Weaning and Allergy Prevention

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There is much to learn about preventing food allergy
De Silva et al. 2014
Objectives

• Weaning recommendations
• Do we follow these recommendations?
• Importance of first tastes as later determinants of later food preference
• Weaning timing/type of foods and NCDs
The recommendations...

Cardiovascular, metabolic, chronic lung diseases and allergic diseases are all collectively known as non-communicable diseases (NCDs). We have seen an increase in all of these NCDs over the past few decades. Early life nutrition play a significant role in the future prevention or development of non-communicable diseases (NCDs).

Prescott et al. 2013
Infant feeding

• Weaning (introduction of solid foods) age and ideal duration of exclusive breast feeding go hand in hand

• Exclusive breastfeeding, based on the WHO definition, refers to:

The practice of feeding only breast milk (including expressed breast milk) and allows the baby to receive vitamins, minerals or medicine. Water, breast milk substitutes, other liquids and solid foods are excluded.

http://www.who.int/nutrition/topics/infantfeeding/en/
WHO recommendation 2001

- **Exclusive breast feeding for 6 months (i.e. no introduction of solid foods) vs. 4-6 months**
  
  - Reduction of gastro-intestinal infections (Belarus)
  
  - No (further) reduction in respiratory infections or atopic disease

# Introduction of solid foods – National Guidelines

<table>
<thead>
<tr>
<th>Country</th>
<th>Introduction of solids</th>
<th>Allergy Advice</th>
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</thead>
</table>
| USA (ADA 2009/AAP Committee on Nutrition 2008) | *ADA*: Complementary foods from 6 months  
*AAPCN*: after 4 months of age, preferably at 6 months of age | ADA None  
*AAPCN* – This includes highly allergenic foods, such as fish, eggs, and foods containing peanut protein. |
| UK (DoH/BDA) | DoH 2007: Weaning should commence around or about 6 months of age. | DoH: If weaning commenced before 6 months: avoid wheat-based foods, eggs, fish, shellfish, nuts, seeds and soft and unpasteurised cheeses. |
| EAACI 2014 (De Silva et al. 2014) | Delaying the introduction of solid foods beyond 4 months did not have preventive benefits in those at high or normal risk. | Therefore, for primary prevention we recommend no withholding or encouraging of exposure to “highly allergenic” foods such as cow’s milk, hen’s egg and peanuts irrespective of atopic heredity, once weaning irrespective of has commenced. |
| Australia (NHMRC2003 and DAA) | NHMRC 2003: Should not be started before the age of 4 months and that they should not be delayed much beyond the age of 6 months.  
DAA: 6 months | NHMRC: Avoid nuts until 3 years if there is a strong family history of nut allergy.  
DAA: None |
Do we follow these guidelines?
<table>
<thead>
<tr>
<th>Country</th>
<th>Solid foods introduced</th>
<th>Introduction of nuts</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA (1993/1994) Skinner et al. 1997 (n=98)</td>
<td>Most infants by six months</td>
<td>By 12 months 6/60 (10%) ate nuts the day before</td>
</tr>
<tr>
<td>USA (2005) IFPS II n~ 3000</td>
<td>83.9% fed cereal foods by 6 months</td>
<td>7% giving nuts by 10 months</td>
</tr>
<tr>
<td></td>
<td>41% by 4 months</td>
<td></td>
</tr>
<tr>
<td>USA (2013) IFS II n=1334</td>
<td>40.4% of mothers introduced solid foods before age 4 months</td>
<td></td>
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</table>

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<tr>
<th>Country</th>
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<tr>
<td>UK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFS (2000) n~9 000</td>
<td>85% at 4 months</td>
<td>Not available 20% of children with fam hx of atopy avoiding peanuts at 3 years</td>
</tr>
<tr>
<td>IOW (2001) n = 969</td>
<td>82.1% by 4 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>all children by 6 months</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFS (2005) n~12 000</td>
<td>51% at 4 months</td>
<td>1% giving nuts by 10 months</td>
</tr>
<tr>
<td></td>
<td>98% by 6 months</td>
<td></td>
</tr>
<tr>
<td>IFS (2010) n~16 000</td>
<td>30% by 4 months</td>
<td>In England only: 29% exclusively breastfed at 6-8 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13% partially breastfed at 6-8 weeks</td>
</tr>
<tr>
<td>DNSIYC 2011 - 2013 (2700)</td>
<td>78% (ever breast fed)</td>
<td>Only 43% breast fed till 3 months</td>
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</tbody>
</table>

Australia

- Updated national allergy guidelines are associated with reduced delay in introduction of solids, egg, and peanut and an increase in partially hydrolyzed formula use among formula-fed infants.

