### Stem

A GP calls you for advice to request for “RAST” Allergy test - to Sultanas, Raisins, Chocolate and Tomatoes. He informs you he has seen a 32 year old lawyer, who is anxious and thinks she is having reactions to lots of different things. She is demanding that she should have an Adrenaline Auto-Injector and he wants the above tests done to reassure her.

You arranged to see the patient in the clinic. She informs you that the first episode happened at around 10:30 in the night when she ate a handful of dry sultanas and within 20 minutes developed significant itching of the palms, facial swelling and a generalised rash, she went to the local A&E, and was treated with antihistamines and steroids. When she woke up next morning, she continued to have significant facial swelling and it took about a further two days for the symptoms to completely resolve.

Since then she has had several similar episodes with various different foods:

1. A chocolate dessert (Gu desert)
2. Mediterranean vegetables with cherry tomatoes
3. Del Monte prepared fruit (piece of pineapple and melon)
4. Chicken kebab dish (with salad + tomato + cucumber + lettuce)
5. Mustard mayo
6. Jamaican bun with raisins
7. Ribena (kind of grape juice)
8. Tesco white chocolate plus strawberry sponge cake

She has attended A&E 6 times with similar episodes.
<table>
<thead>
<tr>
<th>Part</th>
<th>Question</th>
<th>Answer</th>
<th>Marks</th>
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</thead>
</table>
| a)   | What additional information would you need to explore in the clinic? | • Temporal relationship of onset / sequence of symptoms with each of the foods  
• Clarify symptoms and signs (angioedema, wheeze, blood pressure, SaO2)  
• Is there a history of hay fever – spring vs summer  
• Is there a history Asthma – establish severity (use of relievers, admission with asthma attacks)  
• Explore OAS/PFS  
• Establish difference in tolerance of cooked and processed foods.  
• Cofactors’ impact on symptoms : Alcohol, Exercise, NSAIDs, Infection  
• Ethnicity  
• Serum tryptase | 1 1 0.5 +0.5 0.5 +0.5 1 1 1 1 9 |
| b)   | What is your diagnosis / differential diagnosis? List all the possibilities given the clinical scenario | • nsLTP Allergy  
• Allergy to Cross reactive allergen component  
• Food allergy with a potential co-Factor (FDEIA spectrum)  
• Allergy to an unknown allergen  
• Idiopathic Anaphylaxis  
• Spontaneous Urticaria and Angioedema  
• Systemic mastocytosis | 2 1 1 1 1 1 1 8 |
| c)   | What allergy investigations should be performed in this scenario? | Skin prick tests (aeroallergens and relevant foods)  
• Specific IgE testing  
• Allergen component panels (components, ISAC)  
• Total IgE  
• Baseline serum tryptase | 0.5 + 0.5 1 1 1 1 1 5 |
| What are the advantages and limitations of each type of testing? | **Specific IgE**  
Advantages  
- No risk of systemic reaction  
- Multiple tests from a single sample  
- No interference from drugs  
- No interference from dermatographism  
Limitations  
- Predictive values variable  
- Variable specificity and sensitivity  
- CCD interference  
- Challenges in interpretation in patients with high Total IgE  
- Differences in Antigen: Native and Recombinant proteins  
- Differential performance in different platforms (Immunocap, Hycor, Siemens)  
- Limited range  
- Not helpful in non-IgE-mediated reactions | 0.5  
0.5  
0.5  
0.5  
0.5  
0.5  
0.5  
0.5  
6 |
---|---|---|
| **Microarray / Macroarray Specific IgE testing by Panels (ISAC / ALEX)** | Advantages:  
- Improved antigen specificity  
- Clarity True food allergy (Species specific) Vs Cross reactive allergy  
- Multiple tests from a single sample  
- No CCD interference in recombinant proteins | 0.5  
0.5  
0.5  
0.5 |
- **Species specific allergens (e.g.)**
  - Ovomucoid
  - Omega-5-gliadin
  - Ara h1, h2, h3

