

Management of Food Allergy and Intolerance

Cross-reacting Allergens and Co-occurring Allergies

Oral Allergy Syndrome Latex Allergy

Oral Allergy Syndrome

- Clinical symptoms are a result of an IgE mediated reaction in the oral and pharyngeal mucosa
- There is direct contact between the mucosa and raw food in a sensitized person
- Local symptoms triggered include:
 - ♦ Oral itching
 - ◆ Lip swelling
 - Tongue swelling
 - Swelling in the throat ("throat tightening")
 - ◆ In rare cases a systemic reaction (anaphylaxis) may occur



Oral Allergy Syndrome

- Appears as a reaction to raw fruits and vegetables in persons with IgE mediated allergy to pollens (pollinosis)
- Pollens usually trigger rhinitis or asthma in these subjects
- First described in 1942 in patients allergic to birch pollens who experienced oral symptoms when eating apple and hazelnut

Oral Allergy Syndrome

- Syndrome seen more often in persons with birch pollen allergy than those with allergy to other tree pollens
- Also frequently occurs in persons allergic to ragweed pollen

• Seen in adults much more frequently than children

 Reactions to raw fruits and vegetables are the most frequent food allergies with onset in persons over the age of 10 years Oral Allergy Syndrome Cross-reacting allergens

Birch pollen

(also: mugwort, and grass pollens) with:

- Apple
- Stone Fruits (Apricot, Peach, Nectarine, Plum, Cherry)
- ♦ Kiwi Fruit
- Orange Peanut
 Melon Hazelnut
 Watermelon Carrot
 Potato Celery
 Tomato Fennel



Oral Allergy Syndrome Cross-reacting allergens

• Ragweed pollen with: ♦ Banana ♦ Cantaloupe ♦ Honeydew ◆ Watermelon ♦ Other melons ♦ Zucchini ◆ Cucumber



Oral Allergy Syndrome Cause of Symptoms

- The initial reaction is to pollens which react with IgE antibodies bound to mast cells in the mucosa of the upper and lower respiratory tract
- The reaction extends to food antigens with structures similar to those of the pollen antigens
- The plants are not botanically related
- Oral reactivity to the food significantly decreases when food is cooked
- Reactivity of the antigen also depends on ripeness: the antigen becomes more potent as the plant material ages

Latex Allergy

 Allergy to latex is thought to start as a Type IV (contact) hypersensitivity reaction

- Contact is with a 30 kd protein, usually through:
 Abraded (non-intact) skin
 Mucous membrane
 - Or exposed tissue (e.g. during surgery)



Latex Allergy Cross-reacting allergens

- As antigen comes into contact with immune cells, repeated exposure seems to lead to Type I hypersensitivity (IgE mediated allergy)
- Similar 30 kd proteins in foods tend to trigger the same IgE response
- In extreme cases can cause anaphylactic reaction

Latex Allergy Related foods

 Foods that have been shown to contain a similar 30 kd antigen include:

- Avocado
- Banana
- Kiwi fruit
- Fig
- Passion fruit
- Citrus fruits
- Pineapple

- Tomato
- Celery
- Peanut
- Tree nuts
- Chestnut
- Grapes
- Papaya



Common allergens in unrelated plant materials: Summary

 OAS and latex allergy are examples of conditions in which common antigens, expressed in botanically unrelated plants, are capable of eliciting a hypersensitivity reaction

 Previous assumptions that plant foods in the same botanic family are likely to elicit the production of the same antigen- specific IgE are thus questionable Common allergens in unrelated plant materials: Summary

- In practice, when a specific plant food elicits an allergic response, foods in the same botanic family rarely elicit allergy
- It is important to recognize the allergenic potential of antigens common to certain botanically unrelated plant species, and take appropriate measures to avoid exposure of the allergic individual to them

