

Allergy Evaluation-What it all Means & Role of Allergist

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Objectives of Presentation

- Discuss the different options for allergy evaluation.
 - Skin tests
 - Immunocap Testing
- Understand the results of Allergy testing in various allergic diseases.
- Briefly Understand what an Allergist Does

Common Allergic Diseases Seen in the Primary Care Office

- Atopic Dermatitis/Eczema
- Food Allergy
- Allergic Rhinitis
- Allergic Asthma
- Allergic GI Diseases

Factors that Influence Allergies Development and Expression

Host Factors

- Genetic
 - Atopy
 - Airway hyper responsiveness
- Gender
- Obesity

Environmental Factors

- Indoor allergens
- Outdoor allergens
- Occupational sensitizers
- Tobacco smoke
- Air Pollution
- Respiratory Infections
- Diet

Why Perform Allergy Testing?

- Confirm Allergens and answer specific questions.
 - Am I allergic to my dog?
 - Do I have a milk allergy?
 - Have I outgrown my allergy?
 - Do I need medications?
 - Am I penicillin allergic?
 - Do I have a bee sting allergy

Tests Performed in the Diagnostic Allergy Laboratory

- Allergen-specific IgE (over 200 allergen extracts)
 - Pollen (weeds, grasses, trees),
 - Epidermal, dust mites, molds,
 - Foods,
 - Venoms,
 - Drugs,
 - Occupational allergens (*e.g., natural rubber latex*)
- Total Serum IgE (anti-IgE; ABPA)
- Multi-allergen screen for IgE antibody

Diagnostic Allergy Testing



Serological Confirmation of Sensitization

History of RAST Testing

- RAST (**radioallergosorbent test**) invented and marketed in 1974
- The suspected allergen is bound to an insoluble material and the patient's serum is added
- If the serum contains antibodies to the allergen, those antibodies will bind to the allergen
- Radiolabeled anti-human IgE antibody is added where it binds to those IgE antibodies already bound to the insoluble material
- The unbound anti-human IgE antibodies are washed away.
- The amount of radioactivity is proportional to the serum IgE for the allergen

Immuno CAP Specific IgE

- In 1989, Pharmacia Diagnostics AB replaced RAST with a superior test named the ImmunoCAP Specific IgE blood test
- Also describe as CAP RAST or CAP
- In 2013 Component ImmunoCAP available for Peanut.
- 2015 for Tree Nut Component ImmunoCAP

Immuno-Cap Levels

IgE Class	KU/L	% Response	Level of IgE Antibody
0	<0.35	< or = 70	Absent/undetectable
1	0.35-0.70	71-110	Low Level
2	0.71-3.50	111-220	Moderate Level
3	3.51-17.5	221-600	High Level
4	17.6-50	601-2000	Very High Level
5	51-100	2001-6000	Very High Level
6	>100	> 6000	Very High Level

Skin Test Confirmation of Sensitization

Allergy Skin Testing

- Skin testing remains the central test to confirm allergic sensitivity when it can be performed ¹
- Skin testing is fast (15-30 minutes), safe, sensitive and involves minimally invasive procedures which can be cost effective
- When performed correctly, skin testing is reproducible
- Skin testing has demonstrated good correlation with results of nasal challenge² and bronchial challenges ³
- Results of skin test should always be used as an adjunct to the clinical history and physical examination when making the diagnosis of allergic disease