- **Cross reactive allergens (e.g.)**
  - PR10 – Ara h8, Cor a1, Mal d1, Pru p1
  - nsLTP – Ara h9, Pru p3, Cor a8
  - Profilins
  - Tropomysin
  - Albumin

**Limitations:**
- False positives
- Incidental detection of sensitisation
- Challenges in interpretation in patients with high Total IgE
- Differences in Antigen : Native and Recombinant proteins

### Skin prick test
- Skin prick testing (SPT) with extracts
- Prick Prick testing (PPT) with Foods for which there are no available extracts

**Advantages:**
- Quick/instant result (SPT & PPT)
- Ability to test foods for which there is no standard extract (PPT)
Limitations:
- Sensitivity/specificity variable depending on food [False positives and False negatives]
- Small risk of systemic reaction
- Dermatographism can affect interpretation
- Not helpful in non-IgE-mediated reactions
- Limitations in some patients by available skin (eczema etc)
- Lack of standardisation / variability in PPT
- Affected by other drugs (0.5 bonus mark for mentioning one drug)
  - Antihistamines
  - Antidepressants/Antipsychotics
  - Topical steroids
  - Antiemetics (prochlorperazine)

You will be provided some more information during the viva and will be asked four more questions.

1. What laboratory investigations would you like to do for this patient and why?

Information to be provided to the candidates during the viva

Result 1
Result 2

2. Comment on the results

- ISAC Profile looking for Cross-reactive allergen components
  OR

- Specific IgEs to look for Cross reactive allergen components – nsLTP / PR10 / Profilins

- Raised tryptase consistent with MC degranulation, return to
3 Discuss nsLTP Allergy. What food avoidance measures do you advise to someone with nsLTP allergy?

- ISAC result consistent with nsLTP sensitisation
- Clinically consistent with LTP allergy
- Lists examples of foods which contain nsLTP (Peach, Grapes, Peanut, Hazelnut, Tomatos, Kiwi, Sunflower, Wheat etc)
- nsLTPs have high thermal and proteolytic stability
- nsLTP is a PR14 protein
- Recognises nsLTP is widely distributed in plant kingdom: in multiple foods and it is very challenging to provide food avoidance advise in this scenario
- WHO /IUIS Allergen Nomenclature website for nsLTP
- Recognises potential for severe anxiety around foods
- Recognises potential risk of adverse impact on nutrition because of multiple food avoidance
- Able to answer why one may be able to tolerate some nsLTP containing foods but not others – difference in nsLTP epitopes, difference in thresholds
- Will depend on the clinical presentation, indicated if severe reactions

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<tbody>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>57</td>
</tr>
</tbody>
</table>
## CASE – 32 Year lawyer

### 1. Summary of positive IgE results

<table>
<thead>
<tr>
<th>Mainly species-specific food components</th>
<th>Arginine kinase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrimp</td>
<td>Pen m 2</td>
</tr>
<tr>
<td></td>
<td>0.4 ISU-E</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cross-reactive components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid transfer protein (nsLTP)</td>
</tr>
<tr>
<td>Hazelnut</td>
</tr>
<tr>
<td>Walnut</td>
</tr>
<tr>
<td>Peach</td>
</tr>
<tr>
<td>Mugwort</td>
</tr>
<tr>
<td>Plane tree</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ISAC Standardized Units (ISU-E)</th>
<th>Level</th>
</tr>
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<tbody>
<tr>
<td>&lt; 0.3</td>
<td>Undetectable</td>
</tr>
<tr>
<td>0.3 - 0.9</td>
<td>Low</td>
</tr>
<tr>
<td>1 - 14.9</td>
<td>Moderate / High</td>
</tr>
<tr>
<td>≥ 15</td>
<td>Very High</td>
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</tbody>
</table>
Result 2

The serum mast cell tryptase was measured on one occasion in A&E and was 30 ng/mL, and it was 4 ng/mL when measured in the Allergy clinic (reference range 2-14 ng/ml).