

Food Allergy

A GLORIA™ Module

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Learning objectives

At the end of this presentation you will be able to:

- ◆ Recognise the main pathogenic food allergens in adults and children
- ◆ Differentiate between Ig-E mediated, cell-mediated and mixed IgE- and cell-mediated food-related diseases in different organ systems
- ◆ Discuss the diagnosis of food allergy and the limitations of diagnostic techniques
- ◆ Review the treatment of food allergy

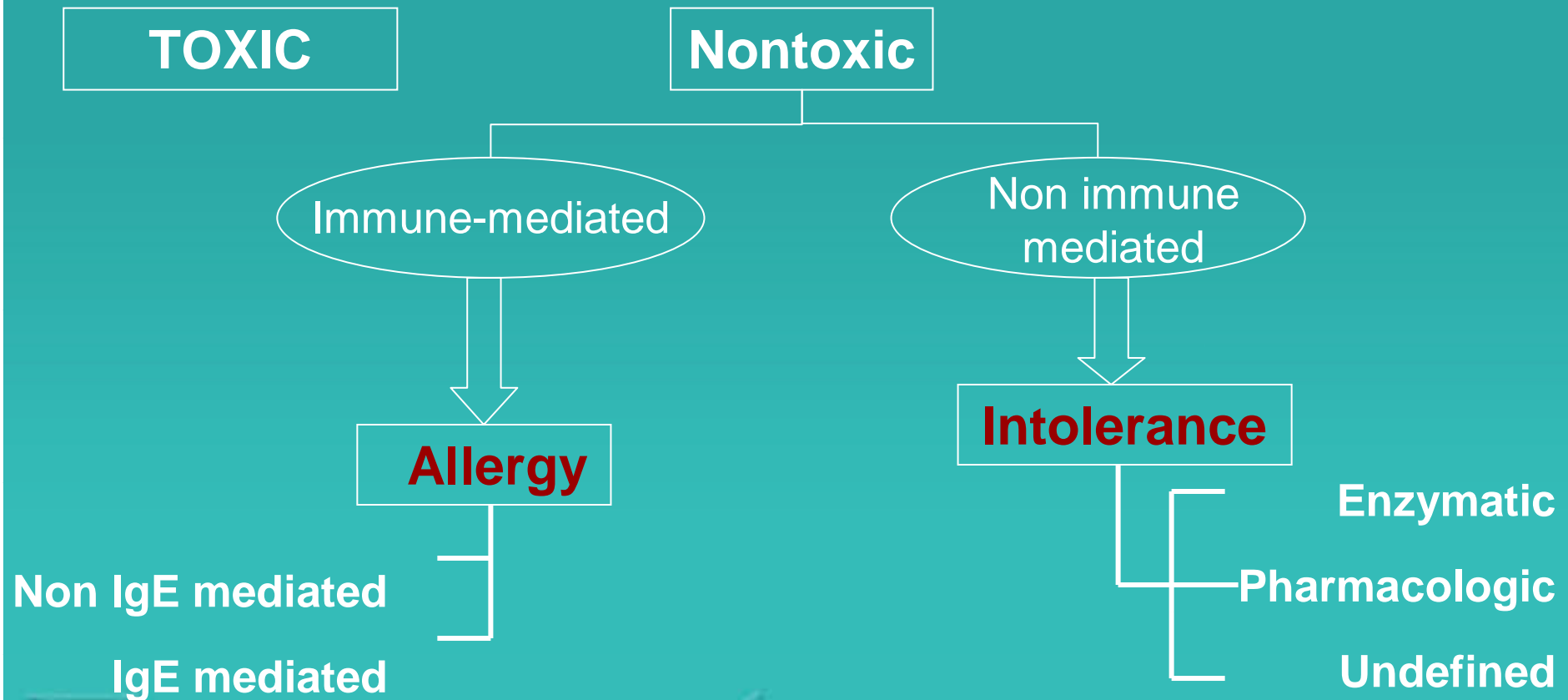
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Adverse reactions to food: Definition

Any abnormal clinical response attributed to ingestion, contact or inhalation of any food, a food derivative or a food additive.

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Adverse reactions to food



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Adverse reaction to food: position paper.
Allergy 1995; 50:623-635

Prevalence of food allergy

Precise prevalence is unknown, but estimates are:

- ◆ Adults: 1.4% - 2.4%
- ◆ Children < 3 years: ~ 6%
- ◆ Atopic dermatitis (mild/severe): ~35%
- ◆ Asthmatic children: 6 - 8%
- ◆ Prevalence depends on: Genetic factors, age, dietary habits, geography and diagnostic procedures

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Adapted from Sampson HA. Adverse Reactions to foods. Allergy Principles and Practice.2003

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Foods more frequently implicated in food allergy

Children

- ✓ Cow's milk
- ✓ Egg
- ✓ Fish
- ✓ Peanut
- ✓ Fruits
- ✓ Legumes
- ✓ Wheat

Adults

- ✓ Fruits
- ✓ Peanuts
- ✓ Tree nuts
- ✓ Fish
- ✓ Shellfish

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Food allergens

Major class 1 food allergens:

- ◆ Primary sensitizers
- ◆ Sensitization may occur in the gastrointestinal tract
- ◆ Water-soluble glycoproteins
- ◆ Molecular weights ranging from 10 to 70 kD
- ◆ Stable to heat, acid and proteases

Class 2 food allergens (cross-reactive):

- ◆ Generally plant-derived proteins
- ◆ Highly heat-labile
- ◆ Difficult to isolate
- ◆ No good, standardized, extracts are available for diagnostic purposes.

