Diet during pregnancy and atopic disease
1. Elimination diet
2. Probiotics
3. LCPUFA
4. Conclusions
Maternal elimination diet during pregnancy?

NO!

- Prescription of an antigen avoidance diet to high-risk woman during pregnancy is unlikely to reduce substantially her risk of giving birth to an atopic child.

- Moreover, such a diet may have an adverse effect on maternal and/or fetal nutrition
  - Kramer MS, Cochrane Library 2002
  - S. Salvatore, K. Keymolen, B. Hauser, Y. Vandenplas
    Intervention during pregnancy and allergic disease in the offspring
    Paediatric Allergy and Immunology 2005;16:558-66

Current evidence does not support a major role for maternal dietary restrictions during pregnancy or lactation.
The impact of government advice to pregnant mothers regarding peanut avoidance on the prevalence of peanut allergy in UK children at school entry.


• Only 36/957 mothers (3.8%) followed the Government's advice by stopping the consumption of peanuts while pregnant.
• 30 children (2.8%; 95% CIs, 1.8% to 3.8%): + SPT.
• 20 children (1.8%; 95% CIs, 1.1% to 2.7%): peanut allergy.
  = highest prevalence for peanut allergy recorded to date.

• It is difficult to ascertain any impact (either positive or negative) of the United Kingdom government advice on the prevalence of peanut allergy in British children aged 4-5 years from 2003 to 2005.
Month of birth – allergic disease / sensitization to aeroallergens
755 Japanese children

Sensitisation

- house dust mites ↓ January – March rest of year (<.01)
- Crytmeria japonica pollen ↑ December – January rest of year (<.05)

Asthma, if born in
November – December : 26 % <-> 17.3 % rest year (<.05)

Allergic rhinitis, if born in
August – October <-> rest of year (<.05)

Allergic conjunctivitis, if born in
December – January (15.8%) <-> 9.1 % rest of year (<.01)

No relation eczema / season of birth
1. Elimination diet
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Probiotics in human milk

- Human milk contains Lactobacilli, Enterococci
- Strains are specific to mother-infant pairs
- Strains isolated from milk are identical to strains in infant faeces, and different from strains isolated from areola skin

Martin R, J. Pediatr 2003; 143:754-8

Breast milk of healthy women is a source of commensal bacteria to the infant gut.


Diversity of the Lactobacillus group in breast milk and vagina of healthy women and potential role in the colonization of the infant gut. Martín R. J Appl Microbiol. 2007;103:2638-44
Probiotics during pregnancy and breast-feeding might confer immunomodulatory protection against atopic disease in the infant.


Lactobacillus rhamnosus strain GG (ATCC 53103)- placebo
4 weeks before birth – during breast feeding (6 months after birth)

<table>
<thead>
<tr>
<th></th>
<th>L.GG</th>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal atopic disease</td>
<td>18/30 (60%)</td>
<td>24/32 (75 %)</td>
</tr>
<tr>
<td>Exclusive breast feeding</td>
<td>3.2</td>
<td>3.2        months</td>
</tr>
<tr>
<td>Total breast feeding</td>
<td>8.3</td>
<td>8.5        months</td>
</tr>
<tr>
<td>Anti-inflammatory transforming growth factor 2</td>
<td>TGF-2</td>
<td>2885</td>
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</table>

At 2 years

<table>
<thead>
<tr>
<th></th>
<th>L.GG</th>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td>eczema</td>
<td>4/27 (15%)</td>
<td>14/30 (47%)</td>
</tr>
<tr>
<td>GI-symptoms</td>
<td>2/28 (7%)</td>
<td>2/31 (6%)</td>
</tr>
<tr>
<td>CMPA</td>
<td>6/29 (21%)</td>
<td>3/31 (10%)</td>
</tr>
<tr>
<td>+ve skin prick</td>
<td>6/26 (23%)</td>
<td>6/29 (21%)</td>
</tr>
<tr>
<td>serum IgE</td>
<td>29</td>
<td>28 kU/l</td>
</tr>
<tr>
<td>Spec IgE Ab (&gt;0.35 kU/l)</td>
<td>8/29 (28%)</td>
<td>11/30 (37%)</td>
</tr>
</tbody>
</table>

- Perinatal administration of Lactob. rhamnosus strain GG (ATCC 53103) reduces incidence of atopic eczema in at-risk children during the first 2 years of life (infancy)
- ? persistence of the potential to prevent atopic eczema at 4 years

- questionnaire + clinical examination: atopic eczema in
  14 / 53  Lactobacillus
  25 / 54  placebo (relative risk 0.57, 95% CI 0.33-0.97)

- Skin prick test reactivity was the same in both groups
  10 / 50  Lactobacillus
  9 / 50  placebo

preventive effect of Lactob GG on atopic eczema extends beyond infancy
Probiotics during the first 7 years of life: a cumulative risk reduction of eczema in a randomized, placebo-controlled trial.

