La dieta del bambino allergico: dai latti speciali allo svezzamento

Diego Peroni
Università di Pisa

diego.peroni@unipi.it

La dimensione del problema
La dieta con latti speciali
Lo svezzamento
Le scelte possibili
Conclusioni
In population-based studies, the likelihood of food sensitization was up to 6 times higher in patients with AD versus healthy control subjects at 3 months of age (odds ratio, 6.18; 95% CI, 2.94-12.98; P < .001).
Does atopic dermatitis cause food allergy? A systematic review.

Tsakok, JACI 2016; 137:1071

In population-based studies, the likelihood of food sensitization was up to 6 times higher in patients with AD versus healthy control subjects at 3 months of age (odds ratio, 6.18; 95% CI, 2.94-12.98; P < .001).

This systematic review confirms a strong and dose-dependent association between AD, food sensitization, and FA. AD of increased severity and chronicity is particularly associated with FA. There is also evidence that AD precedes the development of food sensitization and allergy, in keeping with a causal relationship.
EuroPrevall birth cohort study, children with a suspected HEA and their age-matched controls were evaluated in 9 countries, using a standardized protocol including measurement of - HE-specific serum IgE, -SPT, and -double-blind, placebo-controlled food challenges (DBPCFC)
Incidence and natural history of hen’s egg allergy in the first 2 years of life—the EuroPrevall birth cohort study.
Xepapadaki, Allergy 2016; 71:350.

Incidence of HEA was considerably lower than previously documented, although differences in incidence rates among countries were noted. Half of the children with documented HEA gained tolerance within 1 year postdiagnosis.
Confirmed challenge-proven CMA in <1% of children up to age 2. Affected infants without detectable specific antibodies to cow’s milk were very likely to tolerate cow’s milk one year after diagnosis, whereas only half of those with specific antibodies in serum ‘outgrew’ their disease so soon.

Anaphylaxis in children and adolescents: The European Anaphylaxis Registry. Grabenhenrich JACI 2016; 137:1128

Recorded details of anaphylaxis in 90 tertiary allergy centers in 10 European countries, aiming to oversample the most severe reactions.

Data were retrieved from medical records.

Between July 2007 and March 2015, anaphylaxis was identified in 1970 patients younger than 18 years.

Causes according to age
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Modifying the infant’s diet to prevent food allergy.


Primary Prevention
(prevention of allergic disease in individuals who are not immunologically sensitised)

Secondary Prevention
(prevention of the development of allergic disease or the atopic march in individuals already sensitised)

Tertiary prevention
(the treatment of allergic disease)
The success of elimination diet requires that

- the correct allergen is identified
- the patient maintains a diet completely devoid of all forms of the offending allergen
- and other factors not provoke similar symptoms during the period of study
Formule idrolisate

Cosa sono?

Idrolisi = scissione delle proteine in frammenti < 6.000 Dalton: riduzione potere allergico

Il trattamento di idrolisi consiste nel sottoporre il latte a tre ordini di manipolazioni:
- trattamento enzimatico (mediante l’utilizzo di vari enzimi: pepsina, tripsina, papaina, proteasi batteriche ecc.)
- trattamento termico
- ultrafiltrazione

Si ottengono così tre tipi di latte:

1) Latti parzialmente idrolisati
2) Latti estensivamente idrolisati
3) Formule aminoacidiche
Riduzione della 
ALLERGENICITÀ' di una PROTEINA

Minore è la lunghezza dei peptidi e minore è il peso della proteina........ minore è il residuo allergenico del peptide/proteina
Idrolizzati Proteici

Proteina intatta
Idrolizzato Parziale
Idrolizzato Estensivo
Aminoacidi

Allergenicità
Formule idrolisate

Si differenziano in base alla tipologia di proteine contenute

- Idrolisati parziali
- Idrolisati estensivi
- Idrolisati di caseina
- Idrolisati di sieroproteine
Substitute formulas available in the UK for cow’s milk allergic infants

<table>
<thead>
<tr>
<th>Type of formula</th>
<th>Example (alphabetical order)</th>
<th>Manufacturer</th>
<th>Protein source</th>
<th>Carbohydrate</th>
<th>Minerals (mg/100ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHF²</td>
<td>Aptamil Pepti 1 and 2</td>
<td>Milupa</td>
<td>Hydrolysed whey</td>
<td>Fish oils (omega 3 and 6), Lactose and maltodextrin</td>
<td>Calcium 52, Iron 0.5</td>
</tr>
<tr>
<td></td>
<td>(2 suitable from 6 months)</td>
<td></td>
<td>73% peptides &lt; 1000 Da</td>
<td>Palm, coconut, rapeseed and sunflower oil.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Althéra</td>
<td>Nestlé</td>
<td>Hydrolysed whey</td>
<td>Maltodextrin, lactose</td>
<td>Calcium 41, Iron 0.73</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% peptides &lt; 1000 Da</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nutramigen 1 and 2</td>
<td>Mead Johnson</td>
<td>Hydrolysed casein</td>
<td>Palm, coconut, soya and sunflower oil.</td>
<td>Calcium 77, and 94</td>
</tr>
<tr>
<td></td>
<td>(2 suitable from 6 months)</td>
<td></td>
<td>95% peptides &lt; 1000 Da</td>
<td>Glucose syrup, modified corn starch, fructose. Lactose free</td>
<td>Iron 1.22 and 1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MCT Pepdite</td>
<td>Nutricia SihS</td>
<td>Hydrolysed soya and pork collagen</td>
<td>Coconut, maize, palm kernel and walnut oil. 75% fats MCT. Glucose syrup. Lactose free.</td>
<td>Calcium 49, Iron 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>64% peptides &lt; 1000 Da</td>
<td>Glucose syrup.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pepdite</td>
<td>Nutricia SihS</td>
<td>Hydrolysed soya and pork collagen</td>
<td>Coconut, soya and sunflower oil.</td>
<td>Calcium 45, Iron 1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>64% peptides &lt; 1000 Da</td>
<td>Glucose syrup.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pepti Junior</td>
<td>Cow and Gate</td>
<td>Hydrolysed whey</td>
<td>Coconut, soya and fish oil; 50% MCT. Glucose syrup. Lactose content insignificant</td>
<td>Calcium 76, Iron 1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>57% peptides &lt; 1000 Da</td>
<td>Corn, soya and sunflower oil; 55% MCT. Corn syrup and corn starch. Lactose free.</td>
<td>Calcium 94, Iron 1.8</td>
</tr>
<tr>
<td></td>
<td>Pregestimil</td>
<td>Mead Johnson</td>
<td>Hydrolysed casein</td>
<td>Sunflower and soya oil. 33% MCT Sucrose, modified corn starch. Lactose free.</td>
<td>Calcium 71, Iron 1.2</td>
</tr>
<tr>
<td></td>
<td>Similac Alimentum</td>
<td>Abbott</td>
<td>Hydrolysed casein</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% peptides &lt; 1000 Da</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Advantages

