

Food Allergy Diagnosis and Management

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Children's National

Allergy and Immunology

Objectives

- Food Allergy Diagnosis and Management
 - Overview of Food Allergy Rates and Symptoms
 - Diagnosis:
 - Importance of the history
 - Diagnostic tools available
 - Interpretation of results and natural history
 - Appropriate referrals
 - Current Food Allergy Guidelines
 - Economic impact of food allergy
- Prevention of Food Allergy (Dr. Sharma)
- Mental Health in Food Allergy (Dr. Herbert)

Food Allergy

- **8% Children** (2.4% multiple, 3% severe reactions)
 - Cow's milk 2.2%
 - Peanut 1.8%
 - Tree Nuts 1.7%
- **5% Adults**
 - Shellfish 1.9% (3.1% in Blacks)
 - Fruits 1.6%
 - Vegetables 1.3%
- Overall increase in the rates of FA over time
- IgE sensitization to food (milk, egg, peanut) have remained stable over the decades (80s/90s vs 2005-06)

-Gupta et al. Pediatrics 2011;128:e9-17

-Sicherer JACI 2014;133:291-307

-McGowan J Allergy Clin Immunol Pract 2016; in press

Risk Factors for FA

- Gender (males in children)
- SES (increased with more affluence)
- Race (Asian and Black children)
- Genetics
- Atopy
- Vitamin D
- Dietary fat – omega-3s
- Obesity (inflammatory state)
- Antacids
- Hygiene/Infections
- Timing and Route of exposure to foods
- Place of birth
 - US born
 - children of immigrants
 - arriving before age 2y
- Microbiome, antibiotic use
- Endocrine disruptors/toxins

-Sicherer JACI 2014;133:291-307

-Keet et al JACI 2012;129:169-175.

IgE Mediated

Disorder	Features	Age	Foods	Natural Hx	Tests
Anaphylaxis	Rapid onset, multiorgan	any	PN, TN, F, SF, Milk, Egg (wheat, soy)	variable	SPT, specific, IgE, Component resolved diagnostics (CRD)
Angioedema/urticaria	20% acute 2% chronic	younger			
GI	Immediate vomiting				
Rhinitis, Asthma	Rarely isolated, inhalation	younger occupational	Wheat, egg, seafood		
Oral Allergy	Oral itching, 1% anaphylaxis	older	Fruits, vegetables	persists	Prick-prick
Delayed Meat Induced	6-8 hour delay rare	α -Gal IgE (CHO moiety)			α -Gal IgE
Food-exercise induced anaphylaxis	Only within 2 hours of exercise rare		Wheat, shellfish, celery	persists	Exercise test SPT, IgE

Persistence vs Resolution of IgE mediated FA

- Higher specific IgE levels
- Larger skin prick test
- Reaction on first exposure
- Atopic Dermatitis Severity
- www.cofargroup.org

Mixed IgE-Cell Mediated

Disorder	Features	Age	Foods	Natural Hx	Tests
Atopic Dermatitis	Food induced in 35% of moderate-severe	Infants>Children >Adults	Egg, milk	resolves	SPT, IgE
Eosinophilic GI disease	Biopsy proven eosinophils in GI tissue, dysphagia, reflux, weight loss, impaction	any	Many, milk 70%	persistent	Empiric diets, EGD + Bx, SPT, IgE

Non-IgE Mediated

Disorder	Features	Age	Foods	Natural Hx	Tests
FPIES	<p><u>Chronic exposure:</u> Emesis, diarrhea, poor growth, lethargy</p> <p><u>Re-exposure:</u> 1.5-2 h delay in emesis, hypotension, lethargy</p>	Infancy-toddlerhood	Milk and soy, Solids: rice, oat, banana, other solid foods	resolves	IgE helps with persistence
Food protein induced proctocolitis	Mucousy bloody stools in infants	infancy	Milk, soy +/-BF	resolves	Empiric diet
Celiac Disease	Autoimmune, enteropathy, malabsorption	any	Gliadin (wheat, barley, rye)	lifelong	IgA -TTG, HLA and biopsies
Heiner Syndrome	Rare, pulmonary infiltrates, FTT, anemia	infancy	milk		Milk IgG precipitins

Possible
peanut
reaction

Panel of
food
specific
IgE levels
positive to
10 foods

Patient
avoids 10
foods that
she was
previously
tolerating
and
peanut

Sees
Allergy 3
months
later

Tolerance
now to
the 10
foods is
unknown

Patients
undergoes
repeat
testing

Multiple
OFCs to
confirm
and go
back to
original
diet

**Total
costs
= \$3-
4K**

Economic Impact of Childhood Food Allergy in the United States

- Purpose:
 - To determine the economic impact of childhood food allergy in the United States and caregivers' willingness to pay for food allergy treatment
- Population:
 - Cross-sectional survey of 1643 US caregivers of a child with a current food allergy
 - Caregivers were asked to quantify the direct medical, out-of-pocket, lost labor productivity, and related opportunity costs