Tests for Adverse Reactions to Foods

Rationale and Limitations

Skin tests

Scratch or prick

- Allergen extract applied to skin surface of arm or back
- ◆ Skin is scarified (scratched) or pricked with lancet
- ◆ Allergen encounters mast cells below skin surface
- → Rationale: if allergen-specific IgE is present, allergen plus antibody causes release of mediators (mast cell degranulation), especially histamine
 - Histamine causes reddening and swelling: "wheal and flare" reaction of the skin test
 - \diamond Size of reaction measured (usually 1+ to 4+)

Standard Allergy Tests Skin tests continued



- Manual C

Intradermal tests

- Allergen extract is injected into dermis
- Rationale: release of histamine produces wheal and flare
- Note: many countries do not approve this type of testing because of increased risk of anaphylaxis as allergen introduced directly into blood stream

Controls for all skin tests:

- Negative: medium in which allergen is suspended (usually saline)
- Positive: measured amount of histamine

Reasons for False Positive Skin Tests

- Degranulation of skin mast cells by stimuli that do not degranulate mast cells in the digestive tract
- Differences in the form in which the food is applied to the skin compared to that which encounters immune cells in the digestive tract
- Antigens in fruits and vegetables change when cooked
 Allergen may be derived from an unstable food extract
 Digestive processes can unmask antigens
 Allergen extract contains histamine

False Negative Skin Tests

- Children younger than 2-3 years are more likely to have a negative skin test and positive food challenge than adults
- Adverse reaction is not mediated by IgE
- Commercial allergen may contain no material that the immune system can recognize

Value of Skin Tests in Practice

- Positive predictive accuracy of skin tests rarely exceeds 60%
 - Many practitioners rate them lower
- Tests for highly allergenic foods thought to have close to 100% *negative* predictive accuracy: Such foods include:
 - Egg
 Fish
 Tree nuts

- > Milk
- > Wheat
- ➢ Peanut

Value of Skin Tests in Practice

- Negative skin tests do not rule out the possibility of Type III hypersensitivity reactions, mediated by IgG
- Do not rule out food intolerance (non-immunemediated reactions)

 "Skin tests for food allergy are especially unreliable because of the large number of false positive and false negative reactions"

Status of Skin Testing for Food Allergy: Opinion

• T.J.David 1993

"The fact that skin tests are still in use reflects both the unscientific nature of allergy practice and the lack of reliable and simple tests"

"...it is difficult to see a place for skin testing in the general diagnosis or management of intolerance to food or food additives"

Other Skin Tests

Prick-to-Prick

- ◆ Used for suspected contact allergy
 - e.g. oral allergy syndrome
- Especially where allergen is easily denatured by heat and acid



- Crushing plant tissue during preparation of allergen extracts releases phenols that rapidly cause break-down of protein
- Prick-to prick test transfers "native" allergen
- Sterile needle is inserted into raw food, and the patient's skin is pricked with the same needle

Other Skin Tests



Patch Test for Contact Allergies

- Involves Type IV (delayed) hypersensitivity reaction, requiring cell-to-cell contact
- ◆ Examples:
 - Poison ivy rash
 - Nickel contact dermatitis



- Preservatives, dyes and perfumes in cosmetics
- Allergen is placed on the skin, or applied as an impregnated patch, which is kept in place by adhesive bandage for up to 72 hours
- ◆ Local reddening, swelling, irritation, indicates positive response

Other Skin Tests



• DIMSOFT (dimethylsulfoxide test) for delayed reaction to food ◆ Food extract is suspended in 90% dimethylsulfoxide Aids in skin penetration of allergen ◆ Patch held in place 48-72 hours Especially useful in skin and gastrointestinal reactions which may not have immediate onset symptoms ◆ Especially useful for milk and cereal grains Thought to indicate all 4 Gell and Coombs hypersensitivity reactions

Standard Allergy Tests Blood Tests

ELISA: enzyme-linked immunosorbent assay
RAST: radioallergosorbent test

 Designed to detect and measure levels of allergenspecific IgE

May measure total IgE - thought to be indicative of "atopic potential"

 Some practitioners measure IgG (especially IgG4)