✓ Well tolerated by the vast majority of cow’s milk allergic individuals (approximately 95%)

✓ For prevention, can be used as a supplement or a substitute to breastfeeding in infants at high risk of allergy

✓ Nutritionally adequate

Limitations

✓ High cost

✓ Unpalatable taste

✓ Potential error in reconstitution

✓ High osmolality potential

✓ Can cause allergy in exquisitely milk allergic individuals (5-10%)
Formula aminoacidica

- Idrolisi totale
- Del tutto priva di potere allergenico
- Piuttosto sgradevole
- Facilmente assorbibile → accrescimento soddisfacente anche con quantità inferiori
Substitute formulas available in the UK for cow’s milk allergic infants

<table>
<thead>
<tr>
<th>Type of formula</th>
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<th>Manufacturer</th>
<th>Protein source</th>
<th>Carbohydrate</th>
<th>Minerals (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAF¹</td>
<td>Neocate LCP</td>
<td>Nutricia SHS</td>
<td>Amino acids</td>
<td>Coconut, canola and sunflower oil. Glucose syrup. Lactose free</td>
<td>Calcium 65.6, Iron 1.0</td>
</tr>
<tr>
<td></td>
<td>Neocate Active</td>
<td>Nutricia SHS</td>
<td>Amino acids</td>
<td>Coconut, canola and sunflower oil. Glucose syrup. Lactose free</td>
<td>Calcium 95.1, Iron 1.3</td>
</tr>
<tr>
<td></td>
<td>Neocate Advance</td>
<td>Nutricia SHS</td>
<td>Amino acids</td>
<td>Coconut, canola and sunflower oil. Glucose syrup. Lactose free</td>
<td>Calcium 50, Iron 0.62</td>
</tr>
<tr>
<td></td>
<td>Nutramigen AA</td>
<td>Mead Johnson</td>
<td>Amino acids</td>
<td>Palm, coconut, soya and sunflower oil. Glucose syrup and tapioca starch. Lactose free</td>
<td>Calcium 64, Iron 1.22</td>
</tr>
<tr>
<td>Soya³</td>
<td>Infasoy</td>
<td>Cow and Gate</td>
<td>Whole soya</td>
<td>Glucose syrup. Suitable for vegans</td>
<td>Calcium 54, Iron 0.8, Calcium 67, Iron 0.8</td>
</tr>
<tr>
<td></td>
<td>Wysoy</td>
<td>SMA Nutrition</td>
<td>Whole soya</td>
<td>Glucose syrup.</td>
<td></td>
</tr>
</tbody>
</table>

¹ Amino acid formulas
³ Soya formulas
Advantages
✓ Well tolerated by almost all children allergic to cow's milk
or to multiple foods
✓ For prevention, can be used as a supplement or a substitute to breastfeeding in infants at high risk of allergy
✓ Nutritionally adequate

Limitations
✓ High cost
✓ Unpalatable taste
✓ Potential errors in reconstitution
Idrolisati

Proteina intatta
Idrolizzato Parziale
Idrolizzato Estensivo
Aminoacidi

Costo

Palatabilità
Food items and ingredients that contain cow's milk protein

- Butter, butter fat, butter milk, butter oil
- Casein (curds), caseinates, hydrolysed casein, calcium caseinate, sodium caseinate
- Cheese, cheese powder, cottage cheese
- Cow’s milk (fresh, condensed, dried, evaporated, powdered (infant formulas), UHT)
- Cream, artificial cream, sour cream
- Ghee
- Ice cream
- Lactalbumin, lactoglobulin
- Low-fat milk
- Malted milk
- Margarine
- Milk protein, milk powder, skimmed milk powder, milk solids, non-fat dairy solids, non-fat milk solids, milk sugar
- Whey, hydrolysed whey, whey powder, whey syrup sweetener
- Yogurt, fromage frais
Recommendations on the use of alternative ‘milk’ beverages

1. They are **not suitable** for infants as a main drink **under 1 year of age**. A nutritionally complete formula should always be chosen, preferably to **2 years of age** (although they can be used for cooking).

2. Their use in children should be under the close guidance of a dietitian as shortfalls in energy, protein, calcium, riboflavin, vitamin A and D, and essential fatty acids are likely without an alternative dietary source. Weight and growth should be regularly monitored.

3. They are not available on prescription and therefore should not be suggested to families with financial constraints where a more suitable complete formula can be prescribed.
4. They are not available on prescription and therefore should not be suggested to families with financial constraints where a more suitable complete formula can be prescribed. Their use in older children and adults should be under the supervision of a dietitian to ensure adequate calcium intake.

5. Care should be taken to ensure that specific ingredients are not allergenic to a particular individual, for example nut milks and nut allergy, soya milks and soya allergy.

6. Rice milk should not be used under age 4.5 years due to its natural inorganic arsenic content.
# Recommended calcium intake*

<table>
<thead>
<tr>
<th>Age</th>
<th>Adequate intake (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12 months</td>
<td>525</td>
</tr>
<tr>
<td>1–3 years</td>
<td>350</td>
</tr>
<tr>
<td>4–6 years</td>
<td>450</td>
</tr>
<tr>
<td>7–10 years</td>
<td>550</td>
</tr>
<tr>
<td>11–14 years (male)</td>
<td>1000</td>
</tr>
<tr>
<td>11–14 years (female)</td>
<td>800</td>
</tr>
<tr>
<td>15–18 years (male)</td>
<td>1000</td>
</tr>
<tr>
<td>15–18 years (female)</td>
<td>800</td>
</tr>
</tbody>
</table>

*UK recommendations differ from those of other countries (e.g. US).
Home reintroduction should not be attempted if any of the following features are present:

1) Previous cow’s milk allergy symptoms that significantly affected breathing [cough, wheezing, or swelling of the throat, for example cough, stridor, or choking sensation or throat tightness (in older children)], the gut (i.e. severe vomiting or diarrhoea), or the circulation (faintness, floppiness or shock).
2) A less severe reaction with only trace exposure.
3) Regular asthma preventative inhaler treatment and/or poorly controlled asthma.
4) Multiple or complex allergy.
5) No significant reduction in SPT wheal diameter/sIgE level since diagnosis.
6) High sIgE levels without history of any prior milk exposure (e.g. exclusively breastfed or hypoallergenic formula fed infants with severe eczema).
7) Parents who are unable to comprehend or adhere to the protocol.
8) Children with any of these features should undergo a supervised challenge in hospital.
9) In children at highest risk, a supervised baked milk challenge is preferable.
Problems:

- Inadvertent intake (labeling and level of dietary education);
- Misconceptions about safety of partially hydrolyzed formula, heated milk products, or homologous nonbovine milk formula (eg, goat’s milk formula);
- Taste aversion for treatment formula;
- Poor intake and feeding difficulties or refusal to feed;
- Risk of decreased growth velocity;
- Other confounding food allergies (eg, egg, soy, or wheat).
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La dimensione del problema

La dieta con latti speciali qualcosa di nuovo?

