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Food Allergens

Food Safety

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Who has heard of this company?

Natasha's Law

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Allergy to milk, one death and one recall. The 'lactose-free' issue

Martina Quadrino , 13,
milk allergy
absence of milk in the foods
Died 4/16/22,
carried an adrenaline auto-injector

A salami sandwich in a bar in Fondi (LT) killed Martina despite her precautions, the injection of adrenaline when the first symptoms appeared and the emergency room in the hospital.

Contamination by undeclared allergen, responsibility to be ascertained by the public or the manufacturer.

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Learning Outcomes

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- **Provide an Introduction to adverse food reactions**
- **Examine the individual factors for predisposition**
- **Aware of the legislation governing key allergenic foods**
- **Develop an ability to define and classify allergens**
- **Knowledge of control measures that are implemented to prevent allergens entering into the food chain**
- **Identify emerging issues in food security from allergens and their implications to human health**
- **Recognise bioanalytical approaches used to monitor the presence of allergens in order to protect human health.**

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Adverse reactions to food

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- **1–3 % of adults and 4–6 % of children suffer adverse health effects following the consumption of particular foods or food ingredients.**
- **Such adverse reactions can be broadly categorised as**
  - **immune-mediated food allergies**
  - **non-immune-mediated food intolerances.**
- **The classical food allergy results in a hyper-immune response that is mediated by antibodies, the best known is the peanut allergy.**
- **Food intolerances are often more difficult to characterise as they can be caused by non-proteinaceous food components (lactose for example)**
- **True allergies which are generally the result of a reaction to one or more individual protein components.**

History of adverse reaction to food

- Observed by early Greeks and Romans 2000 years ago
  - Hippocrates documents sensitivity to cow's milk

- In 1906 the first use of the term Allergy – Clemens von Pirquet
  Derived from Greek
  allos meaning 'other or strange'
  ergos meaning 'work or activity'

- 1921 a study was performed on fish (Prausnitz & Kűstner, 1921)
  - Injected normal person with fish extract – no effect
  - Injected serum of fish allergic Heinz Kűstner into Otto Prausnitz then fish caused an allergic reaction
  - Prausnitz-Kustner test – to determine if person has allergic reaction

- In 1966 researchers discovered the role of IgE (immunoglobulin E) an antibody subclass in serum found duing allergic reactions

Further reading
http://www.sciencedirect.com/science/article/pii/S1323893015301027
Saito et al 2013 Mast cells and IgE: From history to today
Allergology International. 2013;62:3-12

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History of adverse reaction to food

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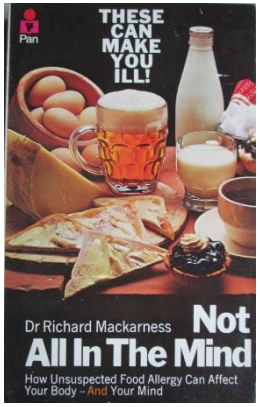
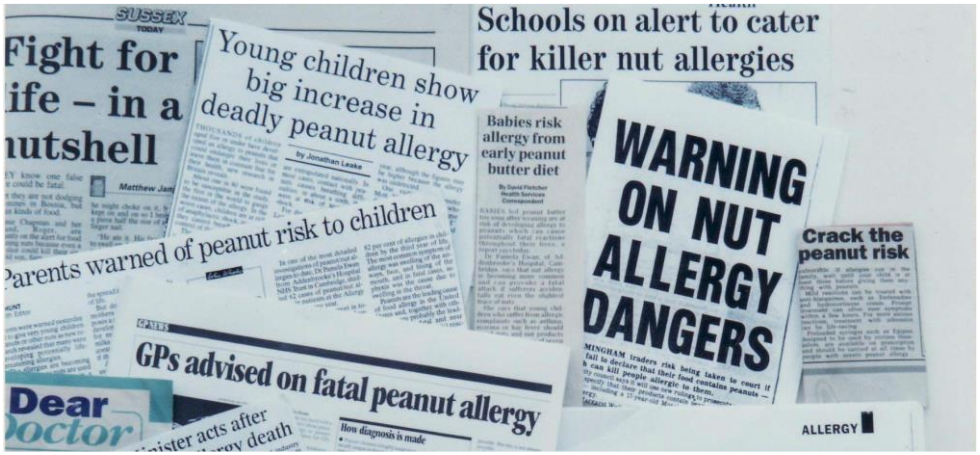
- In 1976 food intolerance in the public eye
- In 1978 Australian researchers Gibson and Clancy published details of an 'exclusion diet' which formed the basis of food intolerance studies
  GIBSON, A.R. and CLANCY, R.L. (1978): An Australian exclusion diet. Med. J. Aust., 1:290-292.
- In 1990s increased media awareness
- In 1995 the European Academy of Allergology and Clinical Immunology suggested a classification on the basis of the responsible pathogenetic mechanism
- In 2000 there was the introduction of EU legislation labelling laws for foods concerning allergens





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Food Allergy Vs Food Intolerance

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Food allergy is a potentially serious immune response to consuming or being in contact with certain foods or food additives.

A food allergy occurs when the immune system:

- identifies a naturally occurring food protein as dangerous and creates antibodies against it
- tries to protect the body against the danger by releasing substances eg histamine, tryptase into the blood when that food is eaten

The reaction is not proportionate to the food consumed

Food Intolerance is an adverse reaction to food that does not involve the immune system and is not life-threatening.

