The Spectrum of Food Allergies

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Background

1. Food allergies are common:
   - Infants: 6-8%; children 2-3%, adults 1% true food allergy
   - Higher prevalence in children: many food allergic children develop immune tolerance
2. Food allergies are increasing:
   - Peanut allergy in UK doubled in 1-2 decades: 1.8%
Background

3. Spectrum changing:

- Multiple food allergies increasing
- “Rare” food allergies are increasing
  e.g. Eosinophilic oesophagitis; FPIES
Allergenic Foods

- Prevalence of food allergies influenced by geography and diet; egg and milk allergy universally common
- Major food allergens are water-soluble glycoproteins (plant or animal sources); generally stable to heat, acid, proteases:
  - “Class 1 allergens”
Allergenic Foods

- Relatively small number of food types cause the majority of reactions:
Allergenic Foods

Young Children
- Cow’s milk
- Hen’s Egg
- Wheat
- Soya
- Peanut
- Treenut
- Sesame
- Kiwi
- (* persistence likely)

Adults
- Fin-fish
- Shellfish
- Treenut
- Peanut
- Fruit and vegetables
Allergenic Foods

- A single food allergen can induce a range of allergic reactions e.g. wheat
Classification of Adverse reactions to Food

- Adverse reaction to food
  - Toxic
    - May occur in all individuals who eat a sufficient quantity of the food
  - Microbiological
  - Pharmalogical
  - Aversion, avoidance and psychological intolerance
  - Food hypersensitivity
    - Non-allergic food hypersensitivity
      - Unknown mechanism
      - Metabolic abnormality e.g. enzyme deficiency
    - Food allergy
      - IgE-mediated food allergy
      - Non-IgE-mediated food allergy
  - Occurs only in some susceptible individuals
Classification of adverse reactions to food

**Adverse Reaction to food**

- May occur in all individuals if they eat sufficient quantity
  - Toxic (e.g. scromboid)
  - Pharmacological (e.g. tyramine)
  - Microbiological (e.g. food poisoning)
- Occurs only in some susceptible individuals
  - Food aversion
  - Food hypersensitivity
Classification of adverse reactions to food

Food Hypersensitivity

- Non-allergic food hypersensitivity
  - Unknown mechanism
  - Metabolic e.g. lactose intolerance

- Food Allergy
  - IgE-mediated
  - Mixed IgE- and non-IgE-mediated
  - Non IgE-mediated
Definitions

- *Food hypersensitivity* has also been described as any reproducible, abnormal, non-psychologically mediated reaction to food.
- *Food allergy* is an immune-mediated food hypersensitivity reaction
Manifestations of food allergies

- **FOOD ALLERGY**
  - **IgE mediated**
    - General
    - Anaphylaxis
    - Cross reactivity syndromes
  - **Mixed IgE and non-IgE mediated**
    - Eosinophilic oesophagitis
    - Eosinophilic gastroenteritis
    - Dietary protein enteropathy
    - Asthma
    - Atopic eczema
  - **Non-IgE mediated**
    - Allergic proctocolitis
    - FPIES
    - Coeliac disease
    - Contact dermatitis
    - Heiner’s syndrome
    - GI motility disorders
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IgE mediated allergic reactions

- Majority of food-induced reactions.
- Release of histamine and mediators from mast cells and basophils produce immediate symptoms (within minutes-2 hours)
IgE mediated allergic reactions

- Some evidence for role of IgE-mediated reaction in intermediate and late symptoms e.g. in atopic dermatitis
- Can involve several organ systems - most common skin and GIT
- Most severe form = anaphylaxis
IgE-mediated allergic reactions

- Large variability in dose/route of exposure required to induce reaction
- Symptoms of FA should occur consistently following ingestion of the causative food allergen→
  - small, sub-threshold quantities of a food allergen/extensively baked, heat-denatured foods may be tolerated
  - modifying factors e.g exercise, alcohol, NSAIDs, viral illness
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IgE mediated: Skin manifestations

