4:45 – 5:30 pm

Managing Pediatric Food Allergy in 2015

SPEAKER
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Presenter Disclosure Information

The following relationships exist related to this presentation:

- Wayne G. Shreffler, MD, PhD: Consultant for Tunitas Therapeutics. Speaker for Mead Johnson.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

PEDIATRIC FOOD ALLERGY

PRI-MED
EAST ANNUAL CONFERENCE

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FOOD ALLERGY

An adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food – NIAID 2011

- **Adverse reactions to foods**
  - Toxic (e.g., scombroid poisoning)
  - Metabolic (e.g., alcohol flush, MSG symptom complex)
  - Non-toxic
    - Intolerance (e.g., lactase deficiency)
    - Psychological (e.g., anxiety / panic)
    - **Immunological (i.e., allergy)**

THE GUIDELINES: SECTION 2

- **What is a food allergy?**
  - **A food allergy is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.**
  - **Skin testing and serum specific IgE antibodies to detect sensitization to foods provide very sensitive means of identifying foods that *may be* responsible for IgE-mediated food-induced allergic reactions.**
  - **Clinical history is needed and when indicated an oral food challenge**

Target Organ	Immediate Sx	Delayed Sx
Cutaneous	Erythema Pruritus Urticaria / Angioedema	Erythema Pruritus Eczematous rash
Ocular	Periorbital edema Tearing / erythema	
Upper Respiratory	Hoarseness Nasal congestion / rhinorrhea / sneeze	
Lower Respiratory	Cough Wheeze Tightness / Increased effort	Cough, dyspnea, wheeze
GI (oral)	Oral pruritus Tongue swelling Angiodema of lip, tongue, palate	
GI (lower)	Nausea, pain, reflux, vomiting, diarrhea	Nausea, pain, reflux, vomiting, diarrhea, hematochezia, irritability, refusal, weight loss
Cardiovascular	Tachycardia / Bradycardia Hypotension / Dizziness / LOC	
Miscellaneous	Impending doom Uterine contractions	

UNDERSTANDING THE NORMOGRAM

IgE testing (and skin testing) tends to be very sensitive but not highly specific

The higher the sIgE (and the larger the skin test) the greater the specificity

- **LR+ = sensitivity / (1 – specificity)**
- **LR- = (1 – sensitivity) / specificity**
- **For sensitivity of 99% and specificity of 50%:**
  - LR+ = 2
  - LR- = 0.02
- **For specificity of 95% and sensitivity of 30%:**
  - LR+ = 6
  - LR- = 0.15

SENSITIZATION ≠ ALLERGY

Allergen-specific IgE may be present in the absence of clinical allergy

- **In some cohorts and some food allergens, positive sIgE may be present 5x – 10x more often than true disease (e.g., young children with eczema)**
- **IgE may be 'falsely' positive for multiple reasons:**
  - affinity, avidity, specific activity
  - specificity
  - other food specific immune factors (cellular, IgG)
  - other innate immune factors (gut barrier)

IMPROVING UPON TESTING

Affinity, Avidity, Specific Activity

- **Skin testing**
- **Basophil activation testing (not-validated)**

Specificity

- **'Component-Resolved' Diagnostics**

Other specific immune factors

- **Specific IgG, IgA, Patch Testing (not-validated)**

Other innate immune factors

- **Skin and intestinal barrier (not-validated)**

COMPONENT ALLERGEN TESTING

Allergen testing to 'peanut' or 'milk' or 'wheat', etc. is of course actually a test of many individual proteins present in that food – some of which are more relevant than others and some of which can actually contribute substantially to false positives.

CASE STUDY

7 year old boy with a history of a suspected FA reaction at age 3 consisting of several hives after eating birthday cake. He had never knowingly ingested peanuts or tree nuts before that. Testing at the time revealed sensitization to peanut, some tree nuts and sesame. He has avoided all ever since without known accidental ingestion or suspected FA reaction.

He has experienced signs/symptoms of spring AR (birch) for the past 2-3 years, controlled with oral anti-histamine

CASE STUDY

PST: peanut 10/17, almond 8/15, hazel nut 8/15, pistachio 5/17, cashew 3/4, walnut 3/4

Brazil nut and pecan were negative

Peanut specific IgE 10 kU/L

CASE STUDY

Ara h 1	<0.1
Ara h 2	<0.1
Ara h 3	<0.1
Ara h 9	<0.1
Ara h 8	14.6

no symptoms on OFC

ANTICIPATORY PRACTICE

- **Early introduction of potentially allergenic foods may reduce the risk of food allergy.**
- **Judicious use of allergy testing with capacity for OFC, allows for more precise diagnosis and fewer food exclusions.**
- **The introduction of modified allergens for carefully selected children may hasten the development of clinical tolerance.**
- **Food immunotherapy is a promising area of research, but is not yet ready for routine clinical treatment.**
- ***Perceived risk often far outweighs actual risk, can skew effective management and should be actively managed.***

Anagnostou, K. *et al. Arch Dis Child* (2014). doi:10.1136/archdischild-2014-306278

ANTICIPATORY TESTING

- **Testing appropriately for those allergens most likely to co-exist**
  - Peanut allergy in those with confirmed egg allergy
  - Tree nut and sesame in those with confirmed peanut allergy (and patterns within tree nuts)
  - Lentil and chick pea with green pea allergy
- **Not avoiding (or testing) where overlap does not seem to exist**
  - Avoidance of fish with confirmed shellfish allergy (and vice versa)
- **Being prepared to follow through with OFCs and not unnecessarily narrowing the diet**

TERTIARY PREVENTION: BAKED MILK / BAKED EGG

Dietary baked milk accelerates the resolution of cow's milk allergy in children.