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Major class 1 food allergens

- ◆ Cow's milk:
Caseins (α , β , κ), α -lactoalbumin, β -lactoglobulin, serum albumin
- ◆ Chicken egg:
Ovomucoid, ovalbumin, ovomucoprotein
- ◆ Peanut:
Vicillin, conglutin, glycinin
- ◆ Soybean:
Glycinin, profilin, trypsin inhibitor
- ◆ Shrimp:
Tropomyosin
- ◆ Lipid transfer proteins (LTPs):
Apple, apricot, peach, plum, corn

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Class 2 food allergens

(Cross-reactive and associated with oral allergy syndrome, latex-fruit syndrome)

- ◆ Pathogen-related protein 2 group (glucanase):
Latex, avocado, banana, chestnut, fig
- ◆ Pathogen-related protein 3 group (chitinase):
Latex (Hes b6), avocado
- ◆ Pathogen-related protein 5 (thaumatin-like):
Cherry, apple, kiwi
- ◆ Birch Bet 1 homologues (pathogen-related proteins 10):
Apple, cherry, apricot, peach, pear, carrot, celery, parsley, hazelnut
- ◆ Birch Bet 2 homologues (celery-mugwort-spice syndrome) profilin:
Latex, celery, potato, pear, peanut, soybean

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Pathogenesis of food hypersensitivity: Gut barrier

- ◆ The immune system associated with this barrier is capable of discriminating among harmless foreign proteins or commensal organisms and dangerous pathogens.
- ◆ Food allergy is an abnormal response of the mucosal immune system to antigens delivered through the oral route.
- ◆ The immature state of the mucosal barrier and immune system might play a role in the increased prevalence of gastrointestinal infections and food allergy in the first few years of life.

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Adapted from J Allergy Clin Immunol.
2004;113:808-809

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Pathogenesis of food hypersensitivity: Gut barrier

- ◆ About 2 % of ingested food antigens are absorbed and transported throughout the body in an immunologically intact form, even through the immature gut.
- ◆ The underlying immunologic mechanisms involved in oral tolerance induction have not been fully elucidated.

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2004;113:808-809

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Food allergy: Clinical manifestations

IgE mediated:

Gastrointestinal:	Oral allergy syndrome, gastrointestinal, anaphylaxis
Cutaneous:	Urticaria, angioedema, morbilliform rashes, flushing
Respiratory:	Rhinoconjunctivitis, bronchospasm, wheezing, anaphylactic shock
Generalized:	Any or all of the above

Mixed IgE and cell mediated:

Gastrointestinal:	Allergic eosinophilic oesophagitis/gastritis/gastroenteritis
Cutaneous:	Atopic eczema
Respiratory:	Asthma

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Food Allergy: Clinical manifestations

Cell mediated

Gastrointestinal:

Food protein-induced:
Enterocolitis/proctocolitis/enteropathy
syndromes, celiac disease

Cutaneous:

Contact dermatitis, herpetiformis
dermatitis

Respiratory:

Food-induced pulmonary hemosiderosis
(Heiner's syndrome)

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Gastrointestinal food hypersensitivities: Oral allergy syndrome (OAS) or pollen- food allergy syndrome

- ◆ Elicited by a variety of plant proteins that cross-react with airborne allergens
- ◆ Pollen allergic patients may develop symptoms following the ingestion of vegetables foods:
 - *Ragweed allergic patients: Fresh melons and bananas*
 - *Birch pollen allergic patients: Raw potatoes, carrots, celery, apples, pears, hazelnuts and kiwi*
- ◆ Immunotherapy for treating the pollen-induced rhinitis may eliminate oral allergy symptoms

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Allergic eosinophilic esophagitis (AEE) and gastroenteritis

- ◆ Characterized by infiltration of the esophagus, stomach and/or intestinal walls with eosinophils, basal zone hyperplasia, papillary elongation, absence of vasculitis and peripheral eosinophilia in about 50 % of patients
- ◆ AEE is seen most frequently during infancy through adolescence and typically presents with chronic gastroesophageal reflux
- ◆ Responsible food allergens may need to be eliminated from the diet for up 8 weeks to bring about resolution of symptoms and up to 12 weeks to bring about normalization of intestinal histology

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Food protein-induced proctocolitis

- ◆ Generally presents in the first few months of life and now is generally due to food proteins passed in maternal breast milk or to milk or soy-based formulas

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Food protein-induced enterocolitis syndrome

