Food Diagnostics and Food Allergy Immunotherapy

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Misconceptions

• Skin testing can only be done (or is only accurate) for children above 2 years or above 5 years of age.

• All types of IgE testing (serum, skin, intradermal) are equivalent in the information they provide

• Allergy testing provides you with severity or degree of allergy; how allergic the patient is

Case 1:
Recently transferred to your practice.
• 2 year old AA male with eczema
• Concerns that food allergy might be a trigger
• Request allergy evaluation
• Prior labs show multiple sensitizations
Case 1

What do you advise?

- Repeat serological testing?
- Referral to nutrition due to multiple food allergy and restrictive diet?
- Screen for additional sensitizations with IgG testing?
- Referral to allergist for skin prick testing?
- Provide parents with information and advise them to continue with dietary restrictions?
- A & E?

Treat the patient not the labs

In general, the sensitivity of serological tests ranges from 60% to 90% and their specificity from 30% to 90%, with a concordance among different immunosassays of 75% to 80%.

- 80% positive sensitization on serological testing
- Only about 20% with clinically relevant food IgE

"Gap" likely due to intrinsic factors or aeroallergen sensitization(s)

American Academy of Pediatrics

What you need to know about the new guidelines for the diagnosis and management of food allergy in the U.S.

2007 Publication

- Discouraged using sIgE to diagnose food allergy
- Discouraged use of "food panel"
- Offered suggestions on when to consider evaluation in pediatric patients

Overview

- The Guidelines, sponsored by the AAO (American Academy of Allergy, Asthma & Immunology) and the AAP (American Academy of Pediatrics), provide recommendations on the diagnosis and management of food allergy.

Definitions

- Food allergy was defined as an adverse health effect occurring from a specific food.
- Food allergens are substances in food that cause immediate adverse reactions in allergic individuals through a reaction of the immune system.

Sensitization and Natural History

- Food allergy is more common in children than adults, but many allergies eventually resolve.
- Allergy to cow’s milk is most common in infants and resolves by the age of 5 years, but may last into the teenage years.

http://www2.aap.org/sections/allergy/allergy_guidelines_final_1.pdf

2007 Publication

- Discouraged using sIgE to diagnose food allergy
- Discouraged use of "food panel"
- Offered suggestions on when to consider food allergy evaluation in pediatric patients.
**IgE Testing Caveats**

- Broad food panels have been shown to have false-positive rates higher than 50%—i.e., in more than half of cases, positive results have no clinical relevance.

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**Allergy**

- Inappropriate Immune Response
- Hypersensitivity reaction (Gel Coombs Classifications)
  - **Type I: Classical Allergy**
    - Short Onset
    - Atopy
    - IgE Bound to Mast cells
  - **Type II: Antibody Dependent/Cytotoxic**
    - IgE/MAC, Complement
    - Antibody binds to cell
  - **Type III: Immune Complex**
    - IgG, Neutrophils
  - **Type IV: Delayed**
    - Cell Mediated

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**IgE Allergy**

- Allergic Reactions
  - Exaggerated or inappropriate immune response
  - Typically IgE & histamine mediated
    - Immediate
    - Onset typically within 30 minutes
  - Due to protein or allergen
    - Protein antigen (i.e. cat or peanut)
    - Fc Epsilon receptor II or FcεRI
    - Histamine
Types of Adverse Food Reactions

**Immediate (typically)**
- Anaphylaxis (systemic)
  - Hives
  - Wheezing
  - Hypotension

**Oral Allergy Syndrome (localized)**
- Itching
- Rash
- Swelling

**Delayed (typically)**
- Celiac Disease
- Heiner's Syndrome
- MPIES (milk induced enterocolitis)
- FPIES
- Dermatitis herpetiformis

**Mixed Immediate & Delayed**
- Eczema
- Eosinophilic Esophagitis

**Immune Mediated Reactions**

**Non-Immune Mediated Reactions**
- Metabolic
  - PKU
  - Galactosemia
  - Fructosemia
- Organic Disease
  - GERD
  - Achalasia
  - Hiatal Hernia
- Infectious
  - Food Poisoning
- Lactase Deficiency

IgE Allergy

Sensitization does not equal clinical allergy!