Example

Lactose intolerance: Trouble digesting milk sugar (lactose)

Symptoms: Might include abdominal cramps, bloating and diarrhea

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Classification of adverse reactions to food

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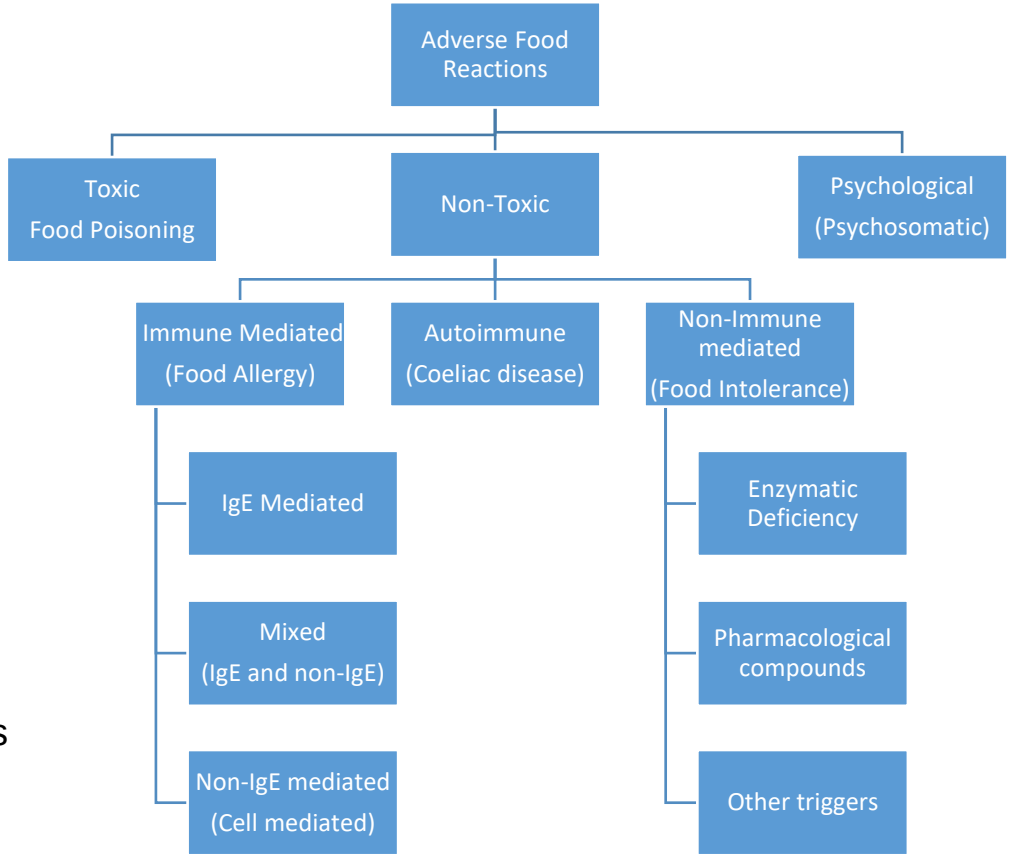
Allergic reactions are classified into IgE-mediated or non-IgE-mediated (cell mediated) or mixed response

Cell mediated - Slower in onset, primarily gastrointestinal reactions

IgE mediated - Causes histamine and other chemicals to be released which trigger allergy symptoms. Rapid in onset, symptoms include urticarial & anaphylaxis



FOOD ALLERGY SYMPTOMS

One or more symptoms:

Can occur within minutes up to hours and be mild to life-threatening

RESPIRATORY TRACT

Swollen throat & mouth

Trouble swallowing

Shortness of breath

Repetitive coughing

Voice change

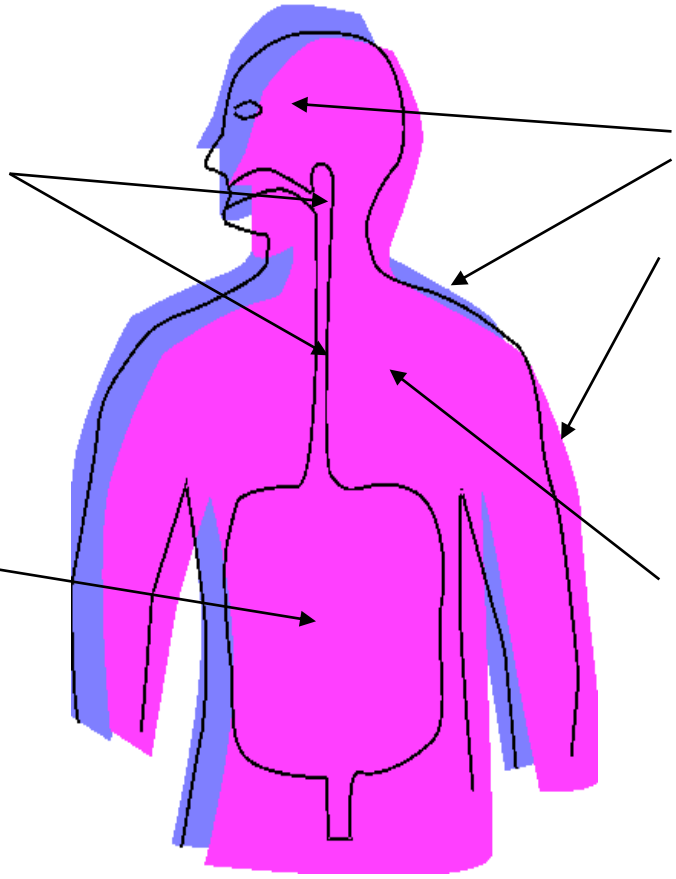
GASTROINTESTINAL TRACT

Nausea & vomiting

Diarrhea

Abdominal cramping

ANAPHYLACTIC SHOCK



SKIN

Swelling

Rhinitis

Conjunctuvitis

Hives

Eczema

Itchy red rash

Rapid heartbeat (tachycardia)