Lo svezzamento

Le scelte possibili

Conclusioni
Hypoallergenicity of an extensively hydrolyzed whey formula. Giampietro, PAI 2001

32 children with proven CMA tested with the extensive hydrolysate whey formula Nutrilon Pepti, Profylac extensive) and Nan HA (partial) whey hydrolysate.

Skin-prick tests (SPTs)

Oral challenge

% of SPTs positivity

- Nutrilon Pepti: 19%
- Profylac: 15%
- Nan HA: 32%
Hypoallergenicity of an extensively hydrolyzed whey formula. Giampietro, PAI 2001

32 children with proven CMA tested with the extensive hydrolysate whey formula Nutrilon Pepti, Profylac extensive) and Nan HA (partial) whey hydrolysate.

Skin-prick tests (SPTs)

Oral challenge

Tolerance after oral challenge

Nutrilon Pepti: 97%
Profylac: 94%
Nan HA: 64%
Most cases of cow’s milk allergy are able to ingest a partially hydrolyzed formula.  

Wheal diameter after skin prick testing with cow’s milk, partially hydrolyzed formula (phCMF), and extensively hydrolyzed formula (ehCMF) in children with cow’s milk allergy who did (n 13, gray bars) or did not develop (n 40, white bars) allergic reactions from the oral provocation test with phCMF.
1.
A seven month-old female presented with concern for milk allergy.

She had been breastfed until age ten weeks and then transitioned to a partially hydrolyzed whey formula (pHWF), Gerber Good Start Gentle®, which she was tolerating well. She had also been successfully introduced to fruits (including bananas), vegetables, and grains.

At age six months, she ingested banana yogurt. Within five minutes, she developed a dry cough, vomiting, and hives over 90% of her body.

Her parents immediately brought her to the pediatrician, who administered oral steroids and antihistamines, and her symptoms resolved. No epinephrine was administered.
2.

A local allergist performed skin testing with the following results (wheal mm/flare mm): plain yogurt 14/30, banana yogurt 12/22, CM 4/8, fresh banana 5/14, commercial banana extract 0/0. Serum specific IgE (sIgE) levels sent to an outside commercial laboratory were: milk 8.01 kUA/L, casein 23.4 kUA/L, alpha-lactoglobulin <0.35 kUA/L, beta-lactoglobulin <0.35 kUA/L, banana <0.35 kUA/L.

The allergist switched from pHWF to an amino acid-based formula, Nutricia Neocate®, and to avoid bananas. The patient did not like the taste of the amino acid-based formula, and her parents became concerned
The patient was then evaluated in our clinic. Skin testing at our practice showed (wheal mm/flare mm): histamine 6/12, saline 0/0, commercial banana extract 4/0, pHWF 2/0. Based on her history, sIgE and skin test results, we diagnosed her with casein-specific CM allergy.

We advised that the patient resume pHWF but to avoid all other CM.

At follow-up several weeks later, she was back on pHWF and eating bananas with appropriate growth.
Profile of milk allergic patient tolerating partially hydrolyzed whey formula. T Lee, JACI prat 2015; 3:116

Casein and whey (α-lactalbumin and β-lactoglobulin) are the main proteins in CM (column CM). pHWF has no casein proteins (column pHWF). The case patient's serum showed binding to only casein proteins in CM (column Pt-pHWF), and no binding to any proteins in pHWF (column Pt-pHWF).
Some patients may be sensitized to individual milk proteins only. In this case, the patient had a casein-specific allergy and was able to tolerate pHWF, which was a more palatable and economical choice. As she had been tolerating pHWF for many months, the initial allergist's advice to switch her to an amino-acid based formula was not necessary and she could have continued on pHWF.

A specific teaching point from this case is that patients should continue tolerated dietary exposures, and test results need to be appropriately interpreted.
Overview recent studies investigating immunomodulating effects of hydrolysates

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year of publication</th>
<th>Described effects</th>
<th>Type of studies</th>
<th>Species in vivo studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iskander et al.</td>
<td>2013</td>
<td>Decline in the LPS-induced IL-8 production in respiratory epithelial cells after the administration of whey protein hydrolysates</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Nielsen et al.</td>
<td>2012</td>
<td>Decrease in expression of inflammation markers in casein hydrolysate treated epithelial cells</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Swiatecka et al.</td>
<td>2012</td>
<td>Hydrolyzed pea protein decreased IL-8 production in CaCo2 cells</td>
<td>In vitro</td>
<td>–</td>
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<tr>
<td>Oseguera-Toledo et al.</td>
<td>2011</td>
<td>LPS-activated macrophages showed a decrease of inflammation markers after administration of hydrolyzed common bean protein</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>de Mejia</td>
<td>2009</td>
<td>Lunasin inhibited inflammatory markers and reduced the production of IL-6 and IL1β in macrophages</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Wong et al.</td>
<td>1989</td>
<td>Whey hydrolysates enhanced proliferation in murine spleen lymphocytes</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Knipping et al.</td>
<td>2012</td>
<td>Whey hydrolysates did not show individual effects on specific cytokines</td>
<td>In vitro</td>
<td>–</td>
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<tr>
<td>Mao et al.</td>
<td>2007</td>
<td>Yak milk hydrolysate increased Th1 cytokine expression, but did not affect Th2 cytokines</td>
<td>In vitro</td>
<td>–</td>
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<tr>
<td>Cian et al.</td>
<td>2012</td>
<td>A seaweed hydrolysate increased IL-10 production in splenocytes, macrophages and T cells.</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Lahart et al.</td>
<td>2011</td>
<td>A casein hydrolysate increased IL-10 production in T cells.</td>
<td>In vitro</td>
<td>–</td>
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<tr>
<td>Duan et al.</td>
<td>2012</td>
<td>β-Lactoglobulin trypsin hydrolysates increased IL-10 production in splenocytes from sensitized mice</td>
<td>In vitro</td>
<td>–</td>
</tr>
<tr>
<td>Ndiaye et al.</td>
<td>2017</td>
<td>Increased amount of IL-10+ cells in the small intestine lamina propria after oral administration of yellow pea protein hydrolysate</td>
<td>In vivo</td>
<td>Mice</td>
</tr>
<tr>
<td>Visser et al.</td>
<td>2012</td>
<td>Decreased in lactulose:mannitol ratio (also compared to AA diet) after casein hydrolysate diet</td>
<td>In vivo</td>
<td>Rats</td>
</tr>
<tr>
<td>Visser et al.</td>
<td>2010</td>
<td>After casein hydrolysate diet</td>
<td>In vivo</td>
<td>Rats</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• decreased lactulose:mannitol ratio</td>
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<tr>
<td></td>
<td></td>
<td>• increased transepithelial electrical resistance in an ileum sample (ex vivo)</td>
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<tr>
<td></td>
<td></td>
<td>• mRNA expression tight junction genes were normalized</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• IL-10 upregulation</td>
<td></td>
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<tr>
<td>Tavares et al.</td>
<td>2013</td>
<td>Anti-inflammatory effects from a whey hydrolysate were observed using a paw edema test</td>
<td>In vivo</td>
<td>Mice</td>
</tr>
<tr>
<td>Wu et al.</td>
<td>2006</td>
<td>IFN-γ/IL-4 ratio increased in spleen T cells from mice fed with chitosan</td>
<td>In vivo</td>
<td>Mice</td>
</tr>
</tbody>
</table>
Peptide IT focuses on the properties of fragmented allergens, which contain T-cell-stimulating epitopes but are not capable of cross-linking IgE on basophils and mast cells. Peptides represent a safer alternative to full allergens, as they produce fewer side effects and increase adherence to therapy.