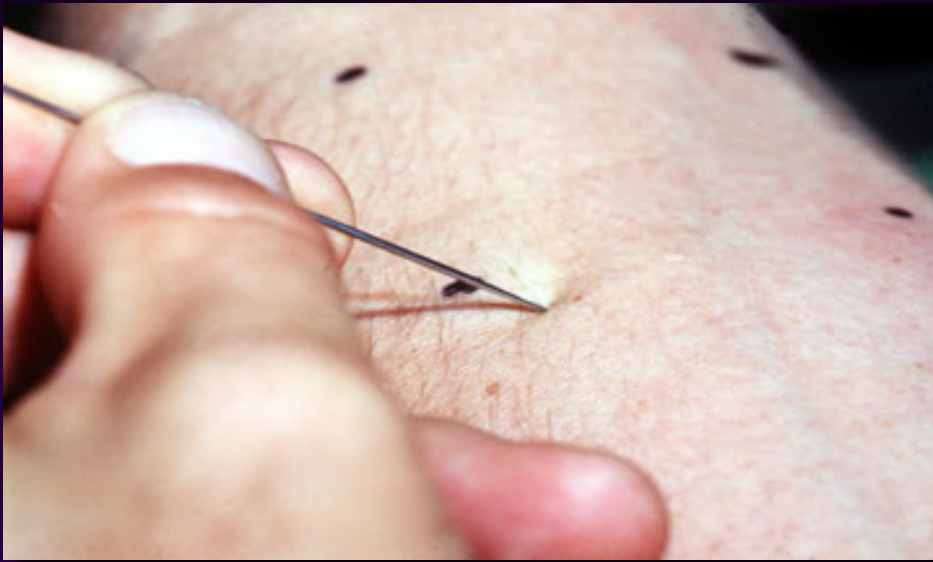
1. Oppenheimer et al, Ann Allergy 2006;S1:6-12

2. Bousquet et al, Clin Allergy 17:529-36, 1987

3. Cockcroft et al, Am Rev Respir Dis 135:264-7., 1987



Skin Testing



Photographs courtesy of Dr. Ed Philpot.

Interpretation of Test Results

- The wheal & flare should be recorded in millimeters
- 3 mm is considered the cut-off for positive, but may overestimate clinical allergy!
- All results should be compared to the negative and positive control
- If negative control is positive the patient has dermatographism, and entire test is invalid
- If histamine control is negative, the results are probably being inhibited by antihistamines (Patients do forget!)
- *Remember that sensitivity (positive skin prick tests) does not mean clinical reactivity or allergy.*

COMPARISON OF SKIN TESTING AND SEROLOGY?

Allergen-Specific IgE

In vitro (lab) and In-Vivo (skin tests)

	<i>In-vitro</i> IgE Antibody Serology	<i>In-vivo</i> SPT
High sensitivity*	Yes	Yes
High specificity*	Yes	Yes
High reproducibility	Yes	Yes
Quantitative results in kIU/L [^]	Yes	No
WHO Standard calibrated	Yes	No
Quality assurance test program	Yes	No
Can be used independently of pharmaceutical treatment	Yes	No
Can be used independently of patient skin status	Yes	No
Time factor	1-7 days	15-30 minutes
Cost factor	more expensive	inexpensive
Usefulness in motivating patients	obscure	dramatic

Results may vary between specific bioassays

[^]Although all are expressed with same units, cannot compare results between different bioassays

Food Allergy Evaluation

Why can't you test my child to
everything????

When to Test/What to Test

**IgE associated clinical disorder?
(Is testing for food allergy appropriate?)**

No

Alternative tests/advice

Yes



Determination of potential triggers

- **Requires careful history, consideration of epidemiology, pathophysiology**
- **Foods tolerated (should not be tested)**
- **Foods not often ingested, more likely triggers**
- **Foods commonly associated with severe reactions:**
- **Peanut, nuts from trees, fish, shellfish, seeds**
- **Common allergens for children with moderate-severe atopic dermatitis:**
- **Egg, milk, wheat, soy**

Selection of serological or skin tests

- **select tests to confirm/exclude suspicions**
- **avoid “panels” of food allergens**
- **avoid testing tolerated foods**

Office Based Evaluation of Food Allergy

- **Primary Care Professional**

- Clinical history (symptoms, food, reaction consistency, alternative explanations, determination if likely IgE mediated)
- Physical examination
- Serological tests for food-specific IgE

- **Allergist**

- Clinical history and physical examination
- Serum and/or skin prick tests for food-specific IgE antibodies
- Diagnostic elimination diets
- Physician-supervised oral food challenges

