Asthma and allergic disease: influence of early nutrition

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• Importance of asthma and allergic disease
• Importance of antenatal influences
• Maternal diet during pregnancy
• Breast feeding
Asthma & allergic disease

Asthma
Eczema (atopic dermatitis)
Hayfever (allergic rhinoconjunctivitis)
Food allergy

Characterised by:
- Tissue inflammation
- Th2 biased immune responses (IL-4, IL-5, IL-13)
- ↑ IgE, ↑ allergen specific IgE
- ↑ eosinophils, allergen skin prick tests
Importance of asthma & allergic disease

- Common: 39% children, 30% adults ≥1 conditions
  - Asthma: 1.1 million children
    - 4.1 million adults
  - Eczema: 30% pre-school children
    - 15-20% school children
    - 7% adults
  - Hayfever: 20% of UK population (10 million)
  - Food allergy: 5% children, 3-4% adults
Importance of asthma & allergic disease

- Expensive: 6% GP consultations, 0.8% of hospital admissions
  10% of NHS primary care prescribing costs

Asthma; NHS £1 billion
Indirect £1.4 billion

Eczema; similar to asthma

Food allergy; $500 million direct & indirect costs
Importance of asthma & allergic disease

• ↑ prevalence

Aberdeen school children 9-12 yrs

18% increase in childhood food allergy from 1997 - 2007
Importance of antenatal influences

1). Associations between birth measurements & asthma/allergy

Godfrey et al (1994)
- Children born in Preston 1935-43 detailed birth measurements
  - $\uparrow$ IgE @ 50
  - Birth head circumference $\uparrow$ 0.30 inches (p=0.004)
  - Birth weight $\uparrow$ 5.6oz (p=0.04)

? Nutritional compromise: sustaining fetal head growth at expense of trunk & limbs, effects on thymus, immune development
Importance of antenatal influences

1). Associations between birth measurements & asthma/allergy

Numerous studies

\[ \downarrow \text{birth weight} \rightarrow \uparrow \text{asthma} \]
\[ \uparrow \text{birth weight, head circumference} \rightarrow \uparrow \text{hayfever, eczema, IgE} \]

Mechanism unclear, not thymus development
Importance of antenatal influences

Fetal measurements at 10 weeks gestation and 5 year wheeze/asthma

Adjusted OR (95% CI)

Q1                Q2                Q3                Q4

CRL quartiles

Wheeze p=0.034
Asthma p=0.026

Thorax 2010; 65: 391.
Importance of antenatal influences

2). Associations between lung function at birth & asthma/wheeze

Never asthma, History of asthma, Asthma at 10 yrs

NEJM 2006; 355:1682
Importance of antenatal influences

3). Associations between cord blood immune responses & allergy (asthma)

Stimulus: PHA

Stimulus: House dust mite
Maternal dietary intake of food allergens

1990s
Concerns that fetal exposure to allergens ⇒ childhood asthma/allergy
Reports of allergic reactions to peanuts on first exposure

Allergens identified in:
- amniotic fluid
- cord blood

Cord blood mononuclear cell responses to allergens

CBMC proliferate after stimulation with allergen.

↑CBMC responses associated with childhood allergic disease
Maternal dietary intake of food allergens
Cord blood mononuclear cell responses to allergens

HR1 allergic parents, allergic children
HR2 allergic parents, non-allergic children
LR non allergic parents and children
Maternal dietary intake of food allergens

Cord blood mononuclear cell responses to allergens

Interpretation:
Exposure & sensitisation to maternally derived food allergens ↑ risk allergy

Department of Health advice, June 1998

*Pregnant women who are allergic should not consume peanuts during pregnancy in order to reduce the risk of peanut allergy in their children*
Cord blood mononuclear cell responses to allergens

BUT:

Perennial allergens

No association: CBMC responses & exposure to dust mite

Seasonal allergens

CBMC non-responders : exposed

CBMC responders : not exposed
Seasonal allergens

Responders not exposed

Responders not exposed

Non-responders but exposed
The systematic review:

no clear evidence to suggest that either maternal exposure, or early or delayed introduction of peanut in the diets of children, impacts upon subsequent development of sensitisation or allergy to peanut.

Br J Nutrition 2010; 103:1278-86.

2009: COT & DoH Advice: pregnant women can eat peanuts
Allergen avoidance

Trials of allergen avoidance during pregnancy & infancy (dietary & aero allergens)

Mono allergen avoidance meta-analysis asthma @ 5 OR 1.22 (95% CI 0.83-1.78)

? flawed concept: early life allergen exposure promotes tolerance trials of allergen exposure underway

J Allergy Clin Immunol 2007;119:1323
Maternal diet during pregnancy: nutrients

Maternal diet during pregnancy

Changing diet contributing to the increase in asthma and allergy?