- **Sensitization**
  - Production of relevant IgE antibody to allergen, not necessarily indicative of clinical reactions

- **Spectrum of Clinical Reactions**
  - **Localized Reactions**
    - Oral Allergy Syndrome
    - Contact Reactions
  - **Organ Specific Reactions**
    - Eczema
    - Eosinophilic Esophagitis
  - **Anaphylaxis**
    - Multiple organ systems involvement

IgE Allergy Testing

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Diagnostic of IgE Food Allergy</th>
<th>Demonstration of IgE Sensitization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin prick testing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>• Scratch or percutaneous testing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>• Intradermal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serological testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• sIgE (specific IgE)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>• RAST, EIA, Immunocap</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>• Component testing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>• Microarray</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Clinical testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food Challenge</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Serum IgG</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Atopic Patch testing</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>ALCAT (antigen leukocyte antibody test)</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
**IgE Allergy Testing**

- **Sensitivity**
  - True positive rate
  - Number of who test positive (affected) from total number of truly positive individuals
  - A highly sensitive test has few false negatives

- **Specificity**
  - True negative rate
  - Number of who test negative from total number of truly negative individuals
  - High specific test has few false positives

- **Positive Predictive Value**
  - Number of truly positive individuals results in the total number of test positive

- **False Positive**
  - Incorrect positive result for an individual who does not have clinical symptoms.

**In vitro IgE allergy testing**

Detection and Wash Count

Plate for Peanut

**slgE testing**

**Scratch/Prick Testing**
- **In vitro**
  - Histamine release from cross-linked IgE bound on mast cells

**Serological Testing**
- **In vivo**
  - Free serum, unbound IgE molecules collected and measured in assay
IgE in vitro Antibody testing

At normal total IgE level, how many keys?

IgE in vitro Antibody testing

At high total IgE level, how many keys?

Elevated total IgE (and other factors) can lead to non-specific binding.

So how to utilize or interpret sIgE values

- Don’t use “Classes (1-6), it’s a trap.
- These have not been shown to have clinical relevance
- Do check total IgE.
- The gives you context
- Characterize and interpret using specific, individualized value(s) for each allergen
Prescott, et al.
- All kids, less than 5 yrs old
- Australia
- Determine sensitization vs clinical reaction.

Prescott, et al.
- Skin prick and sIgE curves based from graded food challenges
- Probability curves created from graded challenges.
- sIgE values can be plotted to give you probabilities or likelihoods.
- Does not tell you severity, threshold or type of reaction(s).

Fig. 2. Probability of a positive challenge test for peanut at a given peanut-specific sIgE (natural log scale).

sIgE Assays
- Clinical cutoffs
- Optimal Decision Points
- Positive predictive values
- Used to trend resolution over time
IgE Allergy Testing

- Clinical cutoffs for likelihood of reaction
- Typically based on age and specific for each food
- Classes (I-VI) are arbitrarily assigned and have no clinical relevance

IgE caveats:
Probability curves vary for food (allergen) to food (allergen).
The relationship is not linear (e.g., 5kU/L does not mean 5% risk of reaction).
Positive predictive value does not equal negative predictive value.

sIgE PPV for sIgE testing

Hamilton et al. 2009. Allergy, Asthma and Clinical Immunology
sIgE typically does not correlate well with severity of reaction.
### IgE Allergy Testing

*Neither tells severity of reaction or threshold for reaction*

<table>
<thead>
<tr>
<th>Test Method</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Prick test</td>
<td>High negative predictive value (&gt;95%)</td>
<td>False positives (sensitized but not clinically reactive)</td>
</tr>
<tr>
<td></td>
<td>Fairly immediate results</td>
<td>Many reagents react to component allergen, not to whole allergen</td>
</tr>
<tr>
<td>Serum IgE</td>
<td>Numerical value to trend</td>
<td>False positives (sensitized but not clinically reactive)</td>
</tr>
<tr>
<td></td>
<td>Assess multiple allergens with one needle stick</td>
<td>Lower specificity than skin prick</td>
</tr>
<tr>
<td></td>
<td>Newer components assays reveal more detailed information</td>
<td>Conventional test measures whole allergen vs component</td>
</tr>
<tr>
<td></td>
<td>Patients can be on meds (eg antihistamines)</td>
<td>Delayed reporting</td>
</tr>
<tr>
<td></td>
<td>Results from various companies may not be equivalent</td>
<td></td>
</tr>
</tbody>
</table>

### Utility of IgE vitro/vivo Antibody testing

**Decision points**
- Skin test results (NPV 95%-99%)
- CAP RAST results—consider challenge if CAP falls to 1/3 of 95% PPV¹

¹Sampson and Ho. *J Allergy Clin Immunol* 1997;100:444-51

### What about total IgE

- As total IgE increases
  - Assay becomes less precise as total IgE climbs
  - As a result less accurate

**Case of 3 y/o with peanut and birch pollen allergy**

![IgE values over time](image_url)
sIgE to IgE ratios?