Table 2. Direct Medical Costs of Childhood Food Allergy^a

Characteristic	Children With Visit, % (SE)	Visits per Child, Mean (SE)	Cost, US\$		
			Visit	Child	Overall Annual (in Millions)
Visits					
Pediatrician	42 (2)	.82 (.05)	112 ^b	92	543
Allergist	41 (2)	.79 (.05)	175 ^b	138	819
Pulmonologist	14 (1)	.07 (.01)	175 ^b	12	71
Nutritionist	17 (1)	.16 (.04)	100 ^b	16	96
Alternative provider	17 (1)	.23 (.05)	100 ^b	23	136
Emergency department	13 (1)	.18 (.02)	711 ^c	129	764
Inpatient hospitalization stays	4 (1)	.05 (.01)	6269 ^c	314	1863
Total direct medical costs				724	4292

^a Direct medical costs are medical costs borne by the health care system associated with the prevention, diagnosis, and treatment of food allergies.

^b Source: Hospital Outpatient Prospective Payment System.⁸

^c Source: Patel et al.²

- Direct medical costs = \$4.3 billion

Table 3. Out-of-Pocket Costs of Childhood Food Allergy^a

Variable	% Reporting Cost (SE)	Mean Direct Out-of-pocket Costs, US\$ (SE)	Cost per Child, US\$	Overall Annual Cost (in Millions), US\$
Visits to the physician's office or health clinic (including copays)	52.5 (2.2)	160 (14)	84	499
Visits to the emergency room (including copays)	16.1 (1.6)	247 (42)	40	235
Overnight stays at the hospital	10 (1.4)	411 (182)	41	244
Travel to and from health care visits (including ambulance use; parking expenses)	27.7 (1.8)	91 (14)	25	149
Epinephrine injectors (Epipen, Epipen Jr)	35.9 (1.9)	87 (4)	31	184
Antihistamines (Allegra, Benadryl, Claritin, Zyrtec)	50.8 (2.2)	62 (4)	32	188
Other prescription/nonprescription medication	29.3 (1.9)	122 (13)	36	211
Non-traditional medicine (such as herbal products)	15 (1.6)	123 (30)	19	110
→ Costs associated with special diets and allergen-free foods	37.7 (2.0)	756 (59)	285	1689
Additional/change in child care	6.7 (0.8)	2158 (323)	145	857
Legal guidance	2.3 (0.6)	402 (122)	9	55
Counseling or mental health services	4.5 (0.7)	571 (123)	26	152
Special summer camp	3 (0.7)	702 (183)	21	125
A change in schools was needed due to this child's food allergy	4.2 (0.7)	2611 (497)	110	650
Other out-of-pocket expenses (eg, cleaning supplies, skin care products, transportation)	9.2 (1.1)	396 (86)	36	216
Any out-of-pocket costs	74.3 (2.1)	1252 (90)	931	5516

^a Out-of-pocket costs: medical costs borne by patient associated with the prevention, diagnosis, and treatment of food allergies. Includes all costs associated with protecting the child from exposure to allergens, including special child care arrangements. The out-of-pocket costs exclude the top 1% of reported costs in each category.

- Cost of special diets = largest out-of-pocket cost

Table 5. Comparison of WTP and Total Reported Costs

Characteristic	Annual Costs, US\$			
	Total (in Billions)	Per Child	95% CI	
			Total (in Billions)	Per Child
WTP ^a	20.8	3504	15.7-25.7	2652-4344
Total costs borne by families	20.5	3457	16.7-24.9	2816-4208
Out-of-pocket costs for treatment ^b	5.5	931	4.7-6.4	793-1080
Lost labor productivity	0.77	130	0.53-1.00	89-175
Opportunity costs ^{b,c}	14.2	2399	10.5-18.4	1771-3104
Total direct medical costs	4.3	724	2.8-6.3	472-1063
Total reported costs	24.8	4184	20.6-29.4	3475-4960

Abbreviation: WTP, willingness to pay.

^a The 95% CIs for WTP estimates were computed using linearized SEs while all other 95% CIs were computed with the probabilistic method. Monthly WTP responses greater than \$10 000 have been excluded.

^b Top 1% of responses from each question in these categories has been excluded.

^c Only the maximum of 4 possible responses was used to calculate any job-related opportunity cost.