T-cell epitope-mapping is the determination of the specific peptide sequences recognized by CD4+ T cells. This can be performed by different methods but, in all cases, it needs to be checked that as many as possible distinct MHC-II molecules, representative of the HLA genotypic frequencies of the patient population of interest, recognize and bind the selected epitopes. There is a minimum core sequence of 9 to 15 amino acids required for recognition by reactive T cells. Consequently, even if linear, soluble, 15-mer IgE-binding peptides are unlikely to act as full epitopes and cause allergic reactions.
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La dimensione del problema
La dieta. Ma cresce?
Lo svezzamento
Le scelte possibili
Conclusioni

diego.peroni@unipi.it
96 children (mean age 4.7) with food allergies.

95 paired controls.

Z scores for weight-for-age, height-for-age and weight-for-height.

Z-Score weight-for-age

0.6

p<0.05

0.1

Food Allergic  Controls
Children with 3 or more food allergies were smaller than those with 2 or less food allergies ($p = 0.04$).
Milk allergy is associated with decreased growth in US children. Robbins KA, JACI 2014;134:1466

- Anthropometric measurements and dietary intake of calcium, vitamin D, total calories, protein, and fat between children with and without reported food allergy by using National Health and Nutrition Examination Survey (NHANES).

- 6189 children aged 2 to 17 years.

Weighted box plots of anthropometric features for children aged 2 to 17 years comparing children with milk allergy versus those without milk allergy.
Milk allergy is associated with decreased growth in US children. Robbins KA, JACI 2014;134:1466

Mean total daily vitamin D intake (D2+D3 [IU])

- **Mean**: 212 (YES) vs. 308 (NO)
  - Difference: 96 IU
  - **p-value**: 0.053

Mean total daily calcium intake (mg)

- **Mean**: 802 (YES) vs. 1047 (NO)
  - Difference: 245 mg
  - **p-value**: <0.001
Practical dietary management of protein energy malnutrition in young children with cow’s milk protein allergy.

Meyer PAI 2012

As children with malnutrition are normally consuming a diet deficient in macro- and micronutrients, multiple deficiencies are common. It would therefore be inappropriate to give only energy and protein supplementation without adequate micronutrients in an attempt to reverse wasting or stunting.
Comparison of nutritional content among breast milk, infant formulas, and milk substitutes occasionally given to toddlers

8 oz = 236 mL

Misdiagnosed Food Allergy Resulting in Severe Malnutrition in an Infant 
Alvares M, Pediatrics 2013;132:e229
La dieta del bambino allergico: dai latti speciali allo svezzamento

Diego Peroni
Università di Pisa

diego.peroni@unipi.it

La dimensione del problema
La dieta con latti speciali
Lo svezzamento
Le scelte possibili
Conclusioni
Modifying the infant's diet to prevent food allergy.


Primary Prevention
(prevention of allergic disease in individuals who are not immunologically sensitised)

Secondary Prevention
(prevention of the development of allergic disease or the atopic march in individuals already sensitised)

Before Sensitisation

Sensitisation

Disease manifestation and progression

Tertiary prevention
(the treatment of allergic disease)

Allergic disease
Modifying the infant’s diet to prevent food allergy.

<table>
<thead>
<tr>
<th>Country</th>
<th>Year data collected</th>
<th>Reference</th>
<th>Proportion of infants introduced to solids before 4 months</th>
<th>Proportion of infants introduced to solids after 6 months</th>
<th>Proportion of infants introduced to allergenic foods before 6 months</th>
<th>Proportion of infants introduced to allergenic foods by 8–10 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>2008–2010</td>
<td>Koplin et al(^a)(^34)</td>
<td>4%</td>
<td>5%</td>
<td>69% cow’s milk; 21% hen’s egg; 15% peanuts; 13% tree nuts; 29% soy</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>2003–2006</td>
<td>de Lauzon-Guillain et al(^a)(^35)</td>
<td>~30%</td>
<td>~30%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>2002–2006</td>
<td>Tromp et al(^a)(^36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>2005–2007</td>
<td>de Lauzon-Guillain et al(^a)(^35)</td>
<td>~4%</td>
<td>~10%</td>
<td>57% cow’s milk; 57% gluten (wheat (39%), barley (13%), rye (16%)); 40% soy; 8% egg; 6% fish; 6% kiwi</td>
<td>n/a</td>
</tr>
<tr>
<td>Ireland</td>
<td>2008–2012</td>
<td>O’Donovan et al(^a)(^37)</td>
<td>18% (&lt;17 weeks)</td>
<td>3% (&gt;26 weeks)</td>
<td>54% cow’s milk; 42% wheat; 10% hen’s egg; 19% fish; 6% kiwi; 0.5% peanuts‡</td>
<td>8% (peanuts)</td>
</tr>
<tr>
<td>Portugal</td>
<td>2005–2006</td>
<td>de Lauzon-Guillain et al(^a)(^35)</td>
<td>~5%</td>
<td>~20%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>2010*</td>
<td>Lennox et al(^a)(^38)</td>
<td>43%</td>
<td></td>
<td>70% cow’s milk; 0.9% hen’s egg; 0.5% peanuts; 0.7% soy; 0.2% fish</td>
<td>8% (peanuts)</td>
</tr>
<tr>
<td></td>
<td>2006–2008‡</td>
<td>†McAndrew et al(^a)(^39)</td>
<td>36.6%‡</td>
<td>1.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>2005–2007</td>
<td>Luccioli et al(^a)(^41)</td>
<td>34%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Modifying the infant’s diet to prevent food allergy.