Value of Blood Tests in Practice

- Blood tests are considered less sensitive than skin tests for identification of specific food allergens
- Anti-food antibodies (especially IgG) are frequently detectable in all humans, usually without any evidence of adverse effect
- In fact, some studies suggest that IgG4 might indicate protection or recovery from IgE-mediated food allergy

Value of Blood Tests in Practice

- There is often poor correlation between high level of antifood IgE and symptoms when the food is eaten
- Many people with clinical signs of food allergy show no elevation in IgE
- Reasons for failure of blood tests to indicate foods responsible for symptoms are the same as those for skin tests

Tests for Intolerance of Food Additives

- There are no reliable skin or blood tests to detect food additive intolerance
- Skin prick tests for *sulfites* are sometimes positive
- A negative skin test does not rule out sulfite sensitivity
- History and oral challenge provocation of symptoms are the only methods for the diagnosis of additive sensitivity at present
- Caution: Challenge may occasionally induce anaphylaxis

Unorthodox Tests

- Many people turn to unorthodox tests when avoidance of foods positive by conventional test methods have been unsuccessful in managing their symptoms
- Tests include:
 - Vega test (electro-acupuncture)
 - biokinesiology (muscle strength)
 - ♦ analysis of hair, urine, saliva
 - ♦ radionics
 - ALCAT (lymphocyte cytotoxicity)



Controversial Tests

Electro-Acupuncture (Vega) Test ◆Utilizes "energy waves" Circuit linking Patient (holding a metal rod) Vial containing food, or other material being tested Meter to measure energy level Technician holding probe held at acupuncture point on patient's other hand • Disturbance in energy flow indicates reactivity

Controversial Tests

Biokinesiology

Assumption: muscles become weak when influenced by the allergen to which the patient reacts

 Patient holds a vial containing the suspect allergen (food)

 Practitioner tests the strength of the patient's other arm in resisting downward pressure

Weakening of resistance indicates a positive (allergic) reaction



Drawbacks of Unreliable Tests

- Diagnostic inaccuracy
- Therapeutic failure
- False diagnosis of allergy
- Creation of fictitious disease entities
- Failure to recognize and treat genuine disease
- Inappropriate and unbalanced diets
- Malnutrition

Consequences of Mismanagement of Adverse Reactions to Foods

- Malnutrition; weight loss, due to extensive elimination diets
- Especially critical in young children where nutritional deficiency at a crucial stage in development can cause permanent damage
- Food phobia due to fear that "the wrong food" will cause permanent damage, and in extreme cases, death
- Frustration and anger with the "medical system" that is perceived as failing them
- Disruption of lifestyle, social and family relationships

Reliable Tests

Elimination and Challenge Protocols

Reliable Identification of Allergenic Foods

 Removal of the suspect foods from the diet, followed by reintroduction is the only way to:
 Identify the culprit food components
 Confirm the accuracy of any allergy tests

 Long-term adherence to a restricted diet *should not* be advocated without clear identification of the culprit food components

Reliable Tests

• Elimination and Challenge Suspected food is removed from diet for specified period of time ◆ Selective elimination • Foods most likely to cause reaction are eliminated • Foods free from these are used as substitutes Nutritionally complete • Usually followed for 4 weeks Few foods elimination • Only 6-8 "low allergenicity foods" allowed Nutritionally incomplete • Diet followed for 7-14 days only
Reliable Tests

Challenge

Double-blind placebo-controlled food challenge (DBPCFC)
Neither patient nor supervisor know the identity of the food
Food is disguised, usually in gelatin capsule
Placebo (e.g. glucose powder) is taken as "negative control"
Sequential Incremental Dose Challenge (SIDC)
Open food challenge

Any food suspected to cause a severe or anaphylactic reaction should be challenged in suitably equipped medical facility

Food Intolerance: Clinical Diagnosis



Elimination and Challenge

Stage 1: Exposure Diary

◆ Record each day, for a minimum of 5-7 days:

- All foods, beverages, medications, and supplements ingested
- Composition of compound dishes and drinks, including additives in manufactured foods
- Approximate quantities of each
- The time of consumption



Exposure Diary (continued)

◆ All symptoms graded on severity:
▶ 1 (mild);
▶ 2 (mild-moderate)
▶ 3 (moderate)
▶ 4 (severe)

◆ Time of onset

How long they last

Record status on waking in the morning.
Was sleep disturbed during the night, and if so, was it due to specific symptoms?