- Attempts to "normalize" improve predictive value of sIgE, especially in patients with elevated total IgE.
- Many studies are retrospective.
- Prospective studies are often small.
- Or ratios not found to be effective predictors.
- Likely does not account for factors such as binding avidity.

sIgE Caveats

- Skin and serum testing (Sicherer et al. Pediatrics 2011)

<table>
<thead>
<tr>
<th>sIgE Testing Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cliniicians and laboratorians should be aware of inherent problems with currently available allergen-specific IgE tests. Following pre-market review, FDA allows these tests on the market but suggests that manufacturers and distributors include limitations in the labeling (package insert) that accompanies each test kit to the clinical laboratorian/physician.</td>
</tr>
<tr>
<td>A definite clinical diagnosis should not be made solely on the basis of an in vitro allergen-specific IgE test result. Diagnosis should be made by the physician only after all clinical and laboratory findings have been evaluated.</td>
</tr>
<tr>
<td>False positive test results in persons who are tested for food allergies may lead to inappropriate dietary restrictions while false negative results in food sensitive persons may result in anaphylactic reactions of varying severity. Identical results for different allergens may not be associated with clinically equivalent manifestations, due to differences in patient sensitivities and IgE binding capacities.</td>
</tr>
</tbody>
</table>
FDA sIgE caveats

- The results of an allergen-specific IgE antibody test should not be used as a definitive guide to select an initial dose for immunotherapy. Prior to implementing such therapy, a skin test with the planned initial dilution of the immunotherapy should be performed to prove that the patient tolerates administration of this allergenic extract.

- Very low levels of allergen-specific IgE antibodies should be evaluated with caution when total IgE values are above 1000 kU/L.

- A positive result may be due to cross-reactivity with other similar allergens and not to the specific allergen tested. The user should be aware of the possibility of clinical cross-reactivity within an allergen family.

- In food allergies, circulating IgE antibodies may remain undetectable despite a convincing clinical history because these antibodies may be directed toward allergens that are revealed or altered during industrial processing, cooking or digestion and therefore do not exist in the original food for which the patient is tested.

- Latex-specific IgE antibodies may show cross-reactivity with ragweed and certain food allergens such as banana, avocado, kiwi and chestnut. Since a latex assay measures allergen-specific IgE, type IV delayed reaction or irritation from latex will not be detected.

When should patient have food allergy testing?

- The clinician might consider food allergens as triggers of AD more commonly in young infants and children. The clinician should be aware that children less than 3 years of age with moderate-to-severe AD, the Food Allergy Expert Panel suggested consideration of limited food allergy testing if the child has a convincing history of food-related management and topical therapy. The child has a reliable history of an immediate systemic reaction after ingestion of the food, or both.

- The clinician should not consider extensive elimination diets based only on positive skin or specific IgE test results because potential nutritional deficiency can occur, and even with multiple positive skin test results, most patients will react to few foods on oral challenge.

IgE Allergy Testing

- Take Home Points

  - Diagnosis of "allergy" is a clinical diagnosis, not laboratory.
  - Serum and skin prick testing is not diagnostic for allergy
  - Broad "panels" are typically not helpful, should not be used for "screening"
  - Sensitization ≠ Allergy
  - Cross reactions can occur
  - Skin good at ruling out systemic IgE mediated allergy
  - Currently, serological assays good for ruling or confirming
Why all this testing and monitoring?

- Discern the type of sensitization the patient has:
  - Oral Allergy Syndrome
    - Cross reactive protein homologues
    - Localized, not systemic reactions
  - Transient (likely to resolve)
    - Cow’s milk 80%
    - Hen’s egg 75%
    - Wheat 60-70%
    - Soy 60-70%
  - Persistent (less than 50% resolve)
    - Peanuts, Tree nuts, Fish, Shellfish

<table>
<thead>
<tr>
<th>Oral Allergy Syndrome</th>
<th>Transient (% resolution)</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melons</td>
<td>Cow’s milk</td>
<td>Peanuts</td>
</tr>
<tr>
<td>Strawberry/Berries</td>
<td>Hen’s Egg</td>
<td>Tree nuts</td>
</tr>
<tr>
<td>Bananas</td>
<td>Wheat</td>
<td>Fish</td>
</tr>
<tr>
<td>Citrus</td>
<td>Soy</td>
<td>Shellfish</td>
</tr>
</tbody>
</table>

IgE Allergy component Testing

Which patient better candidate for tolerating baked milk in foods?