Dizziness

Drop in blood pressure

Loss of consciousness

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ANAPHYLAXIS

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- **Ana (without) Phylaxis (protection)**
- **A serious life threatening allergic reaction that is rapid in onset and may cause death**
- **Food allergies most common cause especially peanuts**
- **Treatment is Epinephrine by injection**
- **EpiPen developed based on Combo-pen for chemical warfare antidote.**
- **Quick administration – a delay can be deadly**
- **Follow-up care and observation for 4-6 hours**
- **Biphasic reactions occur about 20% of the time (symptoms improve or disappear, then the 2nd wave can be worse than 1st)**
- **Emergency management – prevention; mitigation; preparedness; response and recovery**

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Pathophysiology of food hypersensitivity

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- GI Tract forms a barrier to outside environment
- The immune system or gut associated lymphoid tissue associated with the gut barrier is capable of discriminating among harmless foreign proteins or commensal organisms and dangerous pathogens
- **Immune tolerance** describes a state of unresponsiveness of the immune system to substances that have the capacity to elicit an immune response.
- Intact food antigens may penetrate the GI tract but not cause clinical symptoms
- Food allergy is an abnormal response of the mucosal immune system to protein antigens delivered through the oral route
- There is still uncertainty as to why some proteins do not denature and thereby trigger allergic reactions and hypersensitivity while others do
- 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
- Clinical symptoms may develop in genetically predisposed individuals when oral immune tolerance fails

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Types of Hypersensitivity

- Type I: Immediate hypersensitivity
- Type II: Antibody dependent cell mediated cytotoxicity
- Type III: Antigen-antibody complex mediated
- Type IV: Cell-mediated hypersensitivity
- Type V: Receptor mediated

Further reading
http://allergo.lyon.inserm.fr/IMMUNOLOGIE/0.4.re-interpretation.pdf
Rajan (2003) TRENDS in Immunology, 24 (7) 376-379

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Type I: Immediate hypersensitivity

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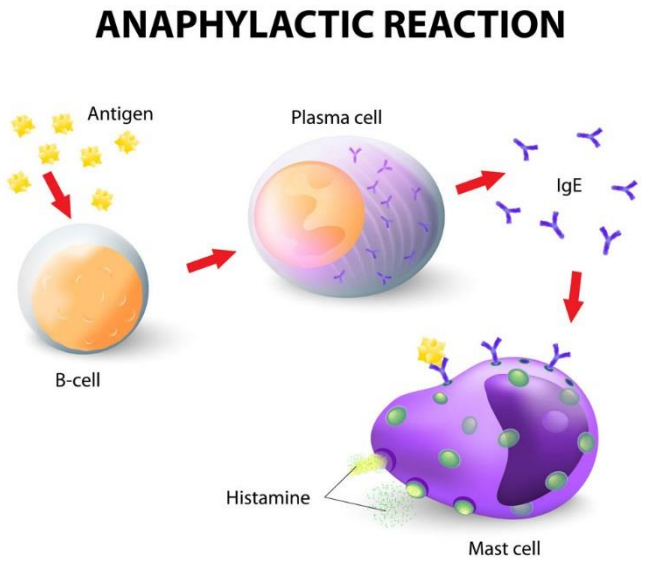
- Failure in oral tolerance leads to excessive food specific IgE antibodies
- These bind receptors on many cells (especially basophils and mast cells)
- Food allergens penetrate the mucosal barrier and bind to these IgE antibodies
- Cellular mediators released
- Systemic effects: cutaneous; respiratory; gastrointestinal and vascular systems



Allergic response: Type I: Immediate hypersensitivity

1. The food is eaten
2. It reaches the stomach and small intestine where the protein are not digested correctly
3. Intact proteins cross the small intestine and reach the blood and lymph system
4. The immune system makes antibodies against the proteins
5. Allergic persons make IgE when non-allergic persons don't
6. IgE binds to the surface of mast cells or basophils which sensitises them

Allergic response: Second Exposure

1. The person eats the food a second time
2. The protein enters the body
3. Binds to and cross-links to two IgE antibodies
4. Causes the basophils to degranulate
5. Granules contain 40 different substances that cause allergic reactions on release
6. Inflammation and swelling due to capillary leakage
   eg Histamine, prostaglandins, bradykinin, TNF, leukotrienes
7. Allergic reaction

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Fatal food induced anaphylaxis

- Most were adolescents or young adults
- History of prior reaction to implicated food
- Only 10% had epinephrine available
- Peanuts and tree nuts for majority (94%)

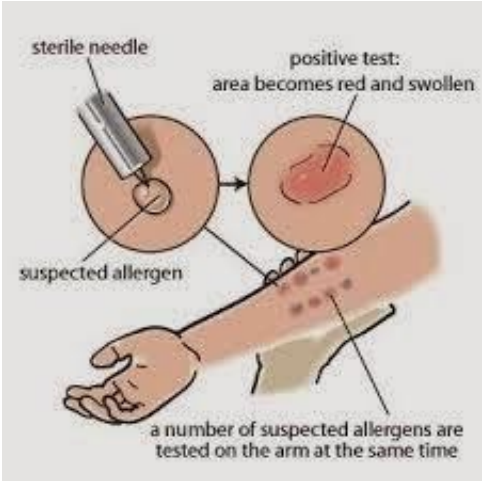
Exercise induced anaphylaxis

- Rare form occurring when patient exercises 2-4 hrs after ingestion of specific food
- Without exercise food not a problem
- Most common in women 15-35 years old
- Common offenders: wheat, celery, shellfish, fish, fruits, milk

ALLERGY Diagnosis

- **Physician - Self / Parental Experience**
- **Medical history, physical exam**
- **Oral food challenge**
- **Elimination diet**
- **Double-blind food challenge**
- **Skin prick test (SPT) - to determine if IgE mediated**

  Allergen extract is applied to the skin & scratched to increase access to blood. If a reaction occurs Inflammation results from the release of histamine and the area becomes red and swollen. Positive control = histamine. Results are determined in 20 mins
- **Lab tests – ImmunoCAP to test for IgE. Allergen extract is applied to a solid phase. Patient serum is added. IgE present binds to the allergen. Antibody is added and binding is measured.**