AFTER FOOD INGESTION:

- Urticaria and/or angioedema
- Pruritis, erythema and flushing
- Morbilliform rash
- Immediate worsening of eczema
IgE mediated: Skin manifestations

AFTER CONTACT WITH FOOD

- Morbilliform rashes and erythema after skin contact to fruit and vegetables (tomato, citrus and berries)

- Acute localised urticaria after contact with food (e.g. seafood, eggs)
IgE-mediated: Gastrointestinal

UPPER GIT

- Angioedema of the lips, tongue, or palate
- Oral pruritis
- Tongue swelling
- Oral allergy syndrome
IgE-mediated: Gastrointestinal

LOWER GIT

- Nausea
- Colicky abdominal pain
- Reflux
- Vomiting
- Diarrhoea
IgE-mediated: Respiratory

UPPER RESPIRATORY TRACT

- Nasal congestion
- Pruritus
- Rhinorrhea
- Sneezing
- Laryngeal oedema → stridor*
- Hoarseness
- Dry staccato cough
IgE-mediated: Respiratory

LOWER RESPIRATORY TRACT*

- Cough
- Chest tightness
- Dyspnoea
- Wheezing**
- Intercostal retractions
- Accessory muscle use

*can be sign of anaphylaxis
**wheeze is seldom in isolation; usually with skin signs
IgE-mediated: Ocular

- Pruritus
- Conjunctival erythema
- Tearing
- Periorbital edema
IgE-mediated: Cardiovascular

- Tachycardia (occasionally bradycardia in anaphylaxis)
- Hypotension
- Dizziness
- Fainting
- Loss of consciousness
IgE-mediated: Neurological

- Change in activity level
- Anxiety
- Feeling of impending doom
- Dizziness, LOC
IgE-mediated: Other

- Metallic taste in mouth
- Uterine cramping
- Urinary urgency
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IgE-mediated: Anaphylaxis

- Acute life-threatening allergic reaction, typically IgE-mediated
- Any food; most common peanut, tree nut, shellfish
- Multiorgan involvement
IgE-mediated: Anaphylaxis

- Acute onset of illness (80-90% skin signs) + at least one of:
  - respiratory compromise (70%)
  - cardiovascular compromise
    (↓BP/ hypotonia, syncope, incontinence) (35%)
  - persistent abdominal symptoms (40%)
IgE-mediated: Anaphylaxis

- Usually immediate (within 2 hours) and uniphasic
- 20% biphasic (second reaction 8-72 hours after initial reaction subsided)
- Rarely protracted over hours to days
IgE-mediated: Anaphylaxis

Risk factors for severe anaphylaxis:

- Previous severe reaction
- Adolescents
- Asthma, especially poorly controlled
- Delayed/no adrenaline
IgE-mediated: Anaphylaxis

Factors modifying severity of reaction:

- Amount of allergen ingested
- Raw vs heated
- Amount and type of other food ingested
- Presence of acute viral illness
- Stress
- Chronic disease: Chronic cardiovascular/respiratory disease /Adrenal insufficiency
- Drugs eg β-blockers
- Alcohol
- Exercise*
IgE-mediated: anaphylaxis

Food-dependent exercise-induced anaphylaxis

- Rare condition in which symptoms develop if food is eaten within 2 hours prior to exercising. (these foods are tolerated in the diet when exercise is not involved)

- ? altered splanchnic flow/ pro-inflammatory mediators/ autonomic dysregulation/ and increased intestinal permeability during exercise
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IgE-mediated: Cross reactivity

- Cross-reactivity = reaction on exposure to a second antigen after sensitisation to the first, because of similar antibody binding epitopes

