Patient derived data - sources strengths and limitations

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Disclosure

In relation to this presentation,

I declare I have the following potential conflict of interest:

Research collaboration with FARRP, Nebraska

A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (eg. owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise), organisational interests and gifts.
Outline

• Case reports

• Case series

• Explicit low dose studies
Low dose reactivity is common in community reactions

<table>
<thead>
<tr>
<th></th>
<th>Hourihane, 1997</th>
<th>Sicherer, 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>598 (%)</td>
<td>42 (%)</td>
</tr>
<tr>
<td>Inhaled</td>
<td>104 (17)</td>
<td>14 (33)</td>
</tr>
<tr>
<td>Non ingestion</td>
<td>405 (68)</td>
<td>8 (19)</td>
</tr>
<tr>
<td>contact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>89 (15)</td>
<td>20 (47)</td>
</tr>
</tbody>
</table>
Baby death nursery fined

A nursery where an allergic child died after eating a milk product has been fined £60,000 and has been ordered to pay £19,000 costs.

Jigsaw Day Nurseries Ltd was sentenced at Aylesbury Crown Court on Thursday.

Thomas Egan, who was five months old, had been diagnosed with an allergy to all dairy products.

A nurse at the Jigsaw Day Nursery in Browns Wood, Milton Keynes, fed Thomas a breakfast cereal, not realising it contained milk.
IgE profile

Allergen

Dose

Exercise

Reaction

Matrix

Asthma

Medication

Infection

6
Hypothetical dose response curve

Dose of allergenic protein

Severity of reaction

- Severe
- Moderate
- Mild

Asthma

“Normal”

Matrix

Antihist

Hourihane and Knulst 2005
Outline

• Case reports

• Case series

• Explicit low dose studies
7 food related anaphylactic deaths (Yunginger, 1988)

• 3 amounts ingested not specified
• 2 bites of chilli (peanut)
• 1 bite of entrée (peanut)
• 1 bite of cake (peanut)

but what’s a bite?
What’s a bite?
What is the difference?
## Fatal doses (g of ingredient)

<table>
<thead>
<tr>
<th>Number of deaths</th>
<th>Dose</th>
<th>0.001</th>
<th>0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuts (32)</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>13</td>
<td>10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other foods (13)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Fatal doses of nuts and other foods

Pumphrey, unpubl
72 reactions survived: dose not related to severity

Hourihane, unpubl
DBPCFCs inducing severe reactions

Bock 1978

- Peanut
  - 100mg, 1g, 1g, 3g, 8g,

- Milk
  - 750 mg, 2g, 8g

- Egg
  - 200mg, 300 mg

Sicherer 2000

- 1st doses >250mg
- 11% of first dose reactions are severe
Outline

• Case reports

• Case series

• Explicit low dose studies
450 peanut low dose challenges
### Table: Allergenic Foods and Their MEDs

<table>
<thead>
<tr>
<th>Allergenic Food</th>
<th>Total No. of Patients with Objective Symptoms</th>
<th>Lowest MED (mg protein)</th>
<th>Highest MED (mg protein)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut</td>
<td>489</td>
<td>0.1</td>
<td>7900</td>
<td>(7, 15, 17, 27, 32-34, 37, 46-53)</td>
</tr>
<tr>
<td>Cows' Milk</td>
<td>222</td>
<td>3.3</td>
<td>13000</td>
<td>(31, 54-68)</td>
</tr>
<tr>
<td>Egg</td>
<td>110</td>
<td>0.21</td>
<td>7700</td>
<td>(31, 46, 54, 55, 58, 66, 69-73)</td>
</tr>
<tr>
<td>Hazelnut</td>
<td>41</td>
<td>1.0</td>
<td>1400</td>
<td>(36, 74)</td>
</tr>
<tr>
<td>Soybean</td>
<td>43</td>
<td>88.0</td>
<td>27000</td>
<td>(63, 75-77)</td>
</tr>
<tr>
<td>Wheat</td>
<td>37</td>
<td>2.6</td>
<td>2500</td>
<td>(78-80)</td>
</tr>
<tr>
<td>Mustard</td>
<td>33</td>
<td>0.26</td>
<td>240</td>
<td>(81-83)</td>
</tr>
<tr>
<td>Shrimp</td>
<td>25</td>
<td>4600</td>
<td>74000</td>
<td>(46, 84)</td>
</tr>
<tr>
<td>Sesame seed</td>
<td>21</td>
<td>1.0</td>
<td>3100</td>
<td>(31, 85-87)</td>
</tr>
<tr>
<td>Fish</td>
<td>15</td>
<td>10.2</td>
<td>1300</td>
<td>(88, 89)</td>
</tr>
<tr>
<td>Celery</td>
<td>12</td>
<td>14.0</td>
<td>560</td>
<td>(90)</td>
</tr>
<tr>
<td>Lupine</td>
<td>9</td>
<td>50.0</td>
<td>3150</td>
<td>(91-93)</td>
</tr>
</tbody>
</table>

Some foods have been studied more than others.
Do adults react differently to children (>6yrs)?

Hourihane, 2005
Males vs females?

Hourihane, 2005
COMPARISON OF PEANUT IN CHOCOLATE CHALLENGES
31.5% FAT and 22.9% FAT

LOG DILUTION INHIBITOR
% INHIBITION

Peanut flour std.
22.9% fat
31.5% fat

Grimshaw, 2004
In low dose DBPCFC, peanut sp IgE level correlates with severity.

$r = 0.6, p < 0.001$
SpIgE is related to severity of elicited reactions

- Outcome of oral food challenges in children in relation to symptom-eliciting allergen dose and allergen-specific IgE
But spIgE not related to MED
Volunteers find low dose challenges “useful”

Most subjects felt DBPCFC had a positive impact on their lives. *All 3 who reported a negative effect reported increased awareness of peanut hazards (which could be interpreted as a positive effect)."
What is the difference?

Dose...

..possibly!
Take home messages

• Thresholds count for every stakeholder

• Thresholds probably vary with circumstances

• Low dose food challenges should be considered the new gold standard DBPCFC
Threshold dose challenges

• Are here to stay

• Try them

  because

• They are intrinsically safer and

• They yield important new information for all concerned
Thanks to

- Allergy Team in Cork
  - Claire Cullinane, Deirdre Daly,
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  - K Allen, Melbourne

- ILSI
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