Even well designed observational birth cohort studies cannot determine causality, only associations. Nevertheless, anecdotal or observational evidence points to lower allergy rates in countries where consumption of dietary allergens as complementary foods starts at an earlier age.
The question

Is there a causal relationship between early consumption and reduced risk of food allergy?

3 RCTs have reported fully:

• Solids Timing for Allergy Research (STAR),
• Learning Early About Peanut (LEAP)
• Enquiring About Tolerance (EAT).
The Solids Timing for Allergy Research (STAR) Study enrolled 86 high-risk infants aged 4-6 months with moderate/severe eczema. Infants received egg powder.

At 12 mo. diagnosis of IgE food allergy:
- Egg ingestion group: 33%
- Controls: 51%

P < 0.11
Palmer DJ, Early regular egg exposure in infants with eczema: a randomized controlled trial.

J Allergy Clin Immunol 2013;132:387

The Solids Timing for Allergy Research STAR Study enrolled 86 high risk infants aged 4-6 months with moderate/severe eczema.

Infants received egg powder

At 12 mo. diagnosis of IgE food allergy

But in the active group 31% had an allergic reaction leading to the study being stopped...

The LEAP Study (Learning early about Peanut)

- 530 high risk infants
- moderate/severe eczema and/or egg allergy
- Aged 4–11 mo.
- Open label peanut consumption or placebo
- At 5 yrs DBPCC

Peanut allergy at DBPCC at 5 yrs

- Open label peanut: 1.9% (p < 0.001)
- Controls: 15.7%

530 high-risk infants age 4-11 months were randomized to open label peanut consumption or placebo. Peanut allergy was significantly lower in the open label group compared to controls (1.9% vs. 15.7%, p < 0.001).
The LEAP Study (Learning early about Peanut)

530 high risk infants moderate/severe eczema and/or egg allergy

Aged 4–11 mo.

Open label peanut consumption or placebo

At 5 yrs DBPCC

Peanut allergy in 98 with SPT peanut positivity

10.6% 35.3%

Open label Peanut Controls


p<0.004

The LEAP Study (Learning early about Peanut)

530 high risk infants

moderate/severe eczema and/or egg allergy

Aged 4–11 mo

Open label peanut consumption or placebo

At 5 yrs DBPCC

Findings led to a consensus communication, providing interim guidance on early peanut introduction and the prevention of peanut allergy in high risk

Peanut allergy in 98 with SPT peanut positivity

35.3%
Enquiring about Tolerance (EAT) Study.  
1303 exclusively breast-fed infants who were 3 months of age and randomly assigned them to the early introduction of six allergenic foods (peanut, cooked egg, cow's milk, sesame, whitefish, and wheat; early-introduction group) or to the current practice recommended in the United Kingdom of exclusive breast-feeding to approximately 6 months of age (standard introduction group).
Enquiring about Tolerance (EAT) Study. However, when the analysis was adjusted for adherence to early introduction...

Food allergy at 1 of the 6 foods between 1-3 yrs

- Standard introduction: 6.4% (p<0.03)
- Early introduction: 2.4%

Graph showing the prevalence of allergy across different study groups.
Suggesting introduction of sufficient amounts of allergenic foods into the infant diet at 3-6 months alongside continued breastfeeding may be effective in the prevention of food allergy.

However, poor adherence to the study protocol highlights the challenges around introducing solids into the diets of infants less than 6 months of age.
Randomized controlled trial of early regular egg intake to prevent egg allergy.

D Palmer JACI 2017

The Starting Time of Egg Protein (STEP) trial.

Infants aged 4 to 6 months were randomly allocated to receive daily pasteurized raw whole egg powder (n 407) or a color-matched rice powder (n 513) to age 10 months.

The primary outcome was IgE-mediated egg allergy defined by a positive pasteurized raw egg challenge and egg sensitization at age 12 months.

Infants with IgE-mediated egg allergy

<table>
<thead>
<tr>
<th>Early Introduction</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>7,0%</td>
<td>10,3%</td>
</tr>
</tbody>
</table>

p<NS
Randomized controlled trial of early regular egg intake to prevent egg allergy.

D Palmer JACI 2017

The Starting Time of Egg Protein (STEP) trial.

Infants aged 4 to 6 months were randomly allocated to receive daily pasteurized raw whole egg powder (n=407) or a color-matched rice powder (n=513) to age 10 months. The primary outcome was IgE-mediated egg allergy defined by a positive pasteurized raw egg challenge and egg sensitization at age 12 months...but all infants followed an egg-free diet and cooked egg was introduced to both groups at age 10 months!
Randomized controlled trial of early regular egg intake to prevent egg allergy.

D Palmer JACI 2017

The Starting Time of Egg Protein (STEP) trial.

Infants aged 4 to 6 months were randomly allocated to receive daily pasteurized raw whole egg powder (n 407) or a color-matched rice powder (n 513) to age 10 months.

The primary outcome was IgE-mediated egg allergy defined by a positive pasteurized raw egg challenge and egg sensitization at age 12 months.

Infants who stopped taking the study powder because of a confirmed allergic reaction:

- Early Introduction: 6.1%
- Placebo: 1.5%
Randomized controlled trial of early regular egg intake to prevent egg allergy.

D Palmer JACI 2017

The Starting Time of Egg Protein (STEP) trial.

Infants aged 4 to 6 months were randomly allocated to receive daily pasteurized raw whole egg powder (n 407) or a color-matched rice powder (n 513) to age 10 months. The primary outcome was IgE-mediated egg allergy defined by a positive pasteurized raw egg challenge and egg sensitization at age 12 months.

Clinical implications: Regular intake of egg protein from age 4 to 6 months does not substantially alter the risk of egg allergy in infants without symptoms of eczema.
Findings from randomised controlled trials investigating the timing of commencement of regular inclusion of peanut and/or egg in infant diets on food allergy outcomes:

Enquiring About Tolerance (EAT), Learning Early About Peanut Allergy (LEAP), Beating Egg Allergy Trial (BEAT), Hen’s Egg Allergy Prevention (HEAP), Solids Timing for Allergy Reduction (STAR), and Starting Time of Egg Protein (STEP) trials.
In the EAT trial, the rate of adherence was the highest for dairy products in the form of yogurt, as opposed to textural food such as egg. This difference may well be due to the rather immature oral motor skills of young infants at 3 to 4 months of age and also to concerns of the parents about choking.

