternal milk, but not formula, regulates the immune response to beta-lactoglobulin in allergy-prone rat pups.

• Breast milk *versus* formula
• Challenge with beta-lactoglobulin at day 4
• Results: Th1 – Th2 markers
• Conclusion: ... introducing an allergenic food with breast milk reduces immunological indicators of an allergic response...
Case

- 9 month old boy
- Totally breastfed
- 1st introduction of CM formula
- One minute after the first “bite”...
Skin prick testing to food allergens in breast-fed young infants with moderate to severe atopic dermatitis.


- 59 infants
- moderate to severe AD
- exclusively breast fed
- mean age: 6.5 months

54/59 (91.5%) positive SPT !!!

Egg  
Cow’s milk  
Peanuts  
Wheat  
Soy
Why egg?

- False positive result
- Through breast milk
- Prenatal sensitization.
- Airborne sensitization
- Direct skin contact
Allergy

GENES (... and more)
Allergy...

“a genetically determined feature”

- Role of epigenetic mechanisms on gene expression
- Role of the environment (pre- & postnatal environment)
Breast milk is the best...
but not able to prevent all allergies.

Can we improve the anti-allergic features of breast milk? If so, how?
Prenatal maternal diet affects asthma risk in offspring

METHYL DONORS:
- folate
- vitamin B12
- choline
- methionine
Primary prevention during pregnancy.

Protective:

- Vitamin E
- Vitamin D
- Zinc
- Mediterranean diet
- Fish
- Bacterial products (probiotics)

(mainly from observational studies)
Maternal dietary antigen avoidance during pregnancy and/or lactation for preventing or treating atopic disease in the child.

Kramer MS, Kakuma R. Cochrane Database Syst Rev 2006; 3: CD000133

- Prescription of an antigen avoidance diet to a high-risk woman during pregnancy and/or lactation is unlikely to reduce substantially her child's risk of atopic diseases, and a diet may adversely affect maternal and/or fetal nutrition.

- How good were the diets?
Candidates to improve the anti-allergic features of breast milk.

1. Safe – Efficient
2. No pharmacological intervention
3. Natural products

1. Bacterial products
2. Allergens (SLIT)
3. Parasites - worms
Probiotics in primary prevention of atopic disease: a randomized placebo-controlled trial.

IgE-mediated reactions persist!

50% decrease...

Figure 2: Treatment effect of Lactobacillus GG on atopic disease
Bars are 95% CI.
Supplementation with *Lactobacillus rhamnosus* or *Bifidobacterium lactis* probiotics in pregnancy increases cord blood interferon-γ and breast milk transforming growth factor-β and immunoglobulin A detection

S. L. Prescott*, K. Wickens†, L. Westcott*, W. Jung*, H. Currie*, P. N. Black‡, T. V. Stanley§, E. A. Mitchell†, P. Fitzharris‡, R. Siebers‡, L. Wu‡, J. Crane‡ and the Probiotic Study Group

*School of Paediatrics and Child Health, University of Western Australia, Perth, Australia, †Wellington Asthma Research Group, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand, ‡Department of Pharmacology and Clinical Pharmacology, University of Auckland, Auckland, New Zealand, §Department of Paediatrics, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand, †Department of Paediatrics, University of Auckland, Auckland, New Zealand and ‡Immunology Department, Auckland Hospital, Auckland, New Zealand
Fig. 4. Comparison of breast milk cytokine levels in study groups. The levels of IL-10, TNF-α and IL-6 are shown in breast milk samples from women in the placebo group (n = 36, clear bars), the B. lactis HN019 group (n = 35, grey bars) and the L. rhamnosus HN001 group (n = 34, crosshatched bars). The data are shown as median, interquartile ranges and 95% confidence intervals, and groups were compared by Mann–Whitney U-test. The proportion (%) with detectable levels is also shown (and compared with chi-square test). All significance levels are all shown in relation to the placebo group, including where both probiotic groups were combined for comparison with the placebo.
A systematic review of the importance of milk TGF-β on immunological outcomes in the infant and young child.

Range of immunological outcomes in infancy and early childhood, such as wheeze, atopy, eczema and the immunoglobulin switch. Twelve human studies were included in the review and 67% showed a positive association with TGF-β1 or TGF-β2 demonstrating protection against allergy-related outcomes in infancy and early childhood. High

Formula versus formula + TGF-beta

TGF-beta in formula results in

1. decreased IgE production & MC activation
2. Increase in Th1 cytokines & IL10.
-Research Agenda -

“To improve the anti-allergic qualities of breast milk”

- Diets
- Supplements (PUFA)
- Bacterial products
Role of immunotherapy?
Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy.


- 134 children (SLIT = 75) with asthma/rhinitis and mono-allergic to HDM
- SLIT for 3 yrs + 3 yrs extra follow-up
- SPT / IgE after 6 yrs.
Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy.


Table 3. Drop-outs and new sensitizations

<table>
<thead>
<tr>
<th>Patients</th>
<th>SIT Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients enrolled</td>
<td>75</td>
<td>63</td>
</tr>
<tr>
<td>Drop-outs</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Patients followed-up for 6 years</td>
<td>69</td>
<td>54</td>
</tr>
<tr>
<td>New sensitizations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>52</td>
<td>18</td>
</tr>
<tr>
<td>Parietaria</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Grass</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Olive tree</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Cat</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Dog</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Alternaria spp.</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Mugwort</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Role of parasitic infections?
Anthelminthic treatment during pregnancy is associated with increased risk of infantile eczema: randomized-controlled trial results.


... that exposure to maternal worm infections *in utero* may protect against eczema and wheeze in infancy.

The results for albendazole are also consistent with a direct drug effect. Further studies are required to investigate mechanisms of these effects, possible benefits of worms or worm products in primary prevention of allergy, and the possibility that routine deworming during pregnancy may promote allergic disease in the offspring.
Research Agenda...

... still extensive.
Research Agenda: Interventions during breast feeding?