Kalliomäki M. J Allergy Clin Immunol 2007;119:1019-21

DBPCR trial, 105 pregnant women (family with ≥1 member with AD) 4-6 weeks before delivery – 6 months postnatal
Lactobacillus GG 53103; 5 x 10^9 CFU 2x/day placebo
94 families (89.5%) completed the trial
Primary endpoint: atopic dermatitis at the age of 2 years

Atopic dermatitis 14/50 (28%) Lactobacillus GG group
12/44 (27.3%) placebo group

Children with recurrent (≥5) episodes of wheezing bronchitis were more frequent in the Lactobacillus GG group (26%; n = 13), as compared with the placebo group (9.1%; n = 4). No difference in IGE or sensitisation
Impact of maternal atopy and probiotic supplementation during pregnancy on infant sensitization: a double-blind placebo-controlled study.


171 mother-infant pairs PCDBR study
• Risk of sensitization ↑ in infants with allergic mothers
  breastfeeding over 6 months [odds ratio (OR=4.83, P=0.005)],
  or exclusively breastfeeding over 2.5 months (OR=3.4, P=0.018).
  compared to non-allergic mothers
• Probiotic supplementation had a protective effect against sensitization
  in infants with a high hereditary risk due to maternal sensitization
  (OR=0.3, P=0.023).
• The concentration of TGF-β2 tended to be ↑ in the colostrum
  of the mothers in the probiotic group compared to placebo
  (probiotic/placebo ratio=1.50, P=0.073).
  Also in subgroup of allergic mothers (prob/plac ratio=1.56, P=0.094)

Probiotic supplementation during pregnancy ↓ sensitisation infants at 12 months
Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis

Lee J. J Allergy Clin Immunol 2008;121: 116-121

21 trials (n: 1898, 0-13 y)

- 6 prevention trials: some efficacy
- 4 treatment trials: no efficacy
1. Elimination diet
2. Probiotics
3. LCPUFA
4. Conclusions
Abnormal fatty acid composition in umbilical cord blood of infants at high risk of atopic disease
Beck M. Acta Paediatr 2000;89:279-84

Breast milk from mothers of children with newly developed atopic eczema has low levels of LCPUFAs
Businco L, J Allergy Clin Immunol 1993;91:1134-9
House dust mite avoidance and omega-3 fatty acids protect for wheezing at 18 months

Mihrshahi S. J Allergy Clin Immunol 2003;111:162-8

616 pregnant women  house dust mite avoidance
+ omega-3 rich fat sources / normal food

Omega-3 rich fat sources result in
9.8 % absolute reduction (95 % CI 1.5 – 18.1) p=0.02
of “any wheeze”

7.8 % absolute reduction (95% CI 0.5 – 15.1) p=0.04
prevalence of “wheeze 1 week”

No effect on serum IgE, atopy, asthma (diagnosis doctor)
Objective:
maternal dietary supplementation with ω-3 PUFAs during pregnancy modifies immune responses in infants

Methods:
randomized, controlled trial
98 atopic, pregnant women: fish oil (3.7 g ω-3 PUFAs per day) placebo
from 20 weeks' gestation until delivery

Neonatal PUFA levels and immunologic response to allergens at birth

Results:
Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial (2)

Dunstan JA. J Allergy Clin Immunol 2003;112:1178-84

Results: 83/98 women completed the study

n-3 PUFAs (mean +/- SD) (% total fatty acids)
Fish oil suppl control
n = 40 n = 43
neonatal erythrocyte membranes 17.75% +/- 1.85% 13.69% +/- 1.22% (<.001)

All neonatal cytokine (IL-5, IL-13, IL-10, and IFN-gamma) responses (to all allergens) tended to be lower in the fish oil group (statistically significant only for IL-10 in response to cat)
Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial (3).


Although this study was not designed to examine clinical effects, we noted that infants in the fish oil group were 3 times less likely to have a positive skin prick test to egg at 1 year of age (odds ratio, 0.34; 95% confidence interval, 0.11 to 1.02; P =.055).