**If feeding these foods is safe,**
- What is the minimal amount needed for inducing tolerance to these foods?
- Will the regimen be as effective if we introduce these foods at a later age but early enough before sensitization may occur?
- How can we improve the preparation of foods to make them easier for parents to administer?
Preventing Food Allergy in Infancy — Early Consumption

In the EAT trial, the rate of adherence was the highest for dairy products in the form of yogurt, as opposed to textural food such as egg. This difference may well be due to the rather immature oral motor skills of young infants at 3 to 4 months of age and also to concerns of the parents about choking.

If feeding these foods is safe,-What is the minimal amount needed for inducing tolerance to these foods?
-Will the regimen be as effective if we introduce these foods at a later age but early enough before sensitization may occur?
-How can we improve the preparation of foods to make them easier for parents to administer?

Evidence is building that early consumption rather than delayed introduction of foods is likely to be more beneficial as a strategy for the primary prevention of food allergy. **So feed your children and hope that they will EAT.**
La dieta del bambino allergico: dai latti speciali allo svezzamento

Diego Peroni
Università di Pisa

diego.peroni@unipi.it
Frequency, severity and causes of unexpected allergic reactions to food: a systematic literature review
Versluis A, CEA 2015;45:347-367

1. the main causal foods: peanut, nuts, egg, fruit/vegetables, milk

2. severe reactions and fatalities occur

3. most reactions place at home, but a significant number also place when eating at friends' houses or in restaurants

4. labelling issues, but also attitude and risky behaviour of patients can attribute to unexpected reactions

✓ 24 studies
(18 observational, 6 qualitative)

✓ food allergic patients aged > 12 years

✓ frequency, severity and causes of unexpected allergic reactions to food
Il paziente non sviluppa reazioni allergiche solo se continua ad assumere regolarmente l'alimento. Il cibo può essere ingerito in:
- normali quantità (tolleranza completa)
- piccole quantità (tolleranza parziale)
senza reazioni allergiche anche dopo un periodo di sospensione.

PERMANENTE?

PRIMO PASSO VERSO LA TOLLERANZA?
Schematic representation of the typical approach to OIT. For SLIT, the overall scheme is similar, with far lower goal doses and a somewhat more rapid dose build-up.
**TABLE III. Milk OIT studies**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Design</th>
<th>Samples size</th>
<th>Subject age (y)</th>
<th>Maintenance dose</th>
<th>Duration</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meglio et al^36</td>
<td>2004</td>
<td>Open label</td>
<td>21</td>
<td>6-10</td>
<td>200 mL</td>
<td>6 mo</td>
<td>72% Desensitization to 200 mL of cow’s milk daily</td>
</tr>
<tr>
<td>Longo et al^37</td>
<td>2008</td>
<td>Randomized, open label</td>
<td>30</td>
<td>5-17</td>
<td>150 mL</td>
<td>10-d Rush escalation, 1 y of maintenance</td>
<td>36% Tolerant (≥150 mL) and 54% partially tolerant (5-150 mL)</td>
</tr>
<tr>
<td>Skripak et al^38</td>
<td>2008</td>
<td>Randomized, placebo controlled</td>
<td>13</td>
<td>6-17</td>
<td>500 mg</td>
<td>23 wk</td>
<td>Median OFC threshold increased from 40 to 5,140 mg after OIT</td>
</tr>
<tr>
<td>Narisety et al^31</td>
<td>2009</td>
<td>Open label (follow-up)</td>
<td>13</td>
<td>6-16</td>
<td>500-4,000 mg</td>
<td>3-17 mo</td>
<td>Median OFC threshold of 7,000 mg (with 33% tolerating 16,000 mg)</td>
</tr>
<tr>
<td>Pajno et al^40</td>
<td>2010</td>
<td>Randomized, placebo controlled</td>
<td>15</td>
<td>4-10</td>
<td>200 mL</td>
<td>18 wk</td>
<td>67% Tolerant to 200 mL of cow’s milk</td>
</tr>
<tr>
<td>Martorell et al^39</td>
<td>2011</td>
<td>Randomized, placebo controlled</td>
<td>30</td>
<td>2-3</td>
<td>200 mL</td>
<td>1 y</td>
<td>90% Showing complete desensitization</td>
</tr>
<tr>
<td>Keet et al^25</td>
<td>2012</td>
<td>Randomized, placebo controlled</td>
<td>20 for OIT</td>
<td>6-17</td>
<td>1,000-2,000 mg</td>
<td>60 wk</td>
<td>70% Desensitized to 8-g OFC, SU in 40% after 6 wk</td>
</tr>
<tr>
<td>Wood et al^41</td>
<td>2015</td>
<td>Omalizumab DBPC, open-label OIT</td>
<td>57</td>
<td>7-32</td>
<td>3,300 mg</td>
<td>24 mo</td>
<td>80% Desensitized to 10-g OFC, SU in 42% after 8 wk</td>
</tr>
</tbody>
</table>
### TABLE IV. SLIT studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Food</th>
<th>Design</th>
<th>Sample size</th>
<th>Subject age (y)</th>
<th>Maintenance dose (mg)</th>
<th>Duration</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrique et al</td>
<td>2005</td>
<td>Hazelnut</td>
<td>Randomized, placebo controlled</td>
<td>23</td>
<td>19-53</td>
<td>13.25</td>
<td>8-12 wk</td>
<td>Significant increase in OFC threshold with active SLIT</td>
</tr>
<tr>
<td>Kim et al</td>
<td>2011</td>
<td>Peanut</td>
<td>Randomized, placebo controlled</td>
<td>18</td>
<td>2-10</td>
<td>2.5</td>
<td>12 mo</td>
<td>OFC threshold 20 times greater SLIT vs placebo (median, 1710 vs 85 mg)</td>
</tr>
<tr>
<td>Fleischer et al</td>
<td>2013</td>
<td>Peanut</td>
<td>Randomized, placebo controlled</td>
<td>37</td>
<td>12-36</td>
<td>1.4-3.7</td>
<td>44 wk</td>
<td>70% Receiving peanut SLIT were responders vs 15% receiving placebo</td>
</tr>
<tr>
<td>Keet et al</td>
<td>2012</td>
<td>Milk</td>
<td>Randomized, SLIT vs OIT</td>
<td>10 for SLIT</td>
<td>6-17</td>
<td>7</td>
<td>60 wk</td>
<td>Median OFC threshold increased 40-fold (2458 mg) from baseline</td>
</tr>
<tr>
<td>Narisety et al</td>
<td>2015</td>
<td>Peanut</td>
<td>DBPC SLIT vs OIT</td>
<td>20</td>
<td>7-13</td>
<td>3.7</td>
<td>12 mo</td>
<td>Median OFC threshold increased from 21 to 496 mg</td>
</tr>
<tr>
<td>Burks et al</td>
<td>2015</td>
<td>Peanut</td>
<td>Open label (follow-up)</td>
<td>37</td>
<td>12-36</td>
<td>1.4-3.7</td>
<td>36 mo</td>
<td>Four (10.8%) of 37 desensitized to 10 g of peanut powder, all 4 with SU</td>
</tr>
</tbody>
</table>
**RASH PHASE: in ospedale**