- ◆ Occurs in infants prior to 3 months of age, but may be delayed in breast-fed babies (milk or soy protein-based formulas are implicated)
- ◆ Symptoms may include irritability, protracted vomiting 1-3 hours after feeding, bloody diarrhoea (leading to dehydration), anaemia, abdominal distension, failure to thrive
- ◆ In adults, shellfish hypersensitivity may provoke a similar syndrome with delayed onset of severe nausea, abdominal cramps and protracted vomiting

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Dietary protein-induced enteropathy (excluding celiac disease)

- ◆ Occurs in first few months of life
- ◆ Diarrhoea (mild to moderate steatorrhea in about 80 % of cases)
- ◆ Poor weight gain
- ◆ Biopsy shows patchy villous atrophy with prominent mononuclear round cell infiltrate, few eosinophils

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Celiac disease

- Extensive enteropathy leading to malabsorption
- Associated with sensitivity to gliadin (wheat, rye and barley)
- Highly associated with HLA-DQ2 ($\alpha 1$ *0501. $\beta 1$ *0201)
- Serology: Anti-gliadin IgA, anti-transglutaminase IgA
- Treatment: Elimination of gluten-containing foods

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Gastrointestinal food hypersensitivities: Infantile colic

- Syndrome of paroxysmal fussiness characterized by inconsolable, agonized crying
- Generally develops in the first 2 to 4 weeks of life and persists through the third to fourth months
- Diagnosis can be established by the implementation of several brief trials of hypoallergenic formula

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*Adapted from J Allergy Clin Immunol. 2004;
113:808-809*

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Cutaneous food hypersensitivities

Acute Urticaria and Angioedema:

- The most common symptoms of food allergic reactions.
- The exact prevalence of these reactions is unknown.
- Acute urticaria due to contact with food is also common.

Chronic Urticaria:

- Food allergy is an infrequent cause of chronic urticaria and angioedema.



Cutaneous food hypersensitivities: Atopic eczema

- ◆ Generally begins in early infancy
- ◆ Characterized by typical distribution, extreme pruritus, and chronically relapsing course
- ◆ Allergen-specific IgE antibodies bound to Langerhans cells play a unique role as “non-traditional” receptors
- ◆ Double blind, placebo-controlled food challenges generally provoke a markedly pruritic, erythematous, morbilliform rash
- ◆ Food allergy plays a pathogenic role in about 35 % of moderate-to-severe atopic dermatitis in children



Respiratory food hypersensitivities: Asthma

- ◆ An uncommon manifestation of food allergy
- ◆ Usually seen with other food-induced symptoms
- ◆ Vapors or steam emitted from cooking food may induced asthmatic reactions
- ◆ Food-induced asthmatic symptoms should be suspected in patients with refractory asthma and history of atopic dermatitis, gastroesophageal reflux, food allergy or feeding problems as an infant, or history of positive skin tests or reactions to food

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Respiratory food hypersensitivities

Rhinoconjunctivitis

- ◆ Usually seen during positive controlled challenge tests, but occasionally reported by patients

Heiner's Syndrome

- ◆ A rare form of food-induced pulmonary hemosiderosis, typically due to cow's milk