Although there was no difference in the frequency of atopic dermatitis at 1 year of age, infants in the fish oil group also had significantly less severe disease (odds ratio, 0.09; 95% confidence interval, 0.01 to 0.94; P =.045).
Comparison of Toll-like receptor- and Th1-/Th-2 related mRNA levels in Spanish versus German pregnant women and neonates


Toll-like receptors bind microbial compounds thereby triggering innate immune response

- Toll-like receptor (TLR) 2 / 4 ↑ Spanish >> German women and neonates
- Spanish women lower IL-4 (Th-2)
- Correlation between TLR2 and TLR4 between mothers/neonates
- Difference due to different microbial exposure in both cities (Granada / Munchen)
- ? Role of different dietary intake (low / high fish intake)

In Spanish women
  more bifidobacteria
  less allergy
than in German women
Maternal diet during pregnancy in relation to eczema and allergic sensitization in the offspring at 2 y of age.

Sausenthaler S. Am J Clin Nutr 2007;85:530-7

<table>
<thead>
<tr>
<th>High intake of</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>margarine</td>
<td>1.49</td>
<td>1.08 - 2.04</td>
</tr>
<tr>
<td>vegetable oils</td>
<td>1.48</td>
<td>1.14 - 1.91</td>
</tr>
<tr>
<td>positively associated with eczema in children at 2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fish</td>
<td>0.75</td>
<td>0.57 – 0.98</td>
</tr>
<tr>
<td>negatively associated with eczema in children at 2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>celery</td>
<td>1.85</td>
<td>1.18 – 2.89</td>
</tr>
<tr>
<td>citrus fruit</td>
<td>1.73</td>
<td>1.18 – 2.53</td>
</tr>
<tr>
<td>increased risk for sensitization food allergens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>deep-frying vegetable fat</td>
<td>1.61</td>
<td>1.02 – 2.54</td>
</tr>
<tr>
<td>raw sweet pepper</td>
<td>2.16</td>
<td>1.20 – 3.90</td>
</tr>
<tr>
<td>citrus fruit</td>
<td>1.72</td>
<td>1.02 – 2.92</td>
</tr>
<tr>
<td>increased risk for sensitization inhalent allergens</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Intake during pregnancy

- Food rich in ω-6 PUFA may ↑
- Food rich in ω-3 PUFA may ↓

The risk of allergic disease in the offspring.
Maternal fish intake during pregnancy and atopy and asthma in infancy.


Cohort of women (n=462) enrolled during pregnancy - offspring followed up to 6 years

- 34% infants: eczema at age 1 year
- 14.3% atopic [SPT + at 6 years]
- 5.7% atopic wheeze at 6 years

After adjusting for confounding factors, fish intake during pregnancy was protective against the
- risk of eczema at age 1 year OR=0.73; 95% CI 0.55-0.98
- + SPT house dust mite (6 yrs) OR=0.68; 95% CI 0.46-1.01
- atopic wheeze (6 yrs) OR=0.55; 95% CI 0.31-0.96

For ↑ in fish intake from 1 x to 2.5 x per week,
the risk of eczema at age 1 year decreased by 37%,
and the risk of positive SPT at age 6 years by 35%.
Maternal fish intake during pregnancy and atopy and asthma in infancy.

- Stratification by breastfeeding showed that fish intake was significantly related to a decrease risk in persistent wheeze among non-breastfed children (P for interaction<0.05).

- No protective effect was observed among breastfed children.

460 children from Menorca age 6.5 years (prospective trial)

- Prevalence rates at 6.5 years of
  - persistent wheeze 13.2 %
  - atopic wheeze 5.8 %
  - atopy 17.0 %

- 1/3rd (36.1%) of mothers had a low quality Mediterranean diet during pregnancy according to the Mediterranean Diet Score, while the rest had a high score.

........

• A “high” Mediterranean Diet Score during pregnancy:
  protective for
  • persistent wheeze (OR 0.22; 95% CI 0.08 to 0.58)
  • atopic wheeze (OR 0.30; 95% CI 0.10 to 0.90)
  • atopy (OR 0.55; 95% CI 0.31 to 0.97)
    after adjusting for potential confounders.

• Childhood adherence to a Mediterranean diet was negatively associated with persistent wheeze and atopy although the associations did not reach statistical significance.
1. Elimination diet
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4. Conclusions
Conclusion

- No data to recommend elimination diet during pregnancy
  - ? Harmfull

- Probiotic supplementation
  - only evaluated strains
  - conflicting data
- Meditarrean diet:
  - food rich in ω-3 PUFA
    may ↓ atopic disease