Hypotheses

1. ‘Antioxidant’ hypothesis: ↓ antioxidants  
   (Thorax 1994;49:171)

2. Lipid hypothesis: ↑ n-6 PUFA, ↓ n-3 PUFA  
   (Eur Respir J 1997;10:6)

3. Vitamin D hypotheses: vitamin D supplements  
   (Allergy 1999;54:757)  
   vitamin D deficiency  
   (JACI 2007;120:1031)

4. Mediterranean diet hypothesis: ↓ Mediterranean diet  
   (Thorax 2007;62:677)
Maternal diet during pregnancy: nutrients

Maternal diet during pregnancy: Vitamin D

Maternal vitamin D intake & recurrent childhood wheeze 2-6 years

Maternal vitamin D intake & childhood asthma 5-6 years

Clinical trials underway, USA, NZ, Europe

Clinical trials underway, USA, NZ, Europe

J Allergy Clin Immunol 2011; 127: 724
Maternal vitamin D status during pregnancy

BUT

- 25(OH) D (>75 vs <30nmol/l) 32 wks gestation associated with:
  - ↑eczema at 9 months: OR 3.26 (1.15-9.29)
  - ↑asthma at 9 years: OR 5.40 (1.09-26.65)

7648 adults age 31
Use of high dose (>2000 IU/d) vitamin D supplements during infancy
Regular vs non/irregular use of vitamin D supplements as infant

<table>
<thead>
<tr>
<th>Condition</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Atopy</td>
<td>1.46 (1.4-2.0)</td>
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<tr>
<td>Allergic rhinitis</td>
<td>1.66 (1.1-1.6)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.35 (0.99-1.8)</td>
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</tbody>
</table>

Eur J Clin Nutr 2008; 62:68
Ann N York Acad Sciences 2004;1037:84
Cord blood 25(OH)D and allergen specific IgE 1-5 years

Tuscon birth cohort n=208

Adjusted OR (95% CI)

<50 50-74.9 75-99.9 ≥100

p=0.02

? U shaped association, low and high deleterious

J Allergy Clin Immunol 2011;128:1093
Maternal diet during pregnancy: nutrients

Maternal diet during pregnancy: Vitamin E

Maternal vitamin E intake & childhood wheeze 2-3 years

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Litorua (E11) 2006</td>
<td>0.700 0.478 1.025 -1.833 0.067</td>
<td></td>
</tr>
<tr>
<td>Martindale (E12) 2005</td>
<td>0.790 0.473 1.319 -0.901 0.368</td>
<td></td>
</tr>
<tr>
<td>Miyake (E15) 2010</td>
<td>0.540 0.322 0.906 -2.338 0.020</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.678 0.519 0.879 -2.918 0.004</td>
<td></td>
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</tbody>
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↓Maternal vitamin E: ↓lung function, ↑wheeze & asthma @ 5 yrs

Pilot trial of vitamin E intervention underway

J Allergy Clin Immunol 2011; 127: 724
*Maternal diet during pregnancy: nutrients*

*Maternal diet during pregnancy: lipids*

Observational studies of maternal dietary lipids during pregnancy & childhood allergy/asthma

Inconsistent, suggestive

Interventional studies
Maternal diet during pregnancy: lipids

Pregnant mothers given placebo or fish oil capsules (n-3 PUFA) from 20 weeks gestation.

J Allergy Clin Immunol 2003; 112: 1178
Maternal diet during pregnancy: lipids

145 pregnant women, high allergy risk pregnancies
Randomised to:
  1.6g EPA + 1.1g DHA (9 caps)/d from 25 wks gestation
  Placebo control

12 month follow up.

n-3 PUFA supplementation
  Positive SPT OR 0.36 (0.14-0.95)
  Positive SPT egg OR 0.31 (0.11-0.89)
  IgE associated eczema OR 0.22 (0.06-0.81)
  Food allergy OR 0.09 (0.01-0.74)

?long term benefits

Acta Pædiatrica 2009; 98: 1461
Maternal diet during pregnancy: lipids

706 pregnant women, high allergy risk pregnancies
Randomised to:
  3 fish oil caps/d 100mg EPA + 800mg DHA from 21 wks gestation
  Placebo control

12 month follow up.
n-3 PUFA supplementation
  allergic disease OR 0.70 (0.45-1.09)
  Positive SPT egg OR 0.62 (0.41-0.93)
  IgE associated eczema OR 0.64 (0.40-1.02)
  Food allergy OR 0.96 (0.41-2.25)

?long term benefits

BMJ 2012;344:e184
Maternal diet during pregnancy: Mediterranean diet

Birth cohort, 482 children in Menorca, 96% follow up at 6.5 yrs

A high Mediterranean Diet Score during pregnancy:
- persistent wheeze OR 0.22 (0.08-0.58)
- allergic wheeze OR 0.30 (0.10-0.90)
- allergic sensitisation OR 0.55 (0.31-0.97)

High level of adherence to a Mediterranean diet during pregnancy protective against asthma-like symptoms and allergy in childhood

Pilot trial of Mediterranean Diet during pregnancy recently completed
Breastfeeding and asthma/allergy in children

Huge number of studies
- Virtually no interventional studies (ethics)
- Systematic reviews, systematic reviews of systematic reviews

- Breastfeeding of high allergic risk infants 3-4 mo
  - ↓ risk of atopic eczema
  - ↓ risk asthma 2-5 yrs

Breastfeeding: ↓ viral associated wheeze up to 4 years

Breastfeeding beyond 3-4 months: no additional benefit.

? Long term benefits
Breastfeeding and asthma/allergy in children

A systematic review long term effects of breastfeeding (>5 years)

31 publications:

breast feeding ≥3months

- wheezing & asthma >5 yr OR 0.97 (0.90–1.04)
- wheeze > 5 yr OR 0.92 (0.86-0.98)
- asthma OR 1.10 (1.00-1.22)
Take home messages

Asthma and allergic disease are common, important & expensive

Antenatal and early life influences appear to play key roles in aetiology

Maternal allergen avoidance appears not to prevent allergic disease

Maternal nutrient intake during pregnancy may influence asthma/allergy

Trials underway/imminent of maternal diet during pregnancy

Breast feeding, effects on asthma/allergy, especially long term, not clear