Pathogenesis: Allergens

- Adults
 - Nuts, peanuts, fish, shellfish, eggs
- Children
 - Eggs, peanuts, milk, soy, fish, wheat
- Societal eating patterns influence development of specific food hypersensitivities
 - Boiled peanuts in Asian cultures,
 - Lack of Peanut Consumption in Sweden

Diagnostic Laboratory Techniques

IgE-Mediated Food Hypersensitivity

- Prick skin tests: Positive tests are “suggestive”
 - Wheal diameter 3 mm > negative control
 - Positive predictive accuracy: < 50%
 - Negative predictive accuracy: > 90%
- Intradermal skin tests: Too non-specific
- IgE RAST: In good lab is similar to skin test
 - Positive: 3+ to 6+ in 6+ scoring system

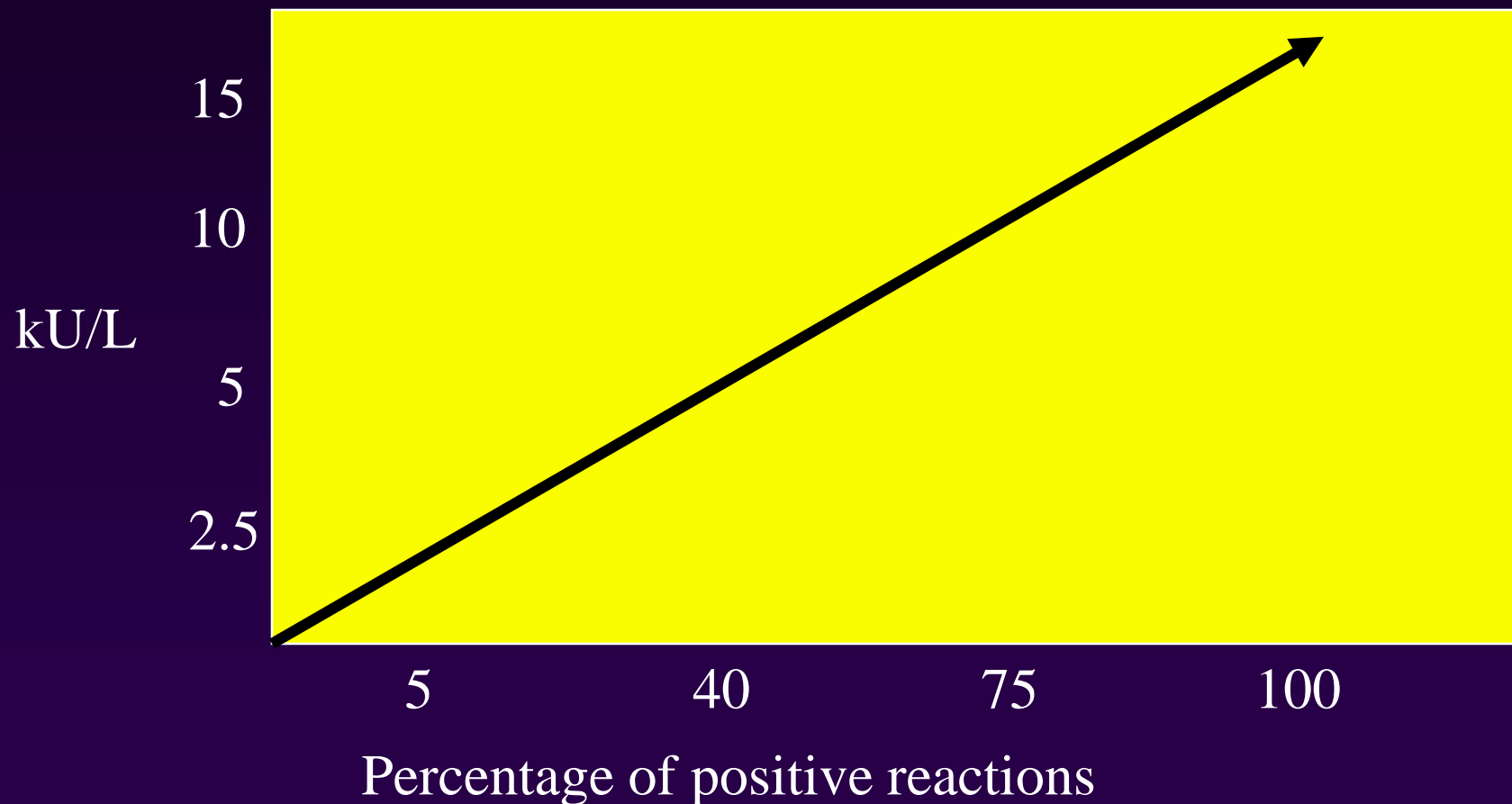
Food-specific IgE concentrations predictive of clinical reactivity (adapted from Sampson HA)