- Patient 1: beta-lac, Casein, a-lac
- Patient 2: beta-lac, Casein

Milk Components

- Heat stable and comprises 80% of the protein in cow’s milk.
IgE Allergy Testing
Component Testing

- Hen’s Egg
  - Over 20 different proteins
- Egg White
  - Ovomucoid: heat stable
  - Ovalbumin: question of heat stability
  - Conalbumin: heat labile
  - Lysozyme: heat labile
- Egg Yolk
  - Lipovitelin, phospholipids
  - IgG, IgA, IgM

IgE Allergy Testing
Component Testing

- Ara h 1, 2, 3: thought to be most relevant in food allergy in USA, many European countries and Asia
- Ara h 6 found to correlate to food allergy in Asia
- Ara h 9: dominant allergy in Spain
- Ara h 8 is Bet V homologue

Case 2:

IgE Allergy component Testing

Which patient better candidate for tolerating boiled milk?

Patient 1

Patient 2
Case 3:

IgE Allergy component Testing

Which patient is most likely to tolerate a food challenge to peanuts and have sensitization to birch pollen:

Patient 1: total IgE in normal range, sIgE to peanut is 10kU/L, sIgE to Ara h 3 is 1.1U/L, sIgE to Ara h 2 is 8.1U/L, sIgE to Ara h 8 is 1.8U/L

Patient 2: total IgE in normal range, sIgE to peanut is 10, sIgE to Ara h 3 is 1.5U/L, sIgE to Ara h 2 is 1.2U/L, sIgE to Ara h 8 is 7.5U/L

Patient 3: total IgE in normal range, sIgE to peanut is 10, sIgE to Ara h 3 is 6.5U/L, sIgE to Ara h 2 is 0.9U/L, sIgE to Ara h 8 is 2.5U/L
IgE Allergy Component Testing

- Assists with delineation of specific allergens/reactions
  - Localized
    - e.g. oral allergy
  - Systemic
    - e.g. anaphylaxis

Cross Reactive Proteins Across Species

<table>
<thead>
<tr>
<th>Component</th>
<th>Substances (Betas homologues)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birch/Alder (Bet V homologues)</td>
<td>Almonds, apple, apricot, carrot, celery, cherries, coriander, fennel, hazelnuts, kiwi, nectarines, peaches, pears, plums, prunes, potatoes, peppers, parsley, peanuts, walnuts, soy, &amp; peanut.</td>
</tr>
<tr>
<td>Weeds (ragweed/mugwort)</td>
<td>Apple, banana, carrots, celery, chamomile tea, coriander, cucumber, dandelions, fennel, kiwi, melons (cantaloupe, honeydew, watermelon), peanut, parsley, sunflower, peppers, &amp; zucchini.</td>
</tr>
<tr>
<td>Potent lysium (evergreen family)</td>
<td>Cashews, peanut, mango, &amp; plum.</td>
</tr>
<tr>
<td>Grasses</td>
<td>Apple, avocado, banana, celery, cherry, kiwi, melons (oranges, peaches &amp; tomatoes.</td>
</tr>
<tr>
<td>Dust mites (bispomucins)</td>
<td>Cockroaches, crab, lobster, shrimp</td>
</tr>
</tbody>
</table>
IgE Allergy Component Testing

Worldwide variations in the proteins associated with anaphylaxis as well as the number of proteins patients were sensitized to.

Advantages

• More detailed information about relevant proteins
• Help identify candidates for desensitization or challenges
• Help patients who may or may not resolve their allergy

Disadvantages

• Can still be affected by high total IgE levels
• Sensitization patterns may vary based on geography/ethnicity
• Positive predictive clinical thresholds not yet establish

What can be done?