Allergens such as chocolate, strawberries and citrus often do not show in positive or double blind studies

Further reading

http://www.jacionline.org/article/S0091-6749(13)01836-8/pdf

Sicherer and Sampson (2014) J ALLERGY CLIN IMMUNOL, 133 (2) 296-307

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Treatment of Food Allergy

In the US a life-threatening food allergy can be considered
a disability under federal laws Rehabilitation Act of 1973, Section 504

The Individuals with Disabilities Education Act (IDEA)
The Americans with Disabilities Act (ADA)
The ADA Amendments of 2008 (ADAA)

School Setting: Treatment is avoidance

Emergency management plan

- Prevention
- Mitigation
- Preparedness
- Response
- Recovery

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Strategies for Food Allergy in School: Avoidance

- Increased supervision during meals, snacks
- No sharing (food, containers, utensils)
- Clean tables, toys, hands (younger children)
- Substitutions: meals, cooking, crafts, science
- Ingredient labels for foods brought in
- Education of staff
- Don't miss the bus: no food parties, ensure communication/supervision

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Strategies for Anaphylaxis in School: Treatment

- Physician-directed protocols
- Review of protocols, assignment of roles
- Medications readily available (not locked)
- Education and review:
  - signs of reaction
  - technique of medication administration
  - basic first aid
  - notification of emergency medical system

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Treatment of Food Allergy

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

Treatment of Food Allergy

- For an individual management of their condition is usually through total avoidance of a specific food containing the allergen
  - No level is deemed safe
  - Very small doses can elicit a response
- 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 ingredients and mislabelling of food products is a concern
- Cross-contamination is a constant worry in production lines

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Future immunomodulatory therapies

- Humanized anti-IgE monoclonal antibody therapy
- "Engineered (mutated) allergen protein immunotherapy
- Antigen-immunostimulatory sequence-modulated immunotherapy
- Peptide immunotherapy
- Plasmid-DNA immunotherapy
- Cytokine-modulated immunotherapy
- Induction of tolerance or oral immunotherapy (milk, egg, hazelnut…….)

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Summary

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- Provided an introduction to adverse food reactions
  - Classification:
    - Psychological, Toxic and Non-toxic
      - Non-toxic:
      - Food Intolerance
        - Non-immune mediated
      - Allergic reactions
        - Immune mediated (Anaphylaxis)
      - Diagnosis
      - Treatment

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Please select from the following list the 14 regulated allergens in Europe

Peanuts	Lupine	Gluten	Mustard
Kiwi	Pineapple	Coffee	Honey
Tea	Crustacean	Mollusc	Potatoes
Pine nuts	Egg	Tomatoes	Sulphites
Fish	Bread	Orange	Beef
Milk	Pork	Shellfish	Soybean
Apple	Sesame	Onions	Celery

Please state the allergen of highest prevalence in your region

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Individual Factors

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Discrepancy between prevalence of perceived and confirmed food allergy

- Age
  - Overall occurrence of food allergy changes with age
  - Increased presence in children under 18 with food allergy
    Approximately 20% increase in last decade
  - Affect ~ 6% of children < 3 years old – soy and cow milk

  - Specific allergies change with age
    - Cows milk – 2.5% with 80% tolerant by their 5th birthday
    - Egg allergy – 1.5% with > 85% tolerant by their 3rd birthday
    - Peanut allergy – 0.5% with clinical tolerance reached in a minority
      Prevalence may actually be increasing in children
    - Shellfish allergy – more common in adults

Individual Factors

Common Allergenic Foods: Infants / Children
Cow's milk
Eggs
Peanuts
Fish
Wheat

Common Allergenic Foods: Adults
Peanuts and nuts
Fish
Crustacea – shrimp, crab, lobster
Molluscs- clams, oyster, scallop
Bananas, kiwi
Apple, pears
Carrots and celery
Wheat

Individual Factors

- Gender
  - Some cases females have a higher prevalence than males

- Ethnicity
  - Differences in the prevalence of food could be due to
    - genetic differences (e.g. in the HLA system)
    - different food habits and
    - different prevalence of food allergy in the country of origin for immigrants
  - Globally a subpopulation of <1% - Data is limited in regions
  - One in 25 Americans, or 4% of the population, has a food allergy
  - In Australia a study of infants found 1 in 10 with a food allergy
  - Chongqing, China - 2.5 % of children showed an allergy to egg & 1.3% to milk

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Individual Factors

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- Genetic background
  - 65% of susceptible people have a close relative with an allergy
  - association between specific food allergies and specific human leucocyte antigen (HLA) types.

- Increased intestinal permeability to macromolecules predisposes exposure
  - Viral gastroenteritis
  - Premature birth
  - Cystic fibrosis
- Higher in children with other atopic disorders
  - 35% of children with moderate to severe atopic dermatitis (eczema)
  - 6% of asthmatic children
- Socioeconomic factors
  - Studies suggest an increased rate of food allergy in higher socioeconomic populations, but evidence is still controversial

- Other factors
  - Physical exercise, alcohol, antibiotics, gastric acidity inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) may increase the likelihood of food-allergic reactions

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Increased Prevalence?

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Theories for the increase in food allergy

- Better diagnosis
- Increased awareness and media attention
- Increases across different demographics
- Changes in the environment
  - Different methods of processing
  - Different methods of preparation
- Hygiene hypothesis

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Global legislation

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Codex Alimentarius is the international food standards agency

It provides a series of international standards for food and agricultural products.

CODEX helps to ensure fair trade and consumer protection internationally.

