How to avoid complete elimination

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Disclosure

I declare that there are no conflicts of interest.
Primary Prevention

• LEAP study for high risk children

<table>
<thead>
<tr>
<th>Skin prick test</th>
<th>Consumption</th>
<th>Avoidance</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>1.9%</td>
<td>13.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive</td>
<td>10.6%</td>
<td>35.3%</td>
<td>0.004</td>
</tr>
</tbody>
</table>


• EAT study for general population

<table>
<thead>
<tr>
<th>Early introduction</th>
<th>Standard introduction</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.6%</td>
<td>7.1%</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Very low dose oral food challenge

• **Usual food allergy management**
• Very low dose OFC to Milk & Wheat
• Heated egg yolk with slightly contaminated with egg white OFC
• Low dose Oral immunotherapy
• Summary
Complete elimination

- Easy to introduce

- Accidental exposure 10-40%/year

- Common food allergens are present in many dishes.

- Complete elimination require correct labeling.
Oral immunotherapy

• Clinical tolerance 25-50%

• Anaphylaxis at home
  10% of patients, 0.05% of doses

• Poor long term adherence over 60% of cases
Very low dose oral food challenge

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• Summary
Stepwise oral food challenge

• Processing (e.g. baking)
  – Baking reduce allergenicity of proteins
  – 70% tolerate baked egg/milk


• Dose
  – Total dose is increased stepwise

### Stepwise oral food challenge

<table>
<thead>
<tr>
<th></th>
<th>Cow’s milk</th>
<th>Wheat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low dose OFC</td>
<td>3 mL heated milk</td>
<td>2 g udon noodles</td>
</tr>
<tr>
<td></td>
<td>10 g butter (100 mg protein)</td>
<td>(52 mg protein)</td>
</tr>
<tr>
<td>Low dose OFC</td>
<td>25 mL heated milk</td>
<td>15 g udon noodles</td>
</tr>
<tr>
<td></td>
<td>(850 mg protein)</td>
<td>(390 mg protein)</td>
</tr>
<tr>
<td>Middle dose OFC</td>
<td>48 g yogurt</td>
<td>50 g udon noodles</td>
</tr>
<tr>
<td></td>
<td>(1700 mg protein)</td>
<td>(1300 mg protein)</td>
</tr>
<tr>
<td>Full dose OFC</td>
<td>200 mL cow’s milk</td>
<td>200 g udon noodles</td>
</tr>
<tr>
<td></td>
<td>(6800 mg protein)</td>
<td>1 slice white bread</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5200 mg protein)</td>
</tr>
</tbody>
</table>

Total dose

Positive rate

0%

100%

Very Low

Tolerance

No reaction

Very Low dose

Tolerance

Allergic reaction

Very Low

Full dose

Tolerance

Food allergy

Tolerance

Allergic reaction

Lower dose

Tolerance

No reaction

Tolerance

Allergic reaction
Very Low dose OFC

32g udon noodles

Amount

Time

0 min

60 min

Low positive rate of Very Low dose OFC to cow’s milk

Low positive rate of Very Low dose OFC to wheat

Tolerance

Very Low dose

Allergic reaction

Can eat

More dose

Positive rate

Total dose

Very Low

Full dose
Very low dose OFC (3mL)

3mL tolerant

3mL reactive

25mL OFC

Complete Elimination

Daily intake

2nd 3mL

25mL OFC

Daily intake
Half of 3mL tolerant tolerated 25 mL of milk.