- Higher socioeconomic status and absence of family history of allergies were associated with better uptake of feeding guidelines.

Tey D 2014
Importance of first tastes and later determinants of food preferences
When are babies ready to be weaned?

• Loss of the neonatal gag reflex
• An ability to propulse food from entry point to the back of the tongue
• Able to masticate more textured foods - at a later stage...?
• Each infant is different...

Koplin and Allen 2013
Variety of tastes

- Taste (sweet, sour, salty, bitter, umami, or savory) preferences have a strong innate component.
- Sweet, umami, and salty substances are *innately preferred*.
- Bitter and sour substances are *innately rejected*.

- This can be modified by pre- and postnatal experiences - learning beginning in utero and continue during early feedings.
- This set the stage for later food choices and are important in establishing life-long food habits.

Beauchamp and Menalla 2009
Importance of introducing new tastes

• Breastfeeding and variety early in weaning increased new food acceptance.
• Frequency of change during weaning was more effective than number of vegetables fed.
• The combination of breastfeeding and high variety produced greatest new food intake. This effect persisted 2 months later.

Maier AS 2008
# Age of introduction - ALSPAC

<table>
<thead>
<tr>
<th>Age solids introduced</th>
<th>Feeding difficulties at 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>29.1%</td>
</tr>
<tr>
<td>6-9 months</td>
<td>38.6%</td>
</tr>
<tr>
<td>&gt;10 months</td>
<td>52.3%</td>
</tr>
</tbody>
</table>

Harris G 2012
The importance of textures

ALSPAC

– Infants introduced to lumps late (≥10 months of age) were more difficult to feed and had more definite food likes and dislikes.

– Children who were introduced to lumpy solids after 9 months of age ate fewer of all ten categories of fruit and vegetables than children introduced to lumpy solids before this age.

– Children introduced to lumpy solids before the age of six months ate more green vegetables, tomatoes and citrus fruits than children introduced after 6 months.

Northstone K, 2001 and Harris, G 2008
General weaning guidance...not to forget

- Infants who are weaned at or near 6 months will need to be moved from smooth pureed foods onto the second stage of weaning more quickly.

- In particular mashed food with soft lumps and soft finger foods and foods high in iron including meat, oily fish and pulses should be introduced from around 6 months.
Oral motor skills: seen dietitian vs. not

Miriam Tarkin unpublished
Weaning and allergy
Modified from Prof Susan Prescott AAAAI 2011/2012

Nutritional factors with immune effects

Healthy diet
Fresh Food

Epigenetics and Genetics
Topical exposure

These may be the subject of future or ongoing (vit D) trials

Disease predisposition
(role in prevention)

Tryptophan ➔ Microbiota ➔ Vitamin A

Konieczna et al. 2012
Healthy eating and solid foods...

- Predominantly home cooked
- Low/negative intake of highly processed adult foods
- Low use of commercial baby foods
- LESS FOOD ALLERGY

Clinical implications: Advocating a healthy infant diet that is predominantly home cooked and provides high levels of fruits and vegetables might be a positive way to protect against food allergy development.

Grimshaw K JACI 2013
Food diversity?

• n= 3142 Finnish children
• By 3 and 4 months of age, food diversity was not associated with any of the allergic end points.
• By 6 months of age, less food diversity was associated with increased risk of allergic rhinitis but not with the other end points.
• By 12 months of age, less food diversity was associated with increased risk of any asthma, atopic asthma, wheeze, and allergic rhinitis.

Nwaru et al. 2014
Breastfeeding duration – the “overlap”
Introduction of solids

- Infants who were diagnosed with food allergy by the time they were 2 years of age were introduced to solids earlier (≤16 weeks of age) and were less likely to be receiving breast milk when cow's milk protein was first introduced into their diet.

Grimshaw et al. 2013
Optimal window for feeding?
Prescott, Tang, Smith et al. PAI 2008

Birth 3-4 6-7 >12 months

↑ risk window ↑ risk resolution

Need more studies:
• May be an **optimal time**, but likely to **vary** (individual & environment)
• Rather than targeting allergens: we need to optimize other **environmental conditions** during allergen encounter:

→ Promote breastfeeding
→ Understand and optimise colonisation
→ Understand and optimise exposure to dietary immunomodulators

Provide more tolerogenic environment
Timing of exposure?