The Codex Alimentarius Commission Committee on Food Labelling has listed the foods and ingredients that cause the most severe reactions and most cases of food hypersensitivity.

a list of ingredients shall be declared on the label.
All ingredients shall be listed in descending order of ingoing weight
Compound ingredients <5% food need not be declared

160 foods are reported to have caused an allergic reaction

Worldwide 90% of allergic reactions, including the most severe ones, are limited to eight foods as agreed on by Codex Alimentarius

These 8 foods should always be declared on the label

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Common Known Food Allergens

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Eight (8) foods cause ninety (90) percent of the food allergic reactions

Manufacturers are required to list these ingredients on the label in **BOLD** text though there are still instances when ingredients may not be listed

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List of Allergens – EU Top 14

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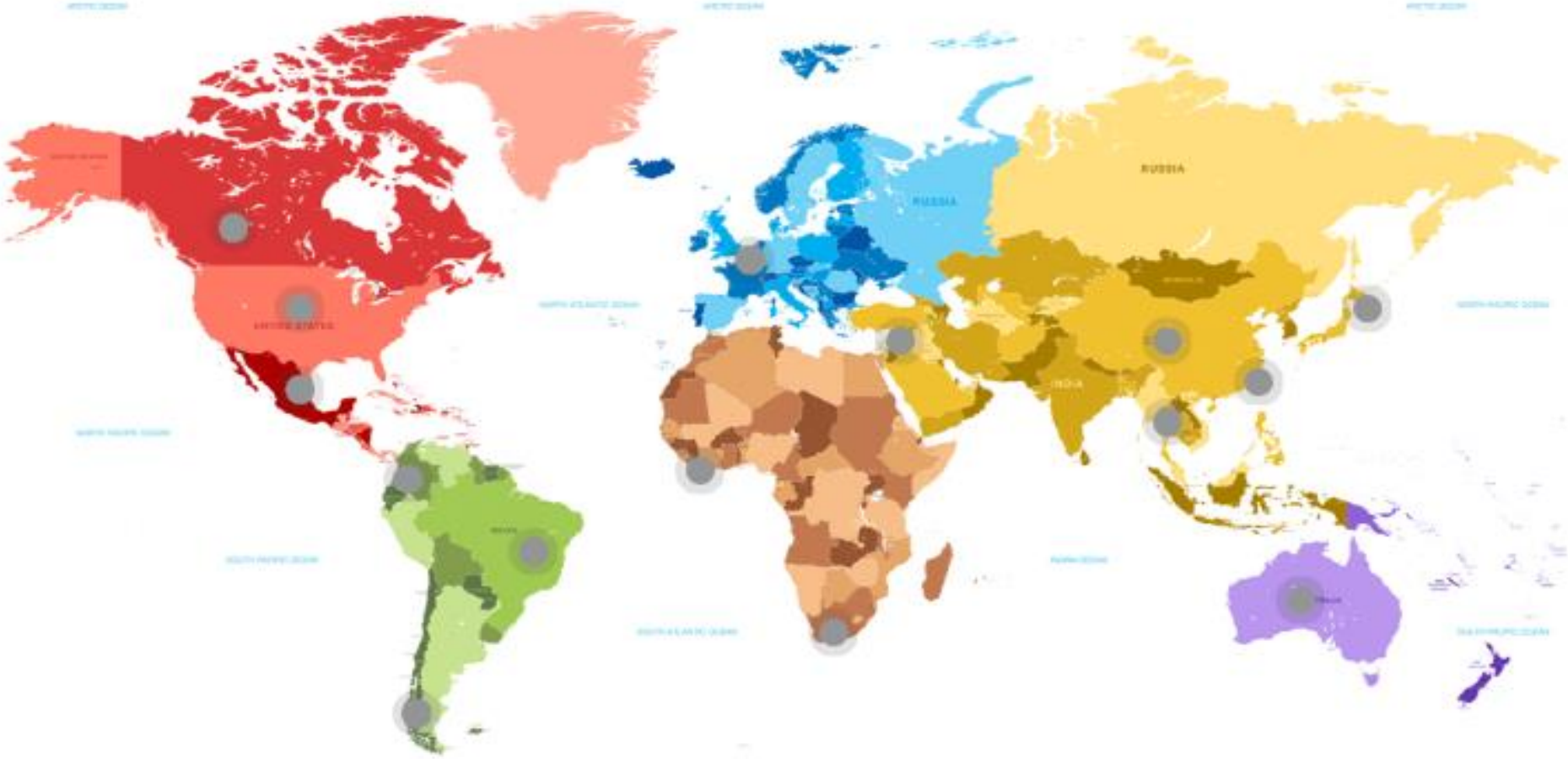
	Codex	Australia	Canada	China	EU	Japan	Korea	Mexico	South Africa	USA
Gluten (Cereals)	X	X	X	X	X	X	X	X	X	X
Crustacean	X	X	X	X	X	X	X	X	X	X
Molluscs			X		X				X	
Egg	X	X	X	X	X	X	X	X	X	X
Fish	X	X	X	X	X		X	X	X	X
Shellfish		X	X	X	X				X	
Peanut	X	X	X	X	X	X	X	X	X	X
Soybean	X	X	X	X	X		X	X	X	X
Milk	X	X	X	X	X	X	X	X	X	X
Tree nuts *	X	X		X	X			X		X
Sulfites	X	X	X		X					
Sesame					X					
Celery			X		X					
Mustard			X		X					
Lupine					X					
Other	X					X	X			

X indicates that the specified allergen is regulated in that country or region

* e.g. Canada: Almond, brazil nut, cashew, hazelnut, macadamia, Queensland nut, pecan, pine nuts, pistachios, walnut

TOP FOOD ALLERGIES AMONG CHILDREN UNDER 18 AROUND THE WORLD



THE TOP EIGHT

DAIRY

EGG

SHELLFISH

FISH

TREE NUTS

SOY

WHEAT

PEANUTS

THESE ACCOUNT FOR MORE THAN 90% OF FOOD ALLERGIES

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Harmonisation Challenges in Legislation

- Geographical differences
- Population variation
- Internal labelling and safety expectations
- Lack of confidence around precautionary labels
- Food fraud

"in this era of globalisation it is not only populations that migrate but also foods as people adopt foreign diets and import exotic products"

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European Legislation

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DIRECTIVE 2000/13/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 20 March 2000 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs

Directive 2003/89/EC of the European Parliament and of the Council of 10 November 2003 amending Directive 2000/13/EC as regards indication of the ingredients present in foodstuffs. OJ L 308, 25.11.2003, p. 15–18.