- Diagnostic Decision Point**

Allergen	[kUA/L]	Sensitivity	Specificity	PPV	NPV
Egg	7	61	95	98	38
-Infants < 2 yrs	2			95	
Milk	15	57	94	95	53
-Infants < 2 yrs	5			95	
Peanut	14	57	100	100	36
Fish	20	25	100	100	89
Soybean	30	44	94	73	82
Wheat	26	61	92	74	87
Tree nuts*	~15			~95	

Diagnostic Decision Point

Value of the Immuno Cap Assay for Peanut Protein



Sample Case

- Connor age 3 with a history of multiple food allergies and recent anaphylaxis to unknown food at a party. Drinks milk with no problem, No exposure to Peanuts or tree nuts, shrimp etc.
- Cap Rast
 - Milk Class II 2.5 kU/L
 - Peanut Class III 7.5 kU/L
 - Cashew Class IV 22.7 kU/L
 - Walnuts Class III 13.2 kU/L
 - Shrimp Class I 0.70 kU/L

Treatment of Food Allergy

- Strict avoidance - teach patients to read labels
- Avoidance of the specific 1 or 2 foods proven to cause the allergy symptom
- Re-challenge at intervals to determine loss of sensitivity
- Re-challenge should be performed in a medical setting if there is any possibility of severe reaction

When to Re-challenge?

- Are skin tests predictive of positive food challenges?
 - Study performed in 467 children suspected of food allergy
 - 555 food challenges
 - Positive in 55% of the patients, negative in 37% and inconclusive in 8%
 - Challenges were **ALWAYS** positive when the skin test diameter was $>8\text{mm}$ for milk, $>7\text{mm}$ for egg, and $>8\text{mm}$ for peanut

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When to Re-challenge?

- Milk and soy allergy in infants
 - Every 6 -12 months depending on initial reactions and intervening period
- Peanuts and tree nuts
 - Depending on exposure and history at 3-5 years of age. **ONLY IN A CONTROLLED SETTING**
- Eggs
 - Challenge eggs in baked goods at 2-3 years of age
 - Eggs as such at 4-5 years of age

Component Immuno-Cap

- Specific proteins now may be isolated and tested.
 - Proflins
 - PR-10 Proteins
 - LTP Proteins
 - Storage Proteins

Increasing risk of systemic reactions

	Profilin	PR-10 protein	LTP	Storage Proteins
PEANUT 	Profilin	Ara h 8	Ara h 9	Ara h 1 Ara h 2 Ara h 3
HAZEL NUT 	Profilin	Cor a 1	Cor a 8	Cor a 9 Cor a 14
WALNUT 	Profilin		Jug r 3	Jug r 1
BRAZIL NUT 	Profilin			Ber e 1
CASHEW NUT 	Profilin			Ana o 3

Peanut (f13)

Ara h 1 + Ara h 2 + Ara h 3
(f422) (f423) (f424)



- Storage proteins
- Stable to heat and digestion
- Associated with severe reactions

Ara h 9 (f427)



- Lipid transfer protein (LTP)
- Stable to heat and digestion
- Associated with both severe and local reactions
- Associated with allergy to peach and peach related fruits

Ara h 8 (f352)