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Anaphylaxis

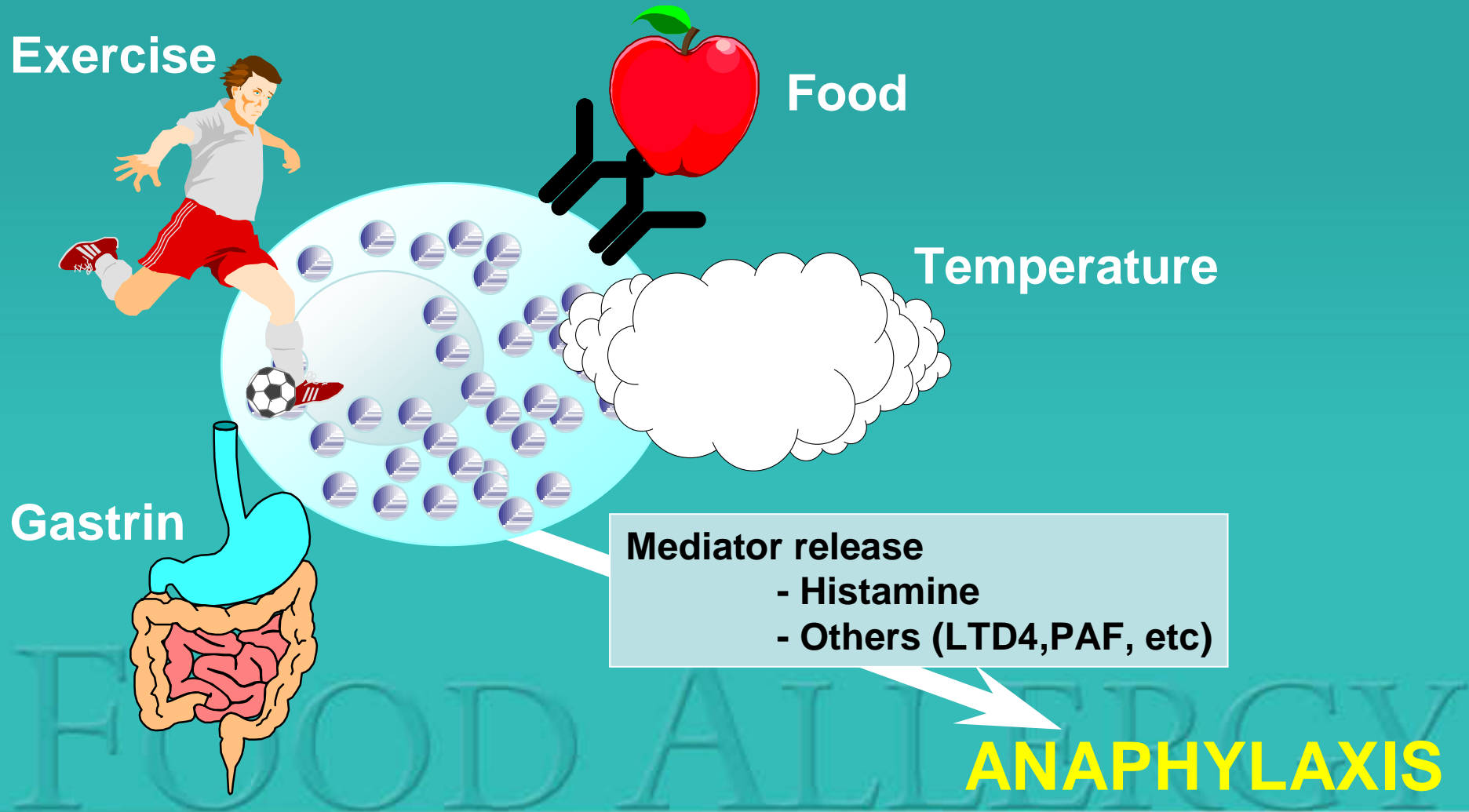
- Food allergies are the cause of at least one-third of anaphylaxis cases seen in hospital emergency
- Variable expression of cutaneous, respiratory and gastrointestinal symptoms, and cardiovascular symptoms including hypotension, vascular collapse and cardiac dysrhythmias
- Serum β -tryptase is rarely elevated in food-induced anaphylaxis

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Adapted from J Allergy Clin Immunol. 2004;113:808-809

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Food allergy: Exercise-induced anaphylaxis



Adapted from Adverse Reactions to Foods Committee.
Spanish Society of Allergy and Clinical Immunology

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Diagnosing food hypersensitivity disorders: IgE-mediated

- 1) Identification and relationship with the food: **Medical history**
- 2) To identify specific IgE: **Skin tests/serum specific IgE**
- 3) To demonstrate that IgE sensitization is responsible for the clinical reaction : **Controlled challenge tests**

Diagnosis is based on the medical history, supported by identification of specific IgE antibodies to the incriminated food allergen.

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*Adapted from Adverse Reactions to Foods Committee,
Spanish Society of Allergy and Clinical Immunology*

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Diagnosing IgE-mediated food hypersensitivity disorders

- ◆ The diagnosis of food allergy cannot be performed on the basis of a non-compatible medical history
- ◆ No diagnostic analysis (skin tests, specific IgE in serum, etc) is of value if it is interpreted without reference to medical history

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*Adapted from Adverse Reactions to Foods Committee,
Spanish Society of Allergy and Clinical Immunology*

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Diagnosing IgE-mediated food hypersensitivity disorders

Medical history: Symptoms

- ◆ Symptoms described by patient
- ◆ Length of time between ingestion and development of symptoms
- ◆ Severity of symptoms
- ◆ Frequency of symptoms
- ◆ Time from last episode

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*Adapted from Adverse Reactions to Foods Committee,
Spanish Society of Allergy and clinical Immunology*

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Diagnosing IgE-mediated food hypersensitivity disorders

Medical history: Timing of reaction

An immediate reaction (1-2 hours) is suggestive of an IgE mediated reaction to foods.

- ◆ It may be preceded by previous tolerance of minimal symptoms
- ◆ It may occur apparently after the first contact



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Diagnosing IgE-mediated Food Hypersensitivity Disorders

- ◆ Identification of food
- ◆ How food was prepared
- ◆ Quantity ingested
- ◆ Previous tolerance
- ◆ Cross-reactions with other food
- ◆ Hidden foods, additives, contaminants

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Diagnosing IgE-mediated Food Hypersensitivity Disorders

- ◆ Age at onset of symptoms
- ◆ Other factors (eg, brought on by exercise)
- ◆ Personal and family history of atopic diseases
- ◆ Risk factors
- ◆ Physical examination: Atopic dermatitis, dermographism, nutritional status

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Clinical symptoms compatible with allergic reaction to food
Immediate reactions (from minutes to 1-2 hours) after
ingestion/contact/inhalation with food
Late gastrointestinal or atopic dermatitis reactions
(>2 hours)
Any age
After last reaction, patient could not tolerate the food

Allergy Assessment

Early correct positive diagnosis allows a suitable diet to be followed and avoids the risks of inappropriate dietary restrictions. **Negative diagnosis** avoids unnecessary dietary restrictions.