- 3mL tolerant (n=41)
- 3mL reactive (n=42)

18 subjects (45%)

0 subjects (0%)
Very low dose OFC (2g)

Daily intake

15g OFC

Complete Elimination

Daily intake

2nd 2g

15g OFC

0

6

12 (months)

2g tolerant

2g reactive
Half of 2g tolerant tolerated 15 g of udon

- 2g tolerant (n=32)
- 2g reactive (n=25)

18 subjects (56%)

0 subjects (0%)

(months)
Anaphylaxis at home

<table>
<thead>
<tr>
<th></th>
<th>Very low dose</th>
<th>Dose escalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow’s milk</td>
<td>2.4% to 3 mL heated milk</td>
<td>7.5% to 4-25 mL heated milk</td>
</tr>
<tr>
<td>Wheat</td>
<td>3.1% to 2 g Udon noodles</td>
<td>0% to 3-15 g Udon noodles</td>
</tr>
</tbody>
</table>

Very low dose oral food challenge

- Usual food allergy management
- Very low dose OFC to Milk & Wheat
- Heated egg yolk with slightly contaminated with egg white OFC
- Low dose Oral immunotherapy
- Summary
Heated egg yolk slightly contaminated with egg white (200mg protein)

WE OFC

Half of a heated whole egg (2200mg protein)

1st EYSEW OFC

EYSEW tolerant

WE OFC (Tolerance evaluation)

Complete Elimination

EYSEW reactive

2nd EYSEW

WE OFC

Daily intake

0  12  24  36 (months)
Almost all of EYSEW tolerant tolerated heated hen’s egg

164 subjects (91.6%)

12 subjects (66.7%)
## Persistent egg allergy at 36 months

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EYSEW OFC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EYSEW reactive</td>
<td>4.6 (1.4-15.0)</td>
<td>0.010</td>
</tr>
<tr>
<td>EYSEW tolerant</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Egg IgE per tenfold increase</td>
<td>3.3 (1.3-8.7)</td>
<td>0.013</td>
</tr>
</tbody>
</table>
Limitation

• Cofactors that lower threshold
  (e.g. medications, exercise, acute infection)


• Natural course predictors by very low dose OFC results
Very low dose oral food challenge

- Usual food allergy management
- Very low dose OFC to Milk & Wheat
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- **Low dose Oral immunotherapy**
- Summary
Build-up (12 months) → Complete elimination (2 weeks) → Maintenance

33% in OIT group achieved sustained tolerance to 25 mL

Baseline

0

12 OIT group

Escalation

25 Control group

Follow up

Build up

Complete milk avoidance

Maintenance

2 weeks of milk avoidance

OFC to 3 mL of milk (194 mg)
7 achieved sustained tolerance

P = 0.018

58% vs 16%

OFC to 25 mL of milk (850 mg)
4 achieved sustained tolerance

P = 0.007

33% vs 0%

OFC to 3 mL of milk (102 mg)
4 achieved tolerance

OFC to 25 mL of milk (850 mg)
None achieved sustained tolerance

37 enrolled OFC
**Milk IgE**

**Casein IgE**

**β-lactoglobulin IgE**

(kUa/L)

- **Milk IgE**
  - Pre: 1.0
  - 1M: 10.0
  - 3M: 100.0
  - 6M: 1.00
  - 12M: 0.01
  - p = 0.044
  - n = 12

- **Casein IgE**
  - Pre: 1.0
  - 1M: 10.0
  - 3M: 100.0
  - 6M: 1.00
  - 12M: 0.01
  - p = 0.039
  - n = 12

- **β-lactoglobulin IgE**
  - Pre: 1.0
  - 1M: 10.0
  - 3M: 100.0
  - 6M: 1.00
  - 12M: 0.01
  - p = 0.033
  - n = 12

**Comparison**

- **Milk IgE** vs **Casein IgE**
  - p = 0.047

- **Milk IgE** vs **β-lactoglobulin IgE**
  - p = 0.044

- **Casein IgE** vs **β-lactoglobulin IgE**
  - p = 0.039
Casein IgG

(p = 0.049)

Casein IgG4

(p = 0.037)

(p = 0.026)
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Summary
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- Very low dose OFC let some food allergic patients avoid complete elimination.

- Very low dose intake could improve food allergy.
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