COMMISSION DIRECTIVE 2007/68/EC of 27 November 2007 amending Annex IIIa to Directive 2000/13/EC of the European Parliament and of the Council as regards certain food ingredients
13 allergenic foods or food groups and sulphur dioxide (listed in Annex IIIa)

Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004 Text with EEA relevance

COMMISSION DELEGATED REGULATION (EU) No 78/2014 of 22 November 2013 amending Annexes II and III to Regulation (EU) No 1169/2011 of the European Parliament and of the Council on the provision of food information to consumers, as regards certain cereals causing allergies or intolerances and foods with added phytosterols, phytosterol esters, phytostanols or phytostanol esters

From 13 December 2014, the EU Food Information for Consumers (EUFIC) Regulation No. 1169/2011 repeals Directive 2000/13/EC as amended by Directives 2003/89/EC 2007/68/EC. requires food businesses to provide allergy information on food sold unpackaged, in for example catering outlets, deli counters, bakeries and sandwich bars.

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Challenges of Labelling

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Challenges of Labelling

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'Free From' to consumer means total absence

Some 'Free from' products have been found to contain traces that may cause a reaction

Food companies wishing to label products 'free from X' must be confident there is virtually no chance of cross-contact.

"Gluten-free" statement will mean the product contains 20ppm or less of gluten.

"Very low gluten" will mean no more than 100ppm.

AOAC International has approved the method
"Gliadin as a Measure of Gluten in Foods" as Official Method 991.19.

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Reference Doses for Legislation

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Food allergies are caused by certain proteins in food.

Reference doses were developed from statistical dose distribution modeling of individual thresholds of patients in clinical oral food challenges.

Translating reference doses into management practice is challenging.

Based on the total protein from an allergic food below which only the most sensitive individual (approx. between 1 and 5%) in the allergic population are likely to experience an adverse reaction.

Reference doses ranged from 0.03 mg for egg protein to 10 mg for shrimp protein

Allergen	Peanut	Milk	Egg	Tree nuts	Soy	Wheat	Mustard	Lupin	Sesame	Crustacea (Shrimp)	Fish
Reference Dose (mg)	0.2	0.1	0.03	0.1	1	1	0.05	4	0.2	10	NA

Allen et al 2014 Allergen reference doses for precautionary labeling (VITAL 2.0): Clinical implications

United States

Food Allergen Labelling and Consumer Protection Act
(FALCPA, 2004) – since 1 January 2006

Shorter list of allergenic food groups; but requires indication of fish, crustacaen and tree nuts

…and other such as Canada, Australia, Japan or Turkey

Focus exclusively on labelling requirements for added ingredients.
Risk management regarding cross contamination is not regulated.
Though legislation should include thresholds or guidances to what constitutes a safe level.

Swiss (Lebensmittelverordnung; 2002)

Action limits: declaration as ingredients – > 1g / kg or L and declaration as contaminants - < 1g / kg or L

Australia

Australian Food and Grocery Council (AFAGC) – industry guidelines in 2007 for allergen management

Action levels: 2 mg / kg for egg, peanut, sesame, treenuts, crustacaen; 5 mg / kg for milk;

10 mg / kg for soy and 20 mg / kg for fish and gluten

The development of acceptable threshold levels is an urgent challenge in the context of international harmonization

To set threshold levels there needs to be a standardisation of measurement for example an indicator protein and analytical reference standards

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Food Allergens

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- Almost all allergens are natural food proteins
  - 10-70 kD glycoproteins
  - Heat resistant, acid stable

- Most food allergens contain multiple proteins which are allergenic

- Characterization of epitopes underway
  - Linear vs conformational epitopes
  - B-cell vs T-cell epitopes

A systematic International Union of Immunological Societies (IUIS) Allergen Nomenclature has been established and adopted by WHO (King et al., 1994).

The official site (http://www.allergen.org) lists all recognised allergens and isoforms

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Food allergens

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Class 1 food allergens:

- Primary sensitizers
- Sensitization may occur through 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

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Food	Allergy causing component (proteins)	Additional Notes
Cow's milk	Caseins (a,b,k) a-lactoalbumin, B-lactoglobulin, serum albumin	No reduction by pasteurisation, condensation, evaporation & dryng
Chicken egg	Ovomucoid, ovalbumin, ovotransferrin	Egg white is more allergenic and no reduction by cooking
Peanuts	Vicillin, conglutin, glycinin	Very heat stable trace sensitivity by individuals
Soybeans	Glycinin, progilin, trypsin inhibitor	
Shrimp	Tropomyosin	
Fish	Parvalbumins	These proteins are conserved in fish species. Very cross reactive and very stable in processing
Lentil	*Vicilin*	
Fruits and other vegetables *(apple, apricot, peach, plum, corn)*	Lipid transfer proteins (LTPs)	

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Class 2 food allergens *(Cross-reactive and associated with oral allergy syndrome, latex-fruit syndrome)*