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Diagnosing IgE-mediated food hypersensitivity disorders

Skin tests

- ◆ **Prick:** Reproducible, sensitive, not irritant
- ◆ **Prick-prick:** Use raw or cooked food. Highly recommended for fruits and vegetables (commercially prepared extracts are generally inadequate because of the lability of the allergens, so the fresh food must be used for skin testing)
- ◆ **Intradermal:** Not indicated.
- ◆ **Patch test:** Atopic dermatitis, delayed reactions, fresh food is recommended

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Diagnosing IgE-mediated food hypersensitivity disorders

- ◆ Skin Prick Tests are used to screen patients for sensitivity to specific foods
- ◆ Allergens eliciting a wheal of at least 3 mm greater than the negative control are considered positive
- ◆ Overall positive predictive accuracy is < 50 %
- ◆ Negative predictive accuracy > 95 % (negative skin test results essentially confirm the absence of IgE-mediated reactions)

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Diagnosing IgE-mediated food hypersensitivity disorders

- ◆ In infants younger than 2 years, skin prick tests to milk, egg, or peanut with wheal diameters of at least 8 mm are more than 95 % predictive of reactivity.
- ◆ In general, negative skin prick test results are extremely useful for excluding IgE-mediated food allergies, but positive skin test results are only suggestive of presence of clinical food allergies.
- ◆ There is no correlation between the size of wheal and the clinical sensitivity in individual patients

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Skin prick testing

Skin Prick Testing 100% Postive Predictive values (PPV)		
Food	100%PPV ≥3yrs (wheal diameter)	100% PPV ≤ 2 yrs (wheal diameter)
Cow's milk	≥8mm	6mm
Egg	≥7mm	5mm
Peanut	≥8mm	4mm

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Sporik et al. Clin Exp Allergy 2000; 30: 1540-6

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Diagnosing IgE-mediated food hypersensitivity disorders

Serum specific IgE (CAP/Radioallergosorbent tests)

- ◆ Sensitivity similar to skin prick tests
- ◆ Good correlation with other procedures
- ◆ Efficiency: Depends on the allergen
- ◆ Indicated if SPT are contraindicated (eg, skin disease, medications)
- ◆ Useful if discrepancy exists between history and SPT
- ◆ The use of quantitative measurements has shown to be predictive, for some allergens, of symptomatic IgE-mediated food allergy

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Table 2. Food-specific IgE concentrations predictive of clinical reactivity [adapted from Sampson HA.[11]

Allergen	[kU _a /L]	Diagnostic Decision Point			
		Sensitivity	Specificity	PPV	NPV
Egg	7	61	95	98	38
- Infants \leq 2 yrs ⁺	2			95	
Milk	15	57	94	95	53
- Infants \leq 2 yrs ⁺⁺	5			95	
Peanut	14	57	100	100	36
Fish	20	25	100	100	69
Soybean	30	44	94	73	62
Wheat	26	61	92	74	67
Tree nuts ⁺⁺⁺	~15	-	-	~95	

+ Boyano MT, et al. *Clin Exp Allergy* 2001; 31(9):1464-9.

++ Garcia-Ara C, et al. *J Allergy Clin Immunol* 2001; 107(1):185-90.

+++ Clark ET et al. *Clin Exp Allergy* 2003; 33:1019-1022.

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Diagnosing IgE-mediated food hypersensitivity disorders

Serum specific IgE (CAP/RAST)

Advantages

- ◆ Multiple determinations with one blood sample
- ◆ Quantitative and comparable measurements
- ◆ Use of recombinant allergens

Disadvantages

- ◆ Cost
- ◆ Results delayed

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Diagnosing IgE-mediated food hypersensitivity disorders

Other Techniques

- ◆ **Histamine release with foods:**
Similar sensitivity and specificity to serum specific IgE
- ◆ **Sulphidoleukotrienes released from basophils with food:**
Not well studied
- ◆ **For monitoring food challenges:**
Plasma and urinary histamine: High sensitivity, low specificity
Serum tryptase: High specificity, low sensitivity

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Diagnosis of non-IgE mediated food allergy

- ◆ Reaction: Slower onset
- ◆ Difficult to distinguish from food intolerance
- ◆ Elimination by challenge testing
- ◆ In-vitro and in-vivo tests: Little progress
- ◆ Cellular Allergen Stimulation Test (CAST), patch tests

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Predictive values of SPT & APT vs DBPCFC in patients with atopic dermatitis

Technique	PPA	NPA
SPT(early reaction)	69%	95%
SPT (late-phase reaction)	41%	81%
APT	81%	93%