• How can we reduce the incidence of food allergies?
• How can we reduce the prevalence of food allergies?
Early induction of Peanuts (LEAP)

- Noted that Jewish children in England had significantly higher rates of peanut allergy than Jewish patients in Israel.
  - Oral ingestion (immunotherapy suspected)
  - Bamba snacks

Peanut Early Introduction

LEAP
- Conducted in England
- Introduction between 4-11 months of age
- Skin prick positive considered 1-4 mm
  - Skin prick greater than 5mm wheal were excluded.
- Required to ingest at least 1gm of peanuts/week in ITT
- Food challenge at 60 months up to 9.4 g of peanut protein in graduated fashion.

Peanut early Intro

- Peanut allergy prevalence at 60 months:
  - Of 263 patients w (-) Skin prick @ start of trial (initially 530 in intent to treat):
    - 13.7% in the avoidance group
    - 1.9% in the consumption group
  - Of 89 patients w (+) Skin prick @ start of trial (initially 98 in intent to treat):
    - 35.3% in the avoidance group
    - 10.6% in consumption group

- Caveats
  - Skin prick + at 1-4 mm
  - Study conducted in high risk population with history of negative skin prick test results
  - Normal for positive skin prick 3mm greater than negative control
  - No mention of distribution of "positive" responses.
  - Not yet reproduced in other countries
  - Other variables could be at play
  - Adherence was quite high
    - >90%
**Peanut Early introduction**

- **Guideline 1**: If patient has severe eczema, egg allergy or both; he/she should have peanuts introduced as early as 4-6 in conjunction with evaluation by Allergist/Immunologist.

- **Guideline 2**: If patient has mild to moderate eczema, he/she can add peanuts around 6 months per family dietary and preference; no compulsion to introduce peanuts. Assessment of mild to moderate eczema can be done by physician; first ingestion can be done under physician supervision.

- **Guideline 3**: If patients have no eczema or food allergy, one can freely add peanut containing foods to the diet.

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**NIAID Interim Guidelines**

**Recommended Approach for Evaluation of Children With Severe Eczema and/or Egg Allergy Before Peanut Introduction**

- Severe eczema or egg allergy

  - Initial steps
  - 
  
- Continued regular dosing

**Potential Treatments and Therapies**

- Currently no FDA approved therapy

  - **Desensitization**
    - Increasing the threshold dose for allergen needed to induce an allergic reaction while on continued exposure.

  - **Tolerance**
    - Induction of long term loss of reactivity even with cessation of therapy.
    - Induction lasting immunological alterations
    - T regulatory cell and TGF beta/IL-10 have been implicated

  - Initiation of therapy
  - Continued regular dosing
  - Initiation of therapy
  - Interval dosing or cessation in dosing with sustained tolerance
Food Allergy Immunotherapy Variants

• Allergen Specific
  ➢ Relevant to specific allergen
    a) OIT
      i. Oral ingestion
    b) SLIT
      ii. Hold under tongue then swallow
    c) EPIT
      iii. Epicutaneous (placement of patch containing miniscule amounts of allergen on skin).

• Allergen non-specific
  ➢ Global/Systemic
    a) Anti-IgE
    b) Chinese herbs

OIT with Extensively Heated Foods

Milk & Egg primarily
70% of egg allergies & 75% of milk allergy can tolerate extensively heated foods.
- Milk
  - Best if casein sensitization is low or absent
- Egg
  - Best if ovomucoid sensitization is low or absent

OIT with Extensively Heated Foods

➢ Baking denatures relevant proteins

Can sometimes be performed at home
Well tolerated in well selected patients
Studies shown to possible accelerate resolution of allergy
Low rate of significant adverse reactions
Literature suggest this can be performed at home with no office visits.

Only for select foods in select patients
Unclear if induces long term tolerance

OIT

• First reported in 1908
• First large clinical trials for OIT, back in 2000s.
• Varying protocols
  ➢ Initial in office dose escalation
  ➢ Build up phase:
    ➢ Dose at home with in office dose increases every 2 weeks.
  ➢ Home Dosing
  ➢ Ongoing maintenance
• Typically goal is about 2-5 peanuts or ~500mg -1gm
Ingestion OIT, why is this not standard of care?

**Disadvantages**
- Most protocols require in-office challenges for dose increases every 2 weeks.
- Children have activity restrictions.
- Inactivity required for 1-3 hours after each dose.
- Dosing is daily most protocols.
- How to dose in patients with asthma, EGID, concurrent illness.
- Most protocols maintenance dosing is indefinite and remains daily.
- In the literature, has the highest rate of report mild and severe adverse reactions of all therapies.
- Cost of frequent in office visits. Every two during escalation; visits for acute reactions.
- Appears to be falling out of favor for newer, safer, more convenient interventions.