Food	Allergy causing component (proteins)
Latex, avocado, banana, chestnut, fig	Pathogen-related protein 2 group (glucanase):
Latex (Hev b6), avocado	Pathogen-related protein 3 group (chitinase):
Cherry, apple, kiwi	Pathogen-related protein 5 (thaumatin-like):
Apple, cherry, apricot, peach, pear, carrot, celery, parsley, hazelnut	Birch Bet v1 homologues (pathogen-related proteins 10):
Latex, celery, potato, pear, peanut, soybean	Birch Bet v2 homologues (celery-mugwort-spice syndrome) profilin:

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Prevalence of clinical cross reactivity among food "families"

Food Allergy	Prevalence of Allergy to > 1 Food in Family
Fish	30-100%
Tree Nut	15-40%
Grain	25%
Legume	5%
Any	11%

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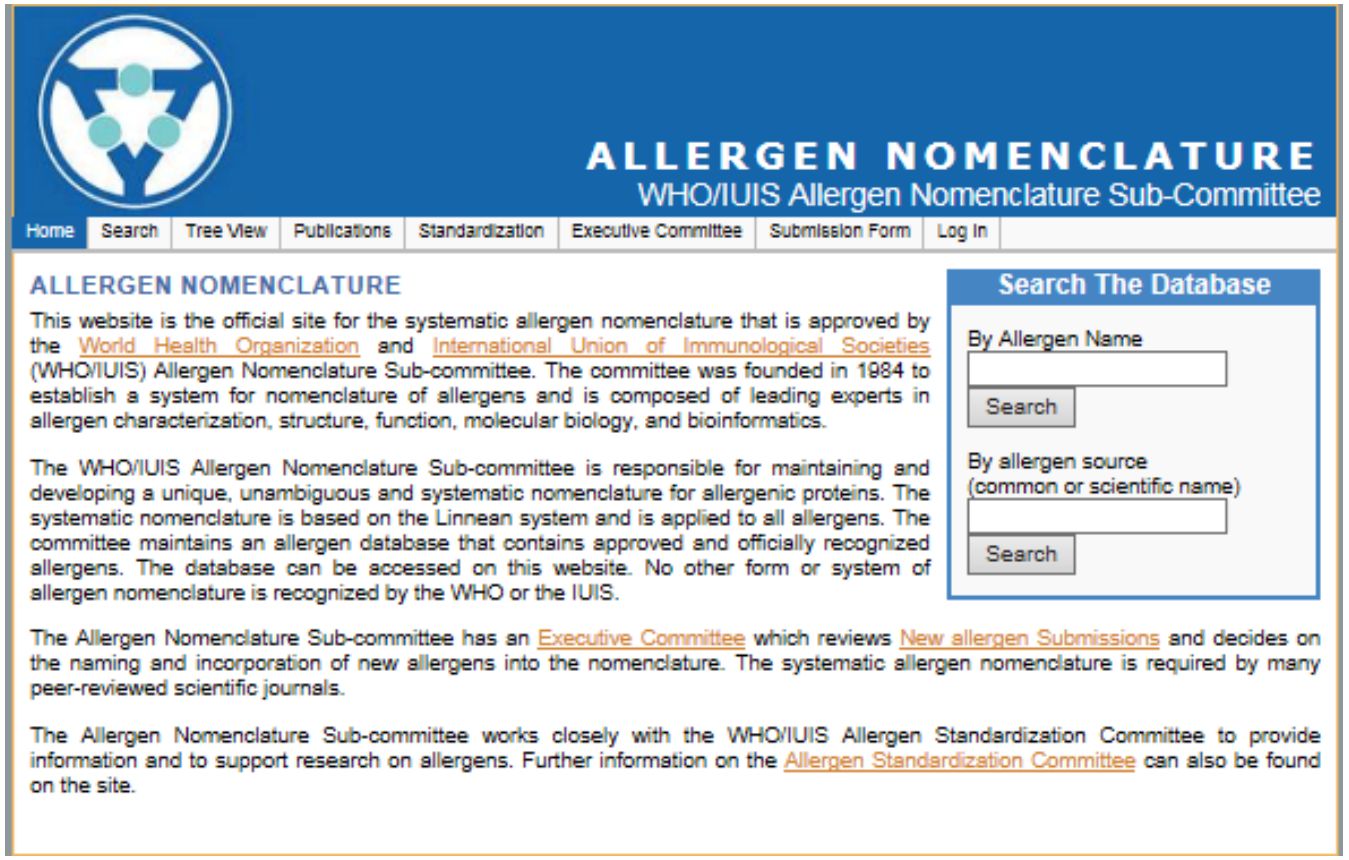
Some cross-reactions between inhalant allergens and food allergens

Inhalant allergy	Food allergy
Birch pollen	Nuts, apple, pear, peach, plum, cherry, carrot, peanut, soy
Ragweed pollen	Melon, banana
Grass pollen	Tomato, peanut, pea, wheat, rye
Latex	Banana, chestnut, kiwi, avocado
Chironomids	Crustaceans