- PR-10 Protein
- Labile to heat and digestion
- Associated with local reactions
- Associated with allergy to birch and birch related tree pollens

Role of Allergy Testing in Atopic Dermatitis

- Skin Testing Preferred
 - Can see positive reaction and can grade ST's
- Immunocap Testing:
 - Unknown decision points
 - Do not run food allergy testing as a screening tool.
 - Many false positives and no “decision points”

Sample Case

Devin age 18 months with AD. No prior hx of anaphylactic reactions to foods

Milk	Class III	3.2 kU/L
Egg	Class IV	17.6 kU/L
Soy	Class I	0.40 kU/L
Peanut	Class III	4.2 kU/L

Atopic Dermatitis - Food Allergy

- 40-50% of patients with severe AD have food allergy as a major trigger
- Food allergy in 20-25% with less severe AD
- Egg allergy is most common, followed by milk, peanut, soy, wheat, and fish
- These 6 foods account for 80-90% of food sensitivities in AD
- 36% react to one food, 26% to 2 foods, 18% to 3 foods, 10% to 4 foods, 10% to 5 or more foods

Gastrointestinal Food Hypersensitivity

IgE-
Mediated



Non-IgE-
Mediated

Immediate GI hypersensitivity
Oral allergy syndrome

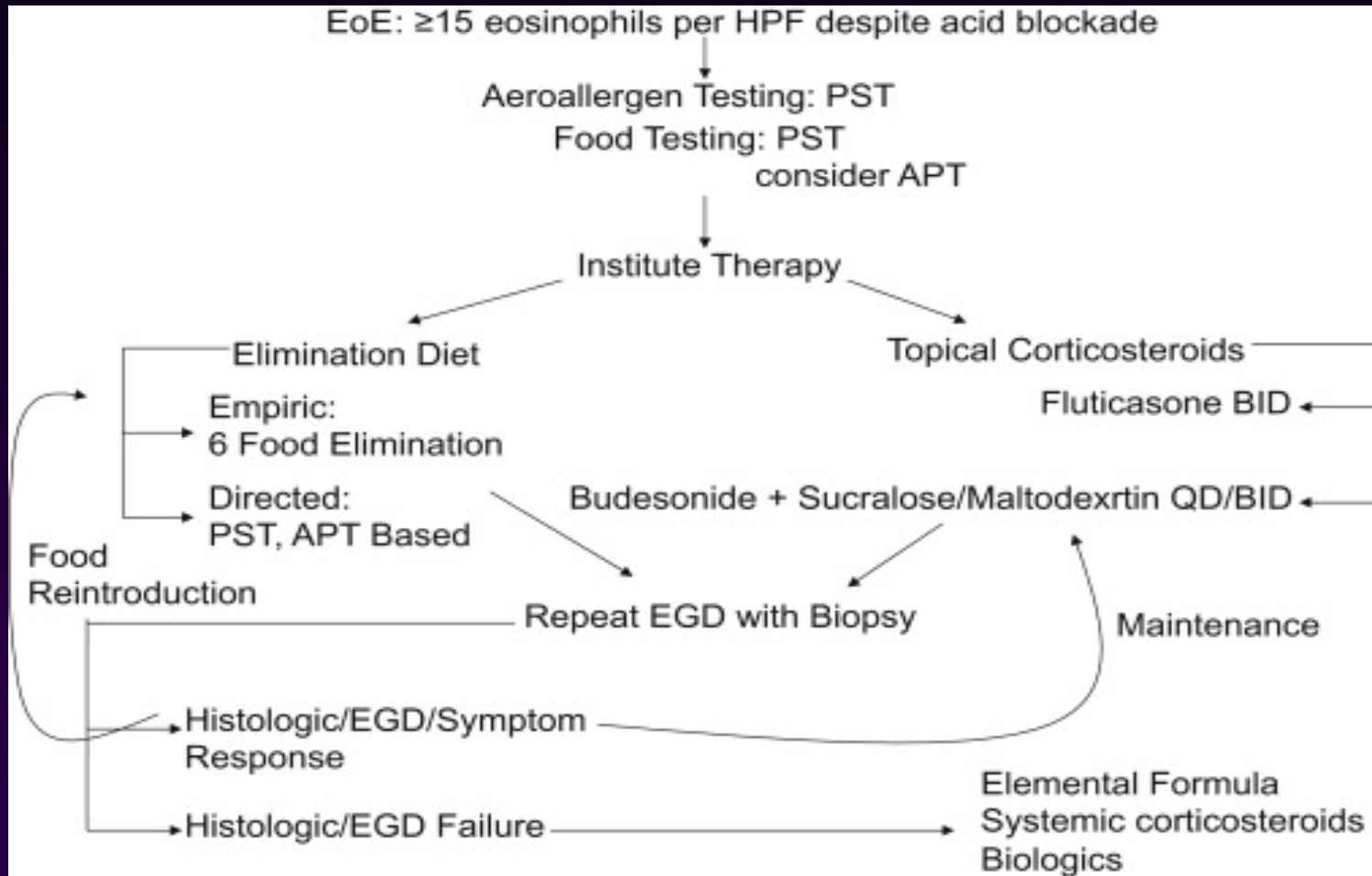
Allergic eosinophilic esophagitis
Allergic eosinophilic gastritis
Allergic eosino-gastroenteritis