**Peanut OIT Adverse Reactions**
- Hoffman et al.
  - The risk of reaction during:
    - Escalation day 93%.
    - Build up 46%.
    - Home dosing 2.5%.
- Blumenstein et al.
  - Rush peanuts OIT: 17 of 22 subjects could not reach the 500 mg dose of peanuts.
  - 18% of subjects dropped out because of side effects from peanut OIT.
- Jones et al.
  - 92% had reactions during initial day, 10% required epi.
  - In office escalation: 56% reacted, 10% given epi.
  - At home dosing: 10% patients given epi.

**SLIT (sublingual immunotherapy)**
- Similar to Ingestion OIT
- Safer than ingestion OIT
- Dosing is almost daily.
- Most protocols maintenance dosing is indefinite and remains daily.
- In the literature, effects do not appear as impressive as other forms of OIT.
- Does not appear to induce long last tolerance if stopped.
- Appears to be falling out of favor.

**AR101**
- Similar to Ingestion OIT
- Safer than ingestion OIT
- Dosing at home.
- Provides "caution" of 5-7 peanuts.
- Clinical trials showing promising results.
- Dosing is almost daily.
- Most protocols maintenance dosing is indefinite and remains daily.
- Does not appear to induce long last tolerance if stopped.
- Cost unknown.
### Epicutaneous immunotherapy

**EPIT**
- Relevant peanut allergens in proprietary patch
- FDA fast-tracked; slated for release 2018
- Milk patch in fast track trials

#### Advantages (peanuts)
- Safest track record of all current immunotherapies
- No systemic reactions
- Dosing at home
- Patch, placed on back for kids; on arm for teens and adults
- Provides “cushion” of 5-15 peanuts
- Clinical trials showing very promising results
- FDA approval and likely insurance coverage.

### EPIT (peanuts)

#### EPIT Advantages
- Jones et al. 2016
  - 52 week trial
  - Tolerance up to ~15 peanuts in 50% of patients in one trial
  - No adverse events
  - Mild localized reactions
  - More robust response in younger children

#### EPIT Disadvantages
- Currently, maintenance dosing is indefinite and remains daily.
- Unknown if it induces long last tolerance if stopped.
- Cost unknown

### Anti-IgE therapy

- Safest track record of all current oral immunotherapies
- Faster dose escalation: “rush phase”
- Can achieve desensitization of full serving of allergenic food
- Effective for multiple foods (milk, eggs, peanuts, tree nuts, soy, sesame, etc)
- Clinical trials showing very promising results
- Can induce long lasting tolerance when therapy is stopped
- Multiple foods addressed at once.
- Less frequent dosing required
- Does involve injection
- Cost of injection can be prohibitive

- Omalizumab (Xolair) currently only anti-IgE available
- Global attenuation of allergic response
Chinese Herb (FAHF-2)

- TCM (traditional Chinese medicine)
- Mix of proprietary herbs
- Appears to attenuate allergic response globally
- Shows some promise with eczemas

Well tolerated
Patients need to be well selected
Can be used in conjunction with other immunotherapies

Effects do not seem as robust as other immunotherapies
Some protocols involve multiple pills, up to 10, three times a day.
Supplement

Table 1: List of drugs with oral challenge efficacy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Oral challenge efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult, 1st generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetirizine</td>
<td>1 mg</td>
<td>1/6</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>20 mg</td>
<td>1/6</td>
</tr>
<tr>
<td>Pramoxine</td>
<td>25 mg</td>
<td>1/6</td>
</tr>
<tr>
<td>Adult, 2nd generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>60 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Loratadine</td>
<td>10 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>10 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>25 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>25 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Cetirizine/oral antihistamine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast</td>
<td>10 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>20 mg</td>
<td>1/2</td>
</tr>
<tr>
<td>Local antihistaminic DNA vaccine</td>
<td>1 mg</td>
<td>1/2 (but suppresses symptoms)</td>
</tr>
<tr>
<td>Adult, 3rd generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>100 mg</td>
<td>1 dose = 1</td>
</tr>
</tbody>
</table>

References:

- https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/Food-Allergy-Guidelines-Summary.pdf