- Overall economic cost of food allergy was estimated at \$24.8 billion annually (\$4184 per year per child)
 - Annual opportunity costs totaled \$14.2 billion, relating to a caregiver needing to leave or change jobs
- Caregivers were willing to pay \$20.8 billion annually for a theoretical effective food allergy treatment

Economic Impact of Childhood Food Allergy in the United States

- *Take Away Points:*
 - *First study to comprehensively quantify the economic impact of childhood food allergy in the United States*
 - *Childhood food allergy in the United States incurs significant direct medical costs to the US health care system and even larger costs to families with a food-allergic child*

History

- Symptoms (ever occur without the food?)
- Dose of the triggering food
- Form of the food
 - Does the patient tolerate the food in a different form (heated, baked, cooked, dried)
- Timing of the reaction (minutes, hours, days)
- Other factors: viral illness, exercise, NSAIDs
- Response to medications (Benadryl, Epi)
- Has the patient tolerated the culprit food (or related food) SINCE the original reaction

Pearls and Pitfalls

- **Pre-test probability is most important**
 - Consider more likely foods for age
 - Consider DDX – lactose intolerance, non-IgE mediated
- **Tolerated foods need not be tested:**
 - milk, egg, soy, wheat, peanut, tree nuts, fish, shellfish, fruits, vegetables, meats
- **Do not discount a negative test with a convincing history**

Cross- Reactivity and Co-Reactivity

Table 1. Natural History of Food Allergy and Cross-Reactivity between Common Food Allergies.

Food	Usual Age at Onset	Cross-Reactivity	Usual Age at Resolution
Hen's egg white	6–24 mo	Other avian eggs	7 yr (75% of cases resolve)*
Cow's milk	6–12 mo	Goat's milk, sheep's milk, buffalo milk	5 yr (76% of cases resolve)*
Peanuts	6–24 mo	Other legumes, peas, lentils; coreactivity with tree nuts	Persistent (20% of cases resolve by 5 yr)
Tree nuts	1–7 yr; in adults, onset occurs after cross-reactivity to birch pollen	Other tree nuts; coreactivity with peanuts	Persistent (9% of cases resolve after 5 yr)
Sesame seeds	6–36 mo	None known; coreactivity with peanuts and tree nuts	Persistent (20% of cases resolve by 7 yr)
Fish	Late childhood and adulthood	Other fish (low cross-reactivity with tuna and swordfish)	Persistent†
Shellfish	Adulthood (in 60% of patients with this allergy)	Other shellfish	Persistent
Wheat‡	6–24 mo	Other grains containing gluten	5 yr (80% of cases resolve)
Soybeans‡	6–24 mo	Other legumes	2 yr (67% of cases resolve)
Kiwi	Any age	Banana, avocado, latex	Unknown
Apples, carrots, and peaches§	Late childhood and adulthood	Birch pollen, other fruits, nuts	Unknown

It might be prudent to test for foods with high co-reactivity if not being consumed but generally avoid testing foods that are cross-reactive (exceptions)

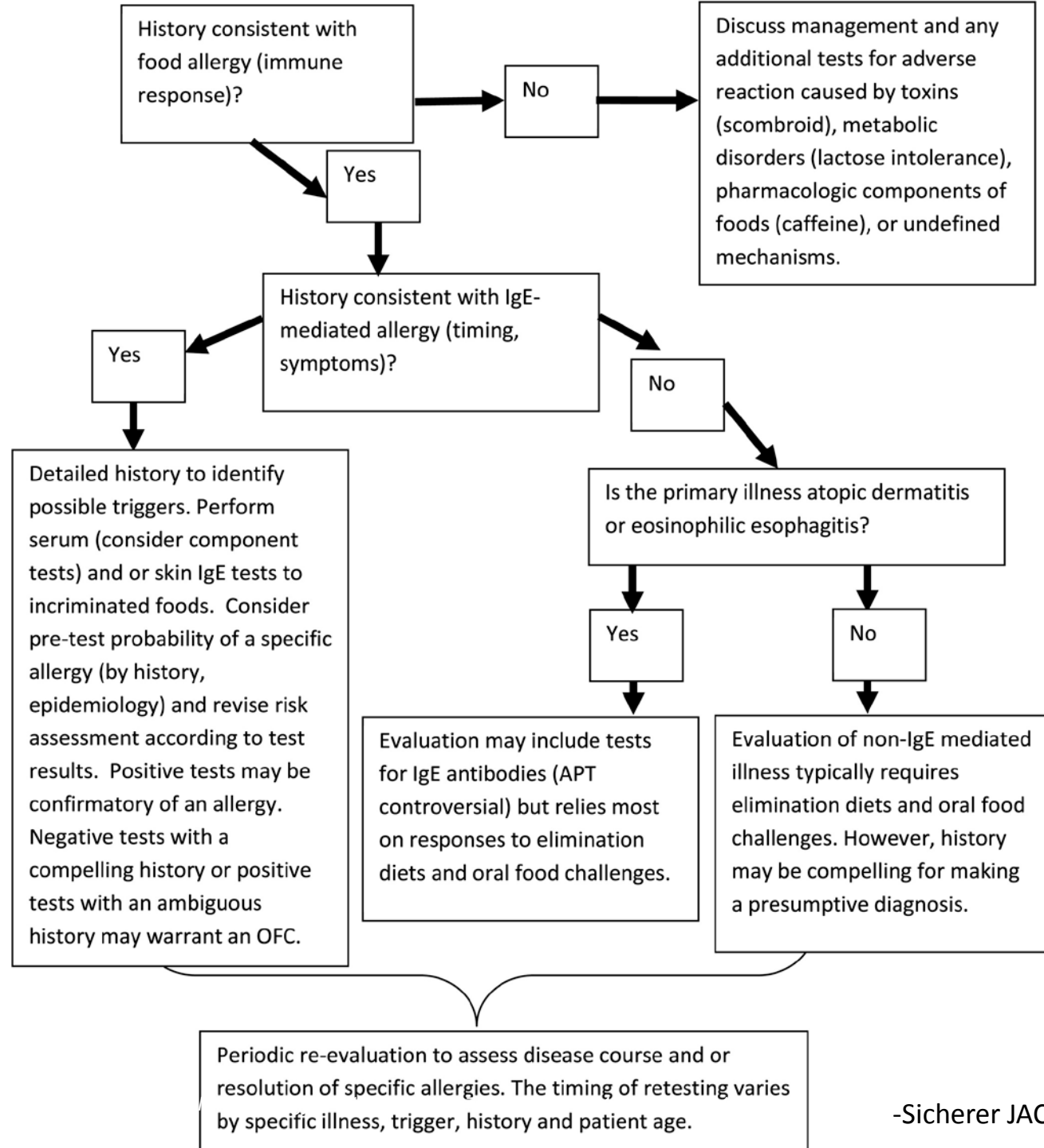
Lack N Engl J Med 2008;359:1252-60.