Enterocolitis syndrome
Dietary protein proctitis
Celiac Disease

Role of Allergy Testing in EoE

- Skin Tests not specific enough
 - Skin tests are “suggestive” of sensitization
 - Positive results- Diet directed
 - Six foods-Implicated in EoE
 - Milk, Wheat, Soy, Egg, Nuts, Fish and Shellfish.
 - Six food Elimination Diet
- Undefined role of ImmunoCAP in EoE no “decision points”
- Atopic Patch Testing- Some clinical benefit in EoE

Figure 1

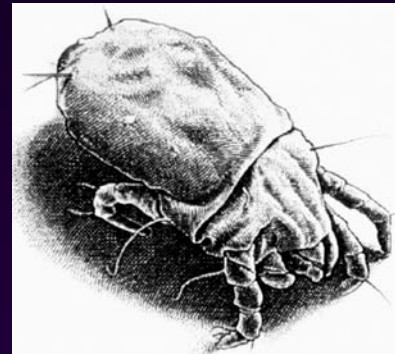


Role of Allergy Testing- Asthma and Allergic Rhinitis

- Skin Prick Testing
 - Still the most useful tool for evaluation
 - Correlates to “Clinical Sensitivity”
 - Clinical challenges with Nasal and Bronchial provocation
- Immunocap Testing
 - Again no clinical “decision points”. Not correlating with clinical sensitivity

Common Asthma Intradermal Skin Testing Antigens

- Mold
- Dust mites
- Pollens
- Cockroach
- Animals
- Feathers



What is an allergist/immunologist?

An allergist/immunologist is a physician certified in either internal medicine or pediatrics, who has completed an additional two years of training in allergy and immunology at an accredited training program and passed the examination given by the American Board of Allergy and Immunology (ABAI).

The allergist/immunologist is uniquely trained in:

- Allergy testing (skin, in-vitro)
- History-allergy test correlation
- Bronchoprovocation testing (e.g. exercise, methacholine)
- Environmental control instructions
- Inhalant immunotherapy
- Immunomodulator therapy (e.g. anti-IgE, IVIG)
- Venom immunotherapy
- Food and drug challenges
- Drug desensitization
- Evaluation of immune competence
- Education (disease, medications, monitoring)
- Management of chronic or recurrent conditions where allergy is not always identified: rhinosinusitis, conjunctivitis, asthma, cough, urticaria/angioedema, eczema, anaphylaxis

Summary

- Depending on the diagnosis allergy testing results are variable
- Skin tests useful for evaluation of most allergic conditions.
- ImmunoCAP for foods has “decision points” but variable for other allergic conditions.

Questions ???