Too early?
- Increased risk
- Birth 3-4?

Too late?
- Increased risk
- Resolution
- >12 months

Factors that influence the capacity for tolerance:
- Gut barriers
- Micro flora
- T-cells
- B-cells
- Breast feeding (continued)
- Genetic predisposition
- Allergen properties (dose, interval, timing, preparation)
- Other Immunological factors (stress/fatty acids/anti-oxidants)

Adapted from Prescott SL 2008
Observational data: Cow’s milk

Prospective study of feeding history of 13,019 infants:

IgE-CMA occurrence as a function of the age of CMP introduction.

- **Group I (Green):** CMP exposure (0 to 14 days)
- **Group II (Yellow):** CMP exposure (15 to 104 days)
- **Group III (Red):** CMP exposure (105 to 194 days)
- **Group IV (Yellow):** CMP exposure (195 to 374 days)

Real need for RCT’s in this area: LEAP and EAT studies in the UK
Observational data: Egg

Egg Introduction and Egg Allergy

“HealthNuts” study, 2589 infants population-based, cross-sectional study

- 4-6 mo
- 7-9 mo
- 10-12 mo
- >12 mo

✓ Effects seen in high-risk and low-risk infants with cooked egg introduction
✓ Adjusted for confounding factors
✓ Confirmed egg allergy

Koplin et al JACI 2010
RCT: Egg

- Introducing egg powder into infant’s diet at 4-8 months.
- A high proportion (31% [15/49]) of infants randomized to receive egg had an allergic reaction to the egg powder and did not continue powder ingestion.
- At 4 months of age, before any known egg ingestion, 36% (24/67) of infants already had egg-specific IgE levels of greater than 0.35 kilounits of antibody (kUA)/L.
- At 12 months, a lower (but not significant) proportion of infants in the egg group (33%) were given a diagnosis of IgE-mediated egg allergy compared with the control group.

Palmer et al. JACI 2013
...and so we have been waiting for this!

• Early evidence, which requires further investigation, suggests that if a window of opportunity for promoting tolerance exists, it may be different for each food.

Koplin and Allen, 2013
Changes in foods included: seen a dietitian vs. not

Following the dietetic consultation, the Number of allergenic foods included in the infant’s diet increased significantly (p=0.001)
AAP 2008

All infants

• There is also little evidence that delaying the timing of the introduction of complementary foods beyond 4 to 6 months of age prevents the occurrence of atopic disease. At present, there are insufficient data to document a protective effect of any dietary intervention beyond 4 to 6 months of age for the development of atopic disease.

• Although solid foods should not be introduced before 4 to 6 months of age, there is no current convincing evidence that delaying their introduction beyond this period has a significant protective effect on the development of atopic disease regardless of whether infants are fed cow milk protein formula or human milk. This includes highly allergenic foods, such as fish, eggs, and foods containing peanut protein.

Greer 2008
AAAAl 2013

• Introduce foods from between 4-6 months
• Single ingredients – one every 3-5 days
• US: rice or oat cereal, yellow/orange vegetables, fruits (eg, apples, pears, and bananas), green vegetables, and then age-appropriate staged foods with meats.
• Acid fruits – “rashes”
AAAAI – allergenic foods

• We do not suggest introducing one of the highly allergenic foods as one of the first complementary foods; however, once a few typical complementary foods (see above bullet) are tolerated, highly allergenic foods may be introduced as complementary foods.
  Fleischer et al. 2013

• Therefore, for primary prevention we recommend no withholding or encouraging of exposure to “highly allergenic” foods such as cow’s milk, hen’s egg and peanuts irrespective of atopic heredity, once weaning has commenced.
  EAACI 2014
A final word about weaning...From Dr Sicherer in 2008!

At present, it seems reasonable to recommend weaning between the age of 4—6 months, based on the needs of the mother and infant. In practical terms, weaning of high risk infants will involve to begin solids with single ingredient infant foods such as fruits, vegetables, and cereal grains, gradually and in progression, which typically results in the more allergenic foods not being introduced immediately at 4 months, and only if there have not been signs of atopic disease.

Scott Sicherer 2008
Special considerations

- Infant with moderate-to-severe atopic dermatitis despite optimized management
- If specific IgE to a food is positive and not has not been eaten = food challenge
- Convincing history and SPT/Specific IgE not supportive
- Sibling with peanut allergy

Fleischer et al. 2013
Finally

• Do introduce solids...but limited information
  – When?
  – Which order?
  – How much?

• Should we follow strict 6 months guidance ...
Key references