- E.g. peanut → treenut
IgE-mediated: Cross reactivity

- **Co-reactivity**: independent sensitisation to more than one allergen

- egg allergy

  ![Co-reactivity](image_url)
IgE-mediated: Cross reactivity

Oral allergy syndrome:
- Cross reaction of airborne allergens with plant proteins (profilins, PR-10 proteins)
- E.g. birch pollen-hazelnut/apple/pear/peach/carrot/cherry/nectarine
- Grass pollen- melon/tomato/orange
IgE-mediated: cross reactivity

Oral allergy syndrome:
- Onset usually in 2\textsuperscript{nd} decade after pollen sensitisation
- Allergens destroyed by acid and heat:
- Symptoms usually mild oropharyngeal
- Rarely systemic symptoms and even anaphylaxis (1.7%)
- Can be reduced by peeling/heat
IgE-mediated: Cross reactivity

Latex Fruit Syndrome

- Latex products
- Fruits (banana, papaya, avo, kiwi, chestnut)

- Shared enzyme chitinase
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Non-IgE mediated reactions

Cell-Mediated Immunity

Antigen Presenting Cell

T Lymphocyte

IL-2

IL-1

TH

IL-2

TH1

IFN-gamma
TNF-beta

Activated Macrophage

Kills Bacteria

Activated NK cell

Kills: Tumor Cells
Virus Infected Cells

Activated Cytotoxic T Cell
Non-IgE mediated reactions

- Involve cell mediated immunity
- Variety of presentations
- Diagnosis by clinical history; improvement on elimination
- No role for SPT/sIgE
- Most commonly involves cow’s milk and soya
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Non-IgE-mediated: allergic proctocolitis

- Usually presents in the first few months of life with fresh blood in the stools + colic
- Otherwise well, thriving baby
- Responds to allergen exclusion.
- Benign; tends to resolve by 1-2 years of age
- Most commonly due to cow’s milk protein allergy
- In both formula and breast fed babies
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Non-IgE-mediated reactions: FPIES

- **Food Protein Induced Enterocolitis Syndrome**
- An acute cell-mediated, gastrointestinal food hypersensitivity characterised by severe protracted diarrhoea and vomiting, pallor and hypotonia
- Onset is typically 1-3 hours after ingestion
- Most commonly cow’s milk and soya; many other triggers described
- May progress to hypovolaemic shock in 15% and ‘sepsis-like’ clinic picture
- Recent recognition of more subtle form, e.g. mild vomiting
Non-IgE-mediated reactions: FPIES

- Characterised by blood neutrophilia, negative stool culture, lack of fever, absence of positive inflammatory markers, and recurrence after reintroduction of the food.
- Symptoms resolve rapidly on a diet free of allergens.
- Most children outgrow the condition within a few years.
- Confirmation of resolution requires a supervised food challenge with facilities to deal with the hypotension and shock that may arise.
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Non-IgE-mediated: Coeliac Disease

- Autoimmune disease in small intestine
- Genetic predisposition HLA DQ2 or DQ8
- Reaction to gliadin (a gluten protein) in wheat, barley, rye
- Presents with malabsorption, chronic diarrhoea, FTT, fatigue, bloating, anaemia
Non-IgE-mediated: Coeliac Disease
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Non-IgE-mediated: contact dermatitis

- Caused by cell-mediated allergic reactions to chemical haptens
- Prolonged/repeated exposure to food allergens
- Common occupational allergy
- E.g. spices, garlic
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Non-IgE mediated: Heiner’s syndrome

Food-protein-induced pulmonary haemosiderosis

• Rare syndrome characterised by recurrent episodes of bleeding into the lungs (leading to haemoptysis and asthma-like symptoms), blood loss from the gut, iron deficiency anaemia, failure to thrive
• Combined cellular and immune-complex reactions, causing alveolar vasculitis.
• Primarily affects infants
• Mostly a reaction to milk
• Reactions to egg and pork have also been reported
Non-IgE mediated: Heiner’s syndrome

- The diagnosis is supported by an improvement on a trial of milk elimination and a positive milk precipitin test.
- Severe cases may be complicated with pulmonary haemosiderosis
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Non-IgE-mediated: GIT motility disorders