Elimination Diet

Based on:

- Detailed medical history
- Analysis of *Exposure Diary*
- Any previous allergy tests
- Foods suspected by the patient
- Formulate diet to exclude all suspect allergens and intolerance triggers
- **Provide** excluded nutrients from alternative sources
- **Duration**: Usually four weeks

Therapeutic Diets

• Certain conditions tend to be associated with specific food components • Suspect food components are those that are probable triggers or mediators of symptoms • Examples: Eczema: highly allergenic foods ◆ Migraine: biogenic amines Urticaria/angioedema: histamine Chronic diarrhea: disaccharides ◆ Asthma: cyclo-oxygenase inhibitors; sulphites

Basic Hypoallergenic ("few foods") Elimination Diet

Only listed foods are allowed No vitamin supplements or non-essential medications **GRAINS**: White rice Tapioca Pears; pear juice FRUITS: Cranberries; cranberry juice **VEGETABLES:** Squash (all varieties) Carrots Parsnips Lettuce MEAT: Lamb Wild game Turkey

Basic Hypoallergenic (*"few foods"*) Elimination Diet (continued)

MEAT	Lentils	
SUBSTITUTES:	Split peas	
	Garbanzo beans (chick peas)	
FLAVOURINGS:	Sea salt	
BEVERAGES:	Distilled water in glass containers	
OILS	Canola oil <i>or</i> olive oil	
	Safflower oil	
OTHER	Agar-agar	
(Make jelly dessert with pears and pear juice)		

Expected Results of Elimination Diet

 Symptoms often worsen on days 2-4 of elimination

- By day 5-7 symptomatic improvement is experienced
- Symptoms disappear after 10-14 days of exclusion

Challenge

- Double-blind Placebo-controlled Food Challenge (DBPCFC)
 - Lyophilized (freeze-dried) food is disguised in gelatin capsules
 - Identical gelatin capsules contain a placebo (glucose powder)
 - Neither the patient nor the supervisor knows the identity of the contents of the capsules
 - Positive test is when the food triggers symptoms when the placebo does not

Challenge

Drawback of DBPCFC
Expensive in time and personnel
Capsule may not provide enough food to elicit a positive reaction
May be other factors involved in eliciting symptoms, e.g. taste and smell

Challenge

Open food challenge
Sequential incremental dose challenge (SIDC)
Determines sensitivity and dose tolerated for each eliminated food in its purest form

Food suspected to have caused a severe or an anaphylactic reaction should only be tested under medical supervision in a facility equipped for resuscitation

Open Food Challenge

- The basic elimination diet, or therapeutic diet continues during this phase
- If an adverse reaction to the test food occurs at any time during the test STOP. Do not continue to eat the test food
- Wait 48 hours after all symptoms have subsided before testing another food

Incremental Dose Challenge

Day 1:

 Morning: Eat a small quantity of the test food Wait four hours, monitoring for adverse reaction; If no symptoms:

- Afternoon: Eat double the quantity of test food eaten in the morning.
 - Wait four hours, monitoring for adverse reaction;
 - If no symptoms:

• Evening: Eat double the quantity of test food eaten at lunch

Incremental Dose Challenge (continued)

Day 2:

Do not eat any of the test food

Continue to eat basic elimination diet

 Monitor for any adverse reactions during the night and day which may be due to a delayed reaction to the test food

Incremental Dose Challenge (continued)

Day 3:

• *If no adverse reactions* have been experienced proceed to testing a new food, starting Day 1

• If the results of Day 1 and/or Day 2 are unclear :