Pearls and Pitfalls

- Positive SPT or food specific IgE indicates *sensitization not clinical allergy*
 - **Indiscriminate food testing is poorly informative**
 - Leads to unnecessary avoidance
 - Nutritional and growth concerns
 - Cascade of further testing
 - Take care not to “over test”
- Specific IgE levels
 - not correlated to severity
 - trended over time to monitor for persistence/resolution

Risk Factors for More Severe Reactions

- Concomitant asthma (asthma + PN allergy → most fatal)
- Amount ingested
- Food form (cooked, raw, or processed)
- Co-ingestion of other foods (fats, alcohol)
- Age of the patient
- Degree of sensitization at the time of ingestion
- Rapidity of absorption, based on whether
 - – The food is taken on an empty stomach
 - – The ingestion is associated with exercise
- Lack or delayed administration of epinephrine
- Lack of skin symptoms
- Denial of symptoms
- Reliance on oral antihistamines alone to treat symptoms



NIAID FA Guidelines: Management

- Education families on:
 - Carrying medications at all times
 - Twin-pak
 - In purse or bag; not in the car
 - Proper use of medications
 - Preparedness
- Provide a written emergency plan
 - <http://www.foodallergy.org/file/emergency-care-plan.pdf>
- Proper dosing of epinephrine:
 - 0.15 mg for ≤ 25 Kg
 - 0.3 mg for > 25 kg
- Benadryl dosing: 1-1.5 mg/kg (max 50 mg)

FA Guidelines: Management

- **Avoidance**

- Label reading, labeling laws, advisory warnings
- Restaurant precautions – “chef cards”, cross-contact
- Travel – medication and safe meal preparedness
- School – written emergency plan, caution with crafts, field trips, mealtimes
- Home – avoid cross-contact
- Educate all care givers
- Vigilance – always have medications ready, medical alert jewelry
- Avoid home trials
- Nutritional counseling and growth monitoring
- Psychological impact – anxiety, bullying, balance in caution

-Sicherer JACI 2014;133:291-307

-J Allergy Clin Immunol 2010;126:S1-S58.

NIAID FA Guidelines: In office Emergency Management

- Elimination of additional allergen exposure
- Immediate IM injection of epinephrine (repeat every 5 min as needed)
- Call 911 or Code team
- Benadryl 1-2 mg/kg
- Albuterol
- Placement patient in a recumbent position with the lower extremities elevated
- Provision of supplemental oxygen
- IV fluids
- Consider H2 Blocker (1-2 mg/kg) and Steroids (1-2 mg/kg)
- EABC OMI

Summary

- You play a key role in patient outcomes for food allergy
- Large Economic impact to food allergy
- The history is the most important part of the evaluation
- Try to decide if it seems to be IgE mediated or not
- Be thoughtful when ordering specific IgE levels or advising avoidance diets
- Provide guidance and education about specific food avoidance, emergency plans and proper medication use when appropriate
- Refer to Allergist for further evaluation and continued management