- Mast cells and eosinophils interact with the enteric nervous system (‘neuro-immune’ interaction) to cause motility disturbance→
  - Vomiting
  - Colic
  - Treatment resistant GORD
  - Constipation
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Mixed IgE/non-IgE

- Symptoms of a more chronic nature, do not resolve quickly, and are not closely associated with ingestion of an offending food.
- IgE plays a role to varying degrees, as well as cellular interactions
- Symptoms typically hours to days after ingestion
- Specific IgE may or may not be helpful in diagnosis
- Diagnosis: -SPT/IgE/patch test
  - elimination-reintroduction diet
  - biopsy
Manifestations of food allergies

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Mixed IgE/non-IgE: eosinophilic oesophagitis

- Presents with GORD symptoms/dysphagia
- Diagnosed by the presence of >15 eosinophils in one high power field of oesophageal biopsy
- Treatment consists of the supervised dietary exclusion and medical treatment.
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Mixed IgE/non-IgE: eosinophilic gastroenteritis

- Eosinophilic gut wall inflammation leads to symptoms including malabsorption, vomiting, abdominal pain and diarrhoea
- EG describes a constellation of symptoms that vary depending on the portion of the GI tract involved and a pathologic infiltration of the GI tract by eosinophils, which may be localized or widespread
- Treated by supervised dietary exclusion in conjunction with drug treatment including steroids, antihistamines and sodium chromoglycate
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Mixed IgE/non-IgE: dietary protein enteropathy

- Food allergy leads to distorted villous architecture and consequent absorption disturbances
- Can lead to protracted diarrhoea, vomiting, bloating and failure to thrive
- Implicated foods include cow’s milk (most commonly in infants), soy, egg, wheat, rice, chicken and fish
- Virtually all affected patients “outgrow” their symptoms by 2 to 3 years of age, therefore follow-up challenges NB
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Mixed IgE/non-IgE: asthma

- Asthma may occur as a result of inhalation of various foods, particularly milk, wheat and seafood vapours e.g. occupational asthma in the food industry.
- Asthma is a risk factor for severe anaphylactic reactions, indeed nearly all severe and fatal food induced reactions occur in patients with underlying asthma.
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Mixed IgE/non-IgE: Atopic Eczema
Mixed IgE/non-IgE: Atopic Eczema

- The relationship between atopic dermatitis and food allergy is complex and not always causal.
- About 60-80% of children with atopic dermatitis are sensitised to food(s); and 30-40% have true food allergy.
- In about half of those with food allergies, the foods can lead to exacerbations of eczema.
- Specific avoidance of foods in some patients with eczema can lead to an improvement of eczema.
Summary Points

- Food allergies can present in a great variety of ways
- Different food allergy “syndromes” have different typical clinical symptoms/diagnostic strategies and clinical course
- Also important to know the “mimics” of food allergies
Quizz time!
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Mrs Smith came in tearfully unhappy
With young Bob—quite a porker of a chappy
“He’s been getting some Nan,
Now my poor little man
Has some speckles of blood in his nappy”
Scenario 1

- Diagnosis?
- Mechanism of Allergy?
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Scenario 2:

Little John at his first birthday bash
Got bored of his vegetable mash
So when Mom didn’t look
Some nice carrot cake he took
Then developed itchy hives in a flash
Scenario 2

- Diagnosis?
- Mechanism of Allergy?
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Scenario 3:

Mr Knead, whose occupation was baking
Noticed that, during morning bread-making,
He got a tight chest
A wheeze even at rest
And now an inhalers he’s taking.
Scenario 3

- Diagnosis?
- Mechanism of Allergy?
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Recommended Reading


- Leonard S. Food Allergy: What you need to know. Medscape Allergy and Clinical Immunology 15/11/2010

- Jackson, William F. Food Allergy. International Life Sciences Institute Europe, Belgium 2003