 Repeat Day 1, using the same food, the same test protocol, but larger doses of the test food

• Day 4:

Monitor for delayed reactions as on Day 2

Sequential Incremental Dose Challenge

 Continue testing in the same manner until all excluded foods, beverages, and additives have been tested

 For each food component, the first day is the test day, and the second is a monitoring day for delayed reactions

Test 1: Casein proteins White Hard Cheese (e.g. Mozzarella or Parmesan)

Block of 6-7 ounces cut into *seven* equal cubes



Morning:1 cubeAfternoon:2 cubesEvening:4 cubes

Test 2: Annatto, biogenic amines, plus casein

 Yellow Aged Cheese (e.g. old Cheddar) Morning: 1 cube
 Afternoon: 2 cubes
 Evening: 4 cubes



Test 3: casein and whey proteins
Lactose-free (lactase treated) milk

◆ 99% Lactose-free milk (LactaidTM; LacteezeTM) or
 ◆ Lactaid drops: 15 drops added to one litre of milk (skim, 1%, 2%, homogenized) left for 24 hours in fridge before test
 Morning: ¼ cup
 Afternoon: ½ cup

Evening: 1 cup

Test 4: lactose in addition to casein and whey proteins

Regular Milk (skim, 1%, 2%, homogenized)



Morning:1/4cupAfternoon:1/2cupEvening:1cup

Test 5: \succ modified milk components \succ reduced lactose (due to action of bacterial β -galactosidase)

♦ Plain yoghurt

Morning:1/4 cupAfternoon:1/2 cupEvening:1 cup



Test 6: Whey proteins

- Whey powder (purchased)
 - Dilute whey powder in water according to package directions (10% wt/vol)

• Test 6A: lactose-free whey

- Add commercial lactase (15 drops per 1 litre)
- ◆ Leave for 24 hrs in the fridge

Morning	¹ / ₄ cup
Afternoon	¹ / ₂ cup
Evening	1 cup

• Test 6B: Lactose (in whey)

• Diluted whey powder (10% wt/vol) in water:

Morning1/4 cupAfternoon1/2 cupEvening1 cup

Test 7: Cottage cheese

 Test for curdled milk with bacterial culture containing casein, whey, and lactose

Morning1/4 cupAfternoon1/2 cupEvening1 cup

Test 8: Ice Cream: vanilla flavour only

◆ Test for complete milk components, sucrose, and additives

Morning Afternoon Evening ¹/₄ cup ¹/₂ cup 1 cup



Sequence of Testing: Egg

Egg: Yolk and white tested separately
Hard boil egg
Separate the yolk from the white



Test 1: egg yolk

 Morning: ½ yolk
 Afternoon: 1 yolk
 Evening: 2 yolks

 Test 2: egg white

Test as for egg yolk

Sequence of Testing: Yeast (Saccharomyces spp.)

• Brewer's and Baker's yeast Purchase debittered brewer's yeast • Dissolve the following quantities in warm water ◆ Add to tolerated beverage (e.g. fruit juice), or cooked fruit (e.g. apple sauce) Morning ¹/₄ teaspoon Afternoon $\frac{1}{2}$ teaspoon 1 teaspoon Evening

Sequence of Testing: Wheat



Test 1: Pure cereal grain

 Puffed wheat; wheat flakes (cooked); Cream of WheatTM(cooked)

Add tolerated fruit juice or milk substitute
 Morning: ¹/₄ cup
 Afternoon: ¹/₂ cup
 Evening: 1 cup

Sequence of Testing: Wheat

Test 2: Wheat Cracker without yeast
♦ e.g. TriscuitTM

Morning: Afternoon: Evening: 1 cracker
 2 crackers
 4 crackers



◆Note; many crackers contain yeast (e.g. Saltines[™]; Ritz[™])

Sequence of Testing: Wheat

Test 3: White Bread

Morning: Afternoon: Evening: ¹/₂ slice1 slice2 slices



if *benzoates* are suspect, use unbleached flour
if *milk proteins* are suspect, use milk-free bread
if *preservatives* are suspect, use preservative-free bread *note:* many commercial breads contain *soya flour*