- Durante il primo giorno:
  intervalli di un’ora tra le dosi

- Successivamente:
  intervalli di due ore

- Oxatomide 1 mg/Kg/die
durante tutto il trattamento

4 reazioni gravi  
con necessità di adrenalina im

---

**PROTOCOLLO**

**TABLE III. In-hospital treatment schedule: Rush phase**

<table>
<thead>
<tr>
<th>Day</th>
<th>Dilution</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 drop of CM in 10 mL of water</td>
<td>5 drops, 10 drops, 1 mL, 2 mL, 5 mL, 10 mL</td>
</tr>
<tr>
<td>2</td>
<td>5 drops of CM in 20 mL of water</td>
<td>2 mL, 4 mL, 8 mL, 16 mL</td>
</tr>
<tr>
<td>3</td>
<td>1 mL of CM in 20 mL of water</td>
<td>2 mL, 4 mL, 8 mL, 12 mL</td>
</tr>
<tr>
<td>4</td>
<td>3 mL of CM in 20 mL of water</td>
<td>3 mL, 6 mL, 9 mL, 10 mL</td>
</tr>
<tr>
<td>5</td>
<td>10 mL of CM in 20 mL of water (1:3)</td>
<td>3 mL, 6 mL, 9 mL</td>
</tr>
<tr>
<td>6</td>
<td>10 mL of CM in 10 mL of water (1:2)</td>
<td>3 mL, 6 mL, 9 mL</td>
</tr>
<tr>
<td>7</td>
<td>No dilution: pure CM (1:1)</td>
<td>2 mL, 4 mL, 6 mL</td>
</tr>
<tr>
<td>8</td>
<td>No dilution: pure CM (1:1)</td>
<td>4 mL, 7 mL, 10 mL</td>
</tr>
<tr>
<td>9</td>
<td>No dilution: pure CM (1:1)</td>
<td>8 mL, 12 mL, 15 mL</td>
</tr>
<tr>
<td>10</td>
<td>No dilution: pure CM (1:1)</td>
<td>13 mL, 16 mL, 20 mL</td>
</tr>
</tbody>
</table>

Doses were administered at 1-hour intervals on the first day and at 2-hour intervals on subsequent days (from the second to the 10th day).

CM, Cow’s milk.
Oral desensitization as a useful treatment in 2-year-old children with cow's milk allergy (Martorell: CEA 2011; 41: 1297)

PROTOCOLLO

- Aumento delle dosi in ospedale
- Mantenimento a domicilio
- Totale: 16 settimane
- Monitoraggio stretto

<table>
<thead>
<tr>
<th>Milk (dilution)</th>
<th>Dose (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
</tr>
<tr>
<td>1/100</td>
<td>1</td>
</tr>
<tr>
<td>In hospital</td>
<td>2</td>
</tr>
<tr>
<td>Doses hourly</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Day 2</td>
<td></td>
</tr>
<tr>
<td>1/10</td>
<td>1.6</td>
</tr>
<tr>
<td>In hospital</td>
<td>3.2</td>
</tr>
<tr>
<td>Doses hourly</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Pure</td>
<td>2.5</td>
</tr>
<tr>
<td>Dose maintained at home, with elevation once a week in hospital</td>
<td></td>
</tr>
<tr>
<td>Pure</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>200</td>
</tr>
<tr>
<td>Total 16 weeks</td>
<td></td>
</tr>
</tbody>
</table>

toleranza completa: >200 ml di latte

tolleranza parziale: 20-200 ml di latte

non tolleranza: <20 ml di latte
18 settimane di trattamento

dose raddoppiate

gioni settimana in ospedale

Table 1. Oral Immunotherapy Protocol

<table>
<thead>
<tr>
<th>Day/week</th>
<th>Dose No.</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/1</td>
<td>1</td>
<td>1 drop&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>7/2</td>
<td>2</td>
<td>2 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>14/3</td>
<td>3</td>
<td>4 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>21/4</td>
<td>4</td>
<td>8 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>28/5</td>
<td>5</td>
<td>16 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>35/6</td>
<td>6</td>
<td>32 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>42/7</td>
<td>7</td>
<td>64 drops&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>49/8</td>
<td>8</td>
<td>5 drops&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>56/9</td>
<td>9</td>
<td>10 drops&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>63/10</td>
<td>10</td>
<td>20 drops&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>70/11</td>
<td>11</td>
<td>2 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>77/12</td>
<td>12</td>
<td>4 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>84/13</td>
<td>13</td>
<td>8 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>91/14</td>
<td>14</td>
<td>16 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>98/15</td>
<td>15</td>
<td>32 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>105/16</td>
<td>16</td>
<td>64 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>112/17</td>
<td>17</td>
<td>128 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>119/18</td>
<td>18</td>
<td>200 mL&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Cow’s milk diluted 1:25.
<sup>b</sup> Undiluted CM.
DESENSIBILIZZAZIONE FRUTTA A GUSCIO (es. nocciola):

T0:    giorno 1: prick test, prick by prick, somministrazione per os da 1-2 mg fino a circa 10 mg (ogni 30 min),
       giorno 2: somministrazione per os da 10 fino a circa 25 mg (ogni 30 minuti)

T1:    dopo 2-3 mesi:
       giorno 1: dalla dose “casalinga” fino a 40 mg (ogni 30 min)
       giorno 2: da 40 mg fino a 50 mg (ogni 30 min)

T2:    dopo 4-5 mesi:
       giorno 1: dalla dose “casalinga” fino a 100-120 mg (ogni 30 min)
       giorno 2: da 100-120 fino a 180-200 (ogni 30 min)

T3:    dopo 6-7 mesi:
       giorno 1: dalla dose “casalinga” fino a 300 mg (ogni 30 min)
       giorno 2: da 300 fino a 400 (ogni 30 min)

T4:    dopo 8-10 mesi:
       giorno 1: dalla dose “casalinga” fino a 500 mg (ogni 30 min)
       giorno 2: da 500 fino a 600 (ogni 30 min)

T5:    dopo 12 mesi:
       giorno 1: dalla dose “casalinga” fino a 900 mg (ogni 30 min)
       giorno 2: da 900 fino a 1200 mg (ogni 30 min)

NB: a casa i genitori devono continuare a fare ingerire gli alimenti meglio se tutti i giorni, ma comunque almeno 2-3 volte la settimana. Devono iniziare per le prime 3 volte con la terzultima dose, poi 3 volte con la penultima e poi con l'ultima dose raggiunta in ambulatorio per i 2-3 mesi successivi.