NPA = Negative predictive accuracy
PPA = Positive predictive accuracy

*Niggemann et al, Allergy 2000;
55::281-285*

Cellular allergen stimulation test (CAST®-ELISA)

- ◆ Commercially available
- ◆ Basophil-based assay, sulphidoleukotriene (SLT) release
- ◆ Non-IgE-mediated reactions, food intolerance, IgE mediated reactions

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*Crockard et al. Clin Exp Allergy 2001;
31:345-350*

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Controlled food challenges: Selection of patients for challenge (IgE- mediated Type I allergy)

- ◆ Challenge should be performed either for establishment or exclusion of the diagnosis, for scientific reasons in clinical trials, or for enabling determination of the sensitivity of the actual patient (threshold value) or for determining the allergenicity of food.
- ◆ The determination of the sensitivity enables tailor-made guidelines for the patient, and opens the possibility of following sensitivity by repeated challenges, especially in children with food allergies which are normally outgrown during childhood (cow's milk or hen's egg).

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Controlled food challenges: Inclusion criteria (IgE-mediated allergy)

Patients of any age with history of adverse reaction to a food:

- ◆ For establishment or exclusion of the diagnosis of food intolerance/allergy;
- ◆ For scientific reasons in clinical studies;
- ◆ For determination of the threshold value or degree of sensitivity;
- ◆ For assessment of tolerance. Once diagnosed, when a patient is suspected to have outgrown clinical allergy - especially in children, whose food allergies are normally outgrown during childhood (eg, milk or hen's egg allergies).

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Controlled food challenges: Inclusion criteria (IgE-mediated Type I allergy)

Patients without specific history of adverse reaction to a food:

- ◆ If any chronic symptom is suspected by the patient or the physician to be food-related
- ◆ If a patient is on an inappropriate elimination diet, without a documented history of adverse food reaction. If the food has to be reintroduced into the diet, and there are reasons to suspect that an adverse reaction is possible
- ◆ If a sensitization to a food is diagnosed and tolerance is not known – for example, sensitization to cross-reactive foods that have not been eaten after the adverse reaction

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Controlled food challenges: exclusion criteria

- When a controlled food challenge is not necessary for diagnosing food allergy
 - ◆ Repetitive reactions with minimal quantities of food with positive SPT/CAP-RAST
 - ◆ Recent (children) severe systemic reaction or anaphylaxis (adults)
- In selected cases where positive test results makes challenge unnecessary (e.g. Children with atopic eczema and positive SPT to egg and specific IgE (CAP) ≤ 17.5 Kua/L)

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Controlled food challenges

Relative Contraindications

- ◆ Diseases where epinephrine is contraindicated
- ◆ Patients treated with beta-blockers
- ◆ Patients with ongoing disease should not be challenged eg, patients with acute infection, unstable angina pectoris or patients with seasonal allergy during the season

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Controlled food challenges

Relative Contraindications

- ◆ Pregnant women
- ◆ Patients taking medication which may enhance, mask, delay or prevent evaluation of a reaction or interfere with treatment of a reaction
- ◆ Patients with chronic atopic disease such as asthma or atopic eczema should only be challenged when disease activity is at a stable and low level

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Controlled food challenges

Methods

- ◆ Trained medical personal
- ◆ Emergency treatment available
- ◆ Patient information and informed consent
- ◆ Early treatment of reactions
- ◆ Observation for at least 2- 4 hours

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Controlled food challenges

Methods

- ◆ Patient without symptoms, and fasting
- ◆ The quantity of food to start the challenge may depend upon the quantity of food that induced the last reaction
- ◆ Is highly recommended to start with minimal doses, with a slight increase at intervals superior to the latency period that the patient has experienced in previous reactions

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Controlled food challenges

Methods

- ◆ The quantity of the last challenge dose will be related to the age of the patient (normal amount)
- ◆ Challenge with different foods on different days
- ◆ In asthma ensure long wash-out periods, $FEV_1 \geq 80\%$, and follow-up with FEV_1 or peak expiratory flow (PEF) hourly for 6 hours
- ◆ Atopic eczema and chronic urticaria: If partial improvement after exclusion diet and on minimal treatment

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Types of challenge testing

- ◆ Double -blind 
- ◆ Single-Blind 
- ◆ Open 
- ◆ Double-blind placebo controlled (DBPCFC)
- ◆ Exercise + oral challenge
- ◆ Inhalation challenge

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Controlled food challenges: Double-blind, placebo-controlled (DBPCFC)

- ◆ DB is the procedure generally recommended, especially if a positive challenge outcome is expected
- ◆ DB is the method of choice for scientific protocols
- ◆ DB is the method of choice when studying late reactions or chronic symptoms, such as atopic eczema, isolated digestive late reactions, or chronic urticaria
- ◆ DB is the only way to conveniently study subjective food-induced complaints, such as acute subjective adverse reactions, chronic fatigue syndrome, multiple chemical sensitivities, migraine or joint complaints

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EAACI Position Paper. Allergy 2004;

59: 690-697

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Controlled food challenges: Eligible patients for DBPCFC include:

1. All patients with suspicion of an immediate, systemic allergic reaction to a food for establishment or exclusion of the diagnosis
2. Infants and children \leq three years: An open challenge controlled and evaluated by a physician is most often sufficient
3. Patients with pollen related oral allergy syndrome as their only symptom should only undergo DBPCFC in selected cases, eg, in cases with discrepancy between the case history and the outcome of in vivo and/or in vitro tests

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Controlled food challenges: Double-blind, placebo-controlled (DBPCFC)

An open challenge may precede DBPCFC in older children and adults because a negative result renders DBPCFC unnecessary

Open challenges should not be applied in cases with a high probability of a positive outcome, or in cases with subjective and/or controversial symptoms only

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Placebo controlled food challenges

Intercalate food and placebo

Active and placebo should have identical characteristics and ensure allergenicity

Masking of food: Appearance, colour, flavor, texture

Placebos: Dextrose, liquids

Vehicles: Capsules (lyophilized)

Liquids (placebo)

There are many recipes published for masking foods.

Capsules: Limit quantity (cereals, dry fruits)

Avoid contact with oral mucosa (not used in oral allergy syndrome)

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Double-blind, placebo-controlled food challenge testing: Limitations

- ◆ Tedious
- ◆ Time-consuming
- ◆ Potential risk
- ◆ Requires specialist unit (research)
- ◆ IgE-mediated or non-IgE-mediated?

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Controlled food challenges: Single-blind challenge

- ◆ Single-blind challenge carries the same difficulties for blinding foods as for double-blind, and introduces subjective bias of the observer
- ◆ It needs additional work (cross-over by an external technician)
- ◆ The recommendation of the European Academy of Allergology and Clinical Immunology is to always perform double-blind food challenge

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*EAACI Position Paper. Allergy 2004;
59: 690-697*

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Controlled food challenges: Open challenge

- ◆ A negative double-blind challenge should always be followed by an open challenge
- ◆ A positive open challenge could be sufficient when dealing with IgE-mediated acute reactions manifesting with objective signs
- ◆ For practical reasons, an open challenge can be the first approach when the probability of a negative outcome is estimated to be very high

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Controlled food challenges: Open challenge

- ◆ In infants and children ≤ 3 years, an open, physician-controlled challenge is often sufficient for suspected immediate type reactions (unless a psychological reaction of the mother is expected)
- ◆ For patients with pollen-related oral allergy syndrome as their only symptom, an open challenge could be sufficient as regular procedure. However, double-blind challenge is recommended for scientific protocols and other selected cases for example, discrepancies between the clinical history and the outcome of diagnostic tests

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Cross reactions with foods

- ◆ **Cross-reactivity:** Certain foods are able to sensitize and elicit reactions and could trigger responses generalized to related foods that contain the same or similar allergens. This has variable clinical relevance.

Cross reactions caused primarily by “Type 1” sensitization

- ◆ Legumes, tree nuts, fish, shellfish, cereal grains, mammalian and avian food products

Cross reactions caused by “Type 2” sensitization

- ◆ Pollen-food allergy syndrome (oral allergy syndrome), latex-food syndrome

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Cross reactivity in food allergy: Clinical relevance