Test 4: Whole Wheat BreadTest as for white bread

Sequence of Testing: Rye

Rye: Test as for wheat:

◆Test 1. Rye Flakes (cooked)



◆ Test 2. Rye Cracker (Ryvita[™] (wheat-free) or Wasa[™] (light)

◆ Test 3. Rye Bread (100% rye flour, wheat-free)

Sequence of Testing: Corn

Test 1: pure grain ◆ corn-on-the-cob • ¹/₄; ¹/₂; 1 cooked cob or: frozen corn niblets: • ¹/₄; ¹/₂; 1 cup cooked Test 2: corn oil ◆ 1, 2, 4 teaspoons added to tolerated food Test 3; corn syrup ◆ 1, 2, 4 teaspoons added to tolerated food

Sequence of Testing: Alcoholic beverages

- Test 1.Distilled alcohol (enhanced antigen uptake)
 Tequila; vodka; gin; white rum
- Test 2. White wine (biogenic amines, especially histamine)
- Test 3. Red wine (biogenic amines, especially tyramine)
- Test 4. Beer, ale, lager (fermented grains)
- Test 5. Cider (fermented apple, pear, peach etc)

Sequence of Testing: Chocolate

Test 1 : Unsweetened ("bitter") baker's chocolate
Melt and add honey (if tolerated) as a sweetener
Solidify on a flat surface (e.g. baking sheet)
Break into squares
Test: 1, 2, 4 squares

• Test 2: Purchased chocolates



Maintenance Diet
Final Diet

• Must exclude all foods and additives to which a positive reaction has been recorded Must be nutritionally complete, providing nutrients from non-allergenic sources • If dose-related intolerances are a problem a 4-day rotation diet may be beneficial ◆ there is no clear consensus on the benefits of rotation diets at present

Important Nutrients in Common Allergens

Equivalent nutrients must be provided from alternative sources when the following foods are eliminated from the diet:

Milk and Milk Products:

Calcium Phosphorus Vitamin D* Vitamin B12 Pantothenic acid

Riboflavin Potassium <u>Smaller amounts:</u> Vitamin A* Vitamin E



*Usually added as fortification to the food product

Important Nutrients in Common Allergens

Egg:

Vitamin B12 Vitamin D Pantothenic acid Biotin

Folacin Riboflavin Selenium Iron Smaller amounts: Vitamin A Vitamin E Vitamin B6 Zinc



Important Nutrients in Common Allergens

<u>Wheat</u>:

Thiamin* Riboflavin* Niacin* Iron* Selenium Chromium

Smaller amounts: Magnesium Folacin Phosphorous Molybdenum



<u>Rice</u>:

Thiamin* Riboflavin* Niacin* Iron*



Important Nutrients in Common Allergens

Peanut:

Niacin Pantothenic acid Vitamin E Magnesium Manganese Chromium Smaller amounts Folacin Biotin Vitamin B6 Copper Phosphorous Potassium

Soybean:

Thiamin Riboflavin Vitamin B6 Folacin Calcium Iron

Phosphorous Magnesium Zinc

Important Nutrients in Common Allergens

Fish and Shellfish:

Niacin Vitamin B6 Vitamin B12 Vitamin E Phosphorous Calcium (in shellfish and fish bones) Selenium

Smaller amounts:

Potassium Magnesium Iron Zinc Vitamin A

Summary

1. Food Allergy: Immune system response Food Intolerance: Usually metabolic dysfunction

2. Diagnostic Laboratory Tests: Often ambiguous because different physiological mechanisms are involved in triggering symptoms

Summary

- 3. Reliable Tests for the Detection of Adverse Food Reactions:
 - Elimination and Challenge
- 4. **Restrict** elimination phase: to a maximum of *four weeks* before challenging:; *two weeks* when a few foods elimination diet is used
- 5. Final diet
 - >Must provide complete nutrition