Arrivati ad una dose accettabile per cui anche la contaminazione non sarebbe un problema ci si può fermare
La dieta del bambino allergico: dai latti speciali allo svezzamento

Diego Peroni
Università di Pisa

diego.peroni@unipi.it

La dimensione del problema
La dieta con latti speciali
Lo svezzamento
Le scelte possibili

Conclusioni
Factors augmenting allergic reactions
Niggemann B, Allergy 2014;69:1582

- Augmenting factors may explain why certain conditions lead to **anaphylaxis**.

- Augmenting factors may exhibit 3 effects:
  1) **lowering the threshold**,  
  2) **increasing the severity**, and  
  3) **reversing acquired clinical tolerance**.

- Common augmenting factors are:  
  - physical exercise,  
  - menstruation,  
  - NSAIDs,  
  - alcohol,  
  - body temperature,  
  - acute infections,  
  - antacids.
Therapeutic options may address causative, preventive, pragmatic, or symptomatic considerations:

- avoid the eliciting food
- take an antihistamine before any situation with a possible risk of augmentation
- separate food and sport (at least for 2 h)
- carry an adrenaline autoinjector at all times
### Table 3  Intervention trials with food allergy as a primary or secondary outcome

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Study name</th>
<th>Location</th>
<th>Recruitment status</th>
<th>Identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>The VITALITY trial</td>
<td>Australia</td>
<td>Recruiting</td>
<td>NCT02112734</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Vitamin A supplementation at birth and atopy in childhood</td>
<td>Guinea Bissau</td>
<td>Active</td>
<td>NCT01779180</td>
</tr>
<tr>
<td>PUFAs</td>
<td>DHA to Optimise Mother Infant Outcomes (DOMInO) trial</td>
<td>Australia</td>
<td>Completed</td>
<td>ACTRN12605000569606</td>
</tr>
<tr>
<td>PUFAs</td>
<td>The Infant Fish Oil Supplementation (IFOS) trial</td>
<td>Australia</td>
<td>Active</td>
<td>ACTRN12606000281594</td>
</tr>
<tr>
<td>PUFAs</td>
<td>Can supplementation with <em>Lactobacillus reuteri</em> and omega-3 fatty acids during pregnancy and lactation reduce the risk of allergic disease in infancy? (PROOM-3)*</td>
<td>Sweden</td>
<td>Recruiting</td>
<td>NCT01542970</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Primary prevention of atopic disease by perinatal administration of probiotics</td>
<td>The Netherlands</td>
<td>Completed</td>
<td>NCT00200954</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Influence of probiotics on atopy, immunological responses and gut microflora, follow-up to 5 years</td>
<td>Singapore</td>
<td>Completed</td>
<td>NCT00365469</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Microbiota as a potential target for food allergy</td>
<td>Italy</td>
<td>Recruiting</td>
<td>NCT02087930</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Effect of lactobacillus GG on atopic march</td>
<td>Italy</td>
<td>Recruiting</td>
<td>NCT01891916</td>
</tr>
<tr>
<td>Prebiotic</td>
<td>Prebiotics in the Prevention of Atopy (PIPA)</td>
<td>Italy</td>
<td>Completed</td>
<td>NCT02116452</td>
</tr>
</tbody>
</table>

†Atopic sensitisation.

PUFA, polyunsaturated fatty acid.
### Diet and asthma: vitamins and methyl donors.


<table>
<thead>
<tr>
<th>Potential mechanisms of action</th>
<th>Observational studies</th>
<th>RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vitamin A</strong></td>
<td>Downregulation of oxidative stress and Th2 (allergic) immune responses</td>
<td>Findings from &gt;20 studies (including three birth cohorts) provide weak evidence for an inverse association between dietary intake and asthma (but not wheeze). Prenatal or postnatal vitamin A supplementation was not significantly associated with asthma, wheeze, or FEV1/FVC in children. Intake of vitamin A and D (as cod liver oil) was associated with incident asthma in a study of adults</td>
</tr>
<tr>
<td><strong>Vitamin C</strong></td>
<td>Downregulation of oxidative stress and Th2 (allergic) immune responses</td>
<td>Findings from more than 30 studies of postnatal dietary intake suggest an inverse association between vitamin C intake and asthma in children and adults, with generally consistent results for wheeze and airway responsiveness but not asthma severity. When studies of prenatal dietary intake are reviewed along with those of postnatal intake, weak and inconsistent evidence exists of an association between vitamin C intake and asthma or atopy in children</td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td>Enhanced steroid responsiveness, antiviral properties, upregulation of T-regulatory cells, prevention of gains in adiposity, effects on lung development or function</td>
<td>Results from six of seven birth cohort studies with sample size &gt;750 mother-child pairs support an inverse association between maternal vitamin D status during pregnancy and asthma or wheeze in childhood. Longer follow-up is necessary to properly assess an association with asthma in all six positive studies. Findings from three studies (one longitudinal) suggest that vitamin D insufficiency or deficiency is associated with increased risk of severe asthma exacerbations</td>
</tr>
<tr>
<td><strong>Vitamin E</strong></td>
<td>Downregulation of oxidative stress, airway inflammation, and Th2 (allergic) immune responses</td>
<td>Findings from &gt;20 studies of postnatal dietary intake suggest an inverse association between vitamin E intake and physician-diagnosed asthma in children and adults, with inconsistent results for wheeze, self-reported asthma, and airway responsiveness. When studies of prenatal dietary intake are reviewed along with those of postnatal intake, weak evidence exists of an inverse association between vitamin E intake and asthma or atopy in children</td>
</tr>
</tbody>
</table>

**RCTs** = randomised controlled trials. FEV1 = forced expiratory volume in 1 second. FVC = forced vital capacity. Th2 = type 2 helper T cell.
Personally, I firmly believe that many issues need to be addressed before food immunotherapy should be used in clinical practice. Systemic reactions occur unpredictably during and after treatment, and at present, it appears that OIT actually increases the risk of systemic reactions compared with practicing avoidance.
Food allergen immunotherapy: Current status and prospects for the future.

R Wood JACI 2016; 137: 973.

It is also unclear whether food immunotherapy, which requires frequent visits and close follow-up, is cost-effective compared with food avoidance or even whether long-term quality of life will be significantly improved.
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Diego Peroni
Università di Pisa

diego.peroni@unipi.it
perodiego@gmail.com