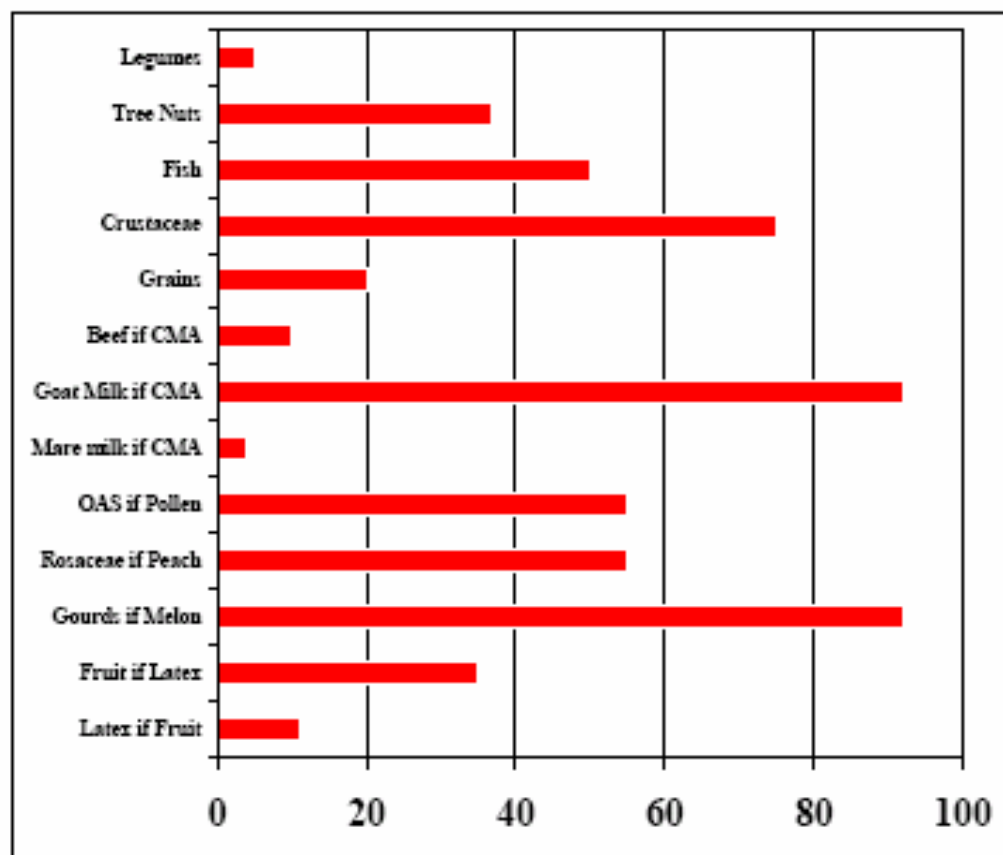


Figure. Approximate rate (%) of reacting to at least one among the related group (limitations and qualifications are explained in the text and in reference 9).

Cross reactions with foods: Clinical implications

- ◆ If the patient is diagnosed with allergy to a food, assessment of clinical sensitization to foods with known cross reactivity is recommended
- ◆ If the patient is diagnosed with allergy to a food with known cross reactivity with another food which he/she is not eating (unknown tolerance), that food must be challenged to assess tolerance

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Food allergy: Treatment

- ◆ Correct diagnosis
- ◆ Treatment of reactions
- ◆ Avoidance
- ◆ Role of dietician
- ◆ Tolerance assessment
- ◆ Immunotherapeutic strategies
- ◆ Prevention

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*Adapted from Adverse Reactions to Foods Committee.
Spanish Society of Allergy and Clinical Immunology*

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Treatment of reactions

- ◆ Epinephrine: 1/1000 w/v, 0,01mg/ kg (Epi-pen®, Adreject®) intramuscularly
- ◆ Emergency ward treatment
- ◆ Oral/parenteral antihistamines
- ◆ Corticosteroids

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Dietary avoidance

- ◆ **Mainstay of treatment**
- ◆ Must be considered as a therapeutic approach
- ◆ Risk-benefit must be assessed
 - ◆ Correct diagnosis is essential
 - ◆ Very restrictive diets can lead to malnutrition

FOOD ALLERGY

Vitamins and minerals which will be affected by restricted diet

Allergen	Vitamin and Minerals
Milk	Vitamin A, vitamin D, riboflavin, pantothenic acid, vitamin B ₁₂ , calcium, & phosphorus
Egg	Vitamin B12, riboflavin, pantothenic acid, biotin, & selenium.
Soy	Thiamin, riboflavin, pyridoxine, folate, calcium, phosphorus, magnesium, iron, & zinc
Wheat	Thiamin, riboflavin, niacin, iron, & folate if fortified
Peanut	Vitamin E, niacin, magnesium, manganese, & chromium

Hidden foods

- ◆ Some foods (allergens) are masked and may be taken unnoticed during diagnostic procedure:
 - ◆ Spices: Mustard, pepper, sesame.
 - ◆ Legumes and tree nuts: Peanut, soy.
 - ◆ Milk protein (protein supplements): Caseine, caseinates.
 - ◆ Vaccines
 - ◆ Kitchen tools, volatile allergens.
- ◆ Parasitized food:
 - ◆ Mites in flour (pasta, pizzas)
 - ◆ *Anisakis simplex* in fish.
 - ◆ Transgenic foods with new proteins.

FOOD ALLERGY

Immunotherapeutic strategies

- ◆ Humanized anti-IgE monoclonal antibody therapy (TNX-901)
- ◆ “Engineered (mutated) allergen protein immunotherapy
- ◆ Antigen-immunostimulatory sequence (CpG)-modulated immunotherapy
- ◆ Peptide immunotherapy
- ◆ Plasmid-DNA immunotherapy
- ◆ Cytokine-modulated immunotherapy

FOOD ALLERGY

Food allergy: Natural history

- ◆ In adults the natural history of food allergy is unknown
- ◆ In children tolerance is frequent after dietary avoidance
- ◆ Milk allergy is outgrown at:
 - 1 yr: 50-60%
 - 2 yr: 70-75%
 - 4 yr: 85%
- ◆ Egg allergy is outgrown:
 - > 6 years: 55%

FOOD ALLERGY

Prevention of food allergy

- ◆ Identify patients at risk (difficult):
 - ◆ There is no reliable or genetic immunological marker
 - ◆ Atopic background in parents, siblings
- ◆ Dietary restriction (milk, egg, fish, nut)
 - ◆ In pregnancy: No benefit
 - ◆ Adverse events on maternal-fetus nutrition
 - ◆ During lactation: Variable effect
- ◆ Prolonged breast feeding?
- ◆ Probiotics??

FOOD ALLERGY

*Adapted from Adverse Reactions to Foods Committee.
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