- **Kim, J. S. *et al. J Allergy Clin Immunol* 128,** 125–1e2 (2011).

Dietary baked egg accelerates resolution of egg allergy in children.

- **Leonard, S. *et al. J Allergy Clin Immunol.* 130,** 473–80.e1 (2012).

ORAL IMMUNOTHERAPY

Prim Care Respir J 2012; 21(1): 41-49

Primary Care RESPIRATORY JOURNAL

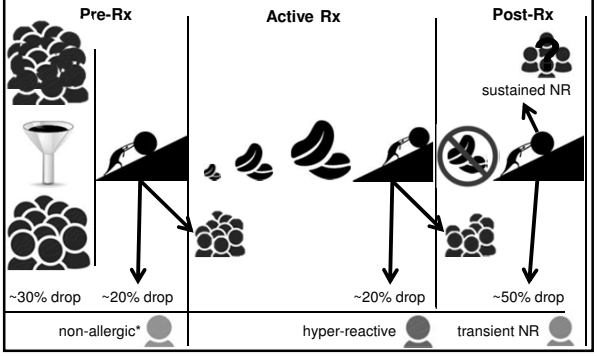
RESEARCH PAPER

Oral immunotherapy for the treatment of peanut allergy: systematic review of six case series studies

***Aziz Sheikh[a], Ulugbek Nurmatov[a], Iris Venderbosch[a], Erik Bischoff[b]**

- 'Desensitization' is achieved in most participants
- Adverse Events are frequent and occasionally serious
- Durable 'tolerance' is the exception, not rule

CHARACTERIZING PATIENTS THROUGH OIT



TERTIARY PREVENTION: RISK MANAGEMENT / REDUCTION

- **Ingestion >>>> Contact**
  - ? Inhalation
- **Adolescence**
  - Risk taking
  - Social conformity
  - ? Endocrine
- **Asthma**
  - Lack of tight control associated with greater reaction severity / airway involvement

WHAT IS MOST LACKING IN MANAGEMENT?

Risk Assessment:

- How allergic??
- How dangerous??
- What are the dangers??
- What is appropriate from a public health perspective?

ASSESSING RISK

RISK

= I + E + D + (IE + ED + ID + IED)

- **I**ntrinsic sensitivity
- **E**xtrinsic modifiers
- **D**ose of exposure

CAN WE BETTER DEFINE THE RISK? ELICITING DOSE

375 peanut allergic individuals 1-21 years old who received an open challenge to 1.5 mg of peanut protein (Boston, Cork, Melbourne)

- ~10X more than major brand cross-contamination
- ~5% of children had some visible reaction
- All reactions were mild and treated with anti-histamine and/or observation
- Allergen component, total IgE, IgG and Basophil reactivity being analyzed

CAN WE BETTER MANAGE THE PERCEPTION OF RISK?

- Contact exposure is much lower risk
- Ingestion of 10's – 100's mg protein is the primary concern for potentially severe reactions

CAN WE BETTER CONTEXTUALIZE THE RISK?

Sarah Gitlin New York 8 December 2013

"This post fails to take something crucial into account: death numbers for food allergies are low not because food allergies are not severe, but because parents and children with life-threatening food allergies are always hyper-vigilant.

Without such strict avoidance, and without always making sure to have their epi-pens with them at all times, death rates would skyrocket. Therefore, Dr. Boyle's remarks are not only wrong but are **outright demeaning and offensive** for the millions of Americans who know that their food allergies have the very real potential to be fatal with any bite, and would be much more likely to be so the instant they let their guards down. What is much worse, his remarks are outright dangerous. Those of us with food allergies count on the rest of the world to help us stay safe, and **trivializing the severity of our condition imperils broader cooperation**."

http://well.blogs.nytimes.com/2013/12/06/food-allergies-less-deadly-than-accidents/?_r=0

WHY ALLERGISTS SHOULD ENGAGE IN THIS AREA

- Better understanding and managing all aspects of risk as well as the perception of risk will lead to the best possible quality of life outcome
- Research outcomes need to be defined based on quality of life improvement that is appropriately linked to real risk reduction
- We need to help our patients advocate as effectively as possible for public health measures that will go furthest improving their safety and quality of life
- We need to develop better methods and biomarkers for risk in order to better focus interventions and educational resources

KEY TAKEAWAY POINTS

- sensitization ≠ clinical allergy
- component testing will improve specificity, but interpretation will still require clinical expertise
- risk stratification remains an important unmet need
- allergen avoidance early in life is NOT recommended
- immunotherapy for FA ≠ current therapy