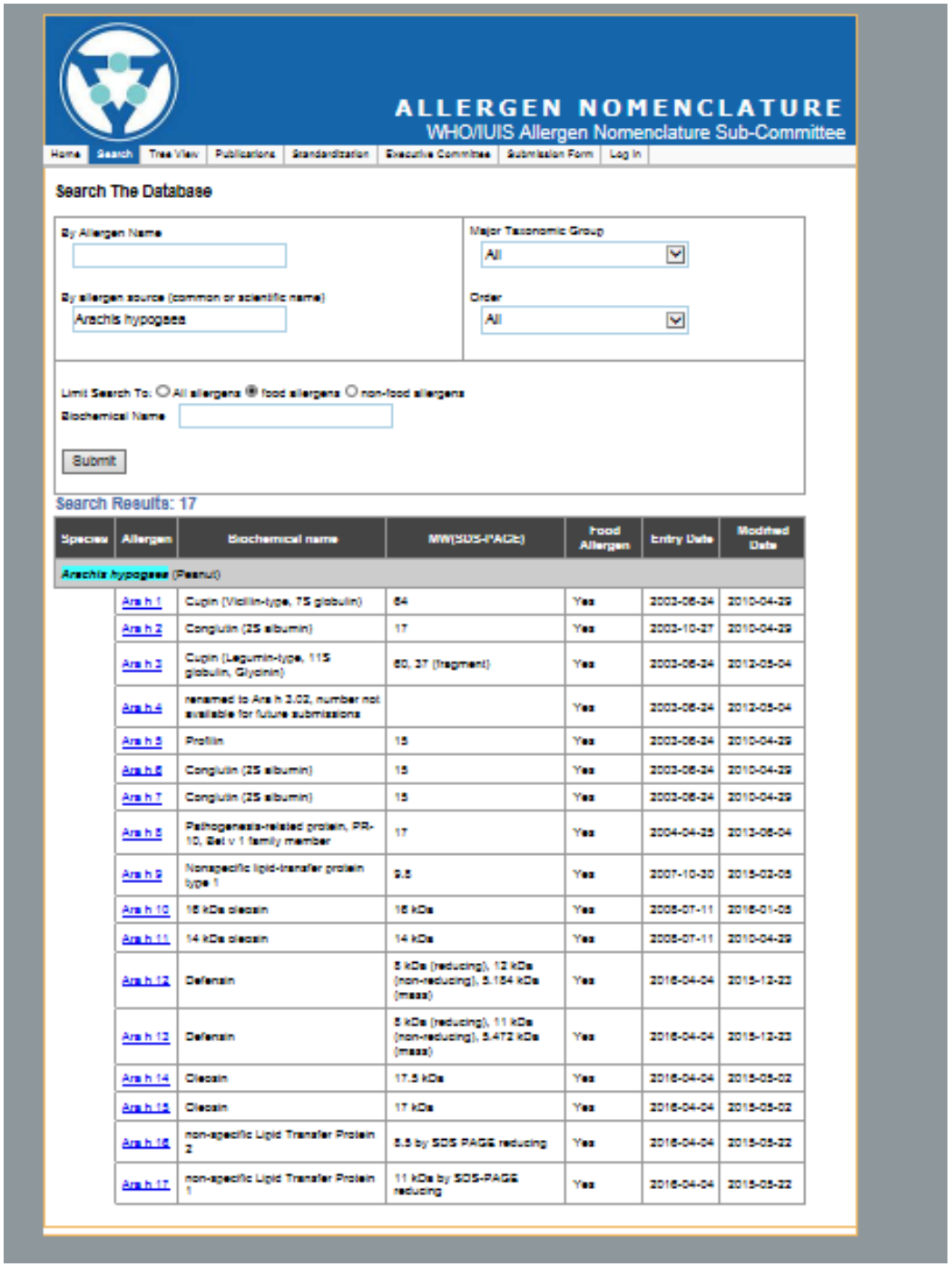
Importance of considering 3-dimensional protein structure in prediction cross-reactivity

Let's have a look at nomenclature

The official site (http://www.allergen.org) lists all recognised allergens and isoforms.



Type common name peanut



ALLERGEN NOMENCLATURE
WHO/IUIS Allergen Nomenclature Sub-Committee

Home | Search | Tree View | Publications | Standardization | Executive Committee | Submission Form | Log In

Search The Database

By Allergen Name

Major Taxonomic Group: All

By allergen source (common or scientific name): Arachis hypogaea

Order: All

Limit Search To: ○ All allergens ◉ food allergens ○ non-food allergens

Biochemical Name

Submit

Search Results: 17

Species	Allergen	Biochemical name	MW(SDS-PAGE)	Food Allergen	Entry Date	Modified Date
Arachis hypogaea (Peanut)						
	Ara h 1	Cupin (Vicilin-type, 7S globulin)	64	Yes	2003-06-24	2010-04-29
	Ara h 2	Conglutin (2S albumin)	17	Yes	2003-10-27	2010-04-29
	Ara h 3	Cupin (Legumin-type, 11S globulin, Glycinin)	60, 37 (fragment)	Yes	2003-06-24	2012-05-04
	Ara h 4	renamed to Ara h 3.02, number not available for future submissions		Yes	2003-06-24	2012-05-04
	Ara h 5	Profilin	15	Yes	2003-06-24	2010-04-29
	Ara h 6	Conglutin (2S albumin)	15	Yes	2003-06-24	2010-04-29
	Ara h 7	Conglutin (2S albumin)	15	Yes	2003-06-24	2010-04-29
	Ara h 8	Pathogenesis-related protein, PR-10, Bet v 1 family member	17	Yes	2004-04-25	2013-06-04
	Ara h 9	Nonspecific lipid-transfer protein type 1	9.5	Yes	2007-10-30	2015-02-05
	Ara h 10	16 kDa oleosin	16 kDa	Yes	2005-07-11	2016-01-05
	Ara h 11	14 kDa oleosin	14 kDa	Yes	2005-07-11	2010-04-29
	Ara h 12	Defensin	5 kDa (reducing), 12 kDa (non-reducing), 5.154 kDa (mass)	Yes	2016-04-04	2015-12-23
	Ara h 13	Defensin	5 kDa (reducing), 11 kDa (non-reducing), 5.472 kDa (mass)	Yes	2016-04-04	2015-12-23
	Ara h 14	Oleosin	17.5 kDa	Yes	2016-04-04	2015-05-02
	Ara h 15	Oleosin	17 kDa	Yes	2016-04-04	2015-05-02
	Ara h 16	non-specific Lipid Transfer Protein 2	9.5 by SDS PAGE reducing	Yes	2016-04-04	2015-05-22
	Ara h 17	non-specific Lipid Transfer Protein 1	11 kDa by SDS-PAGE reducing	Yes	2016-04-04	2015-05-22

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With all these proteins identified
How do you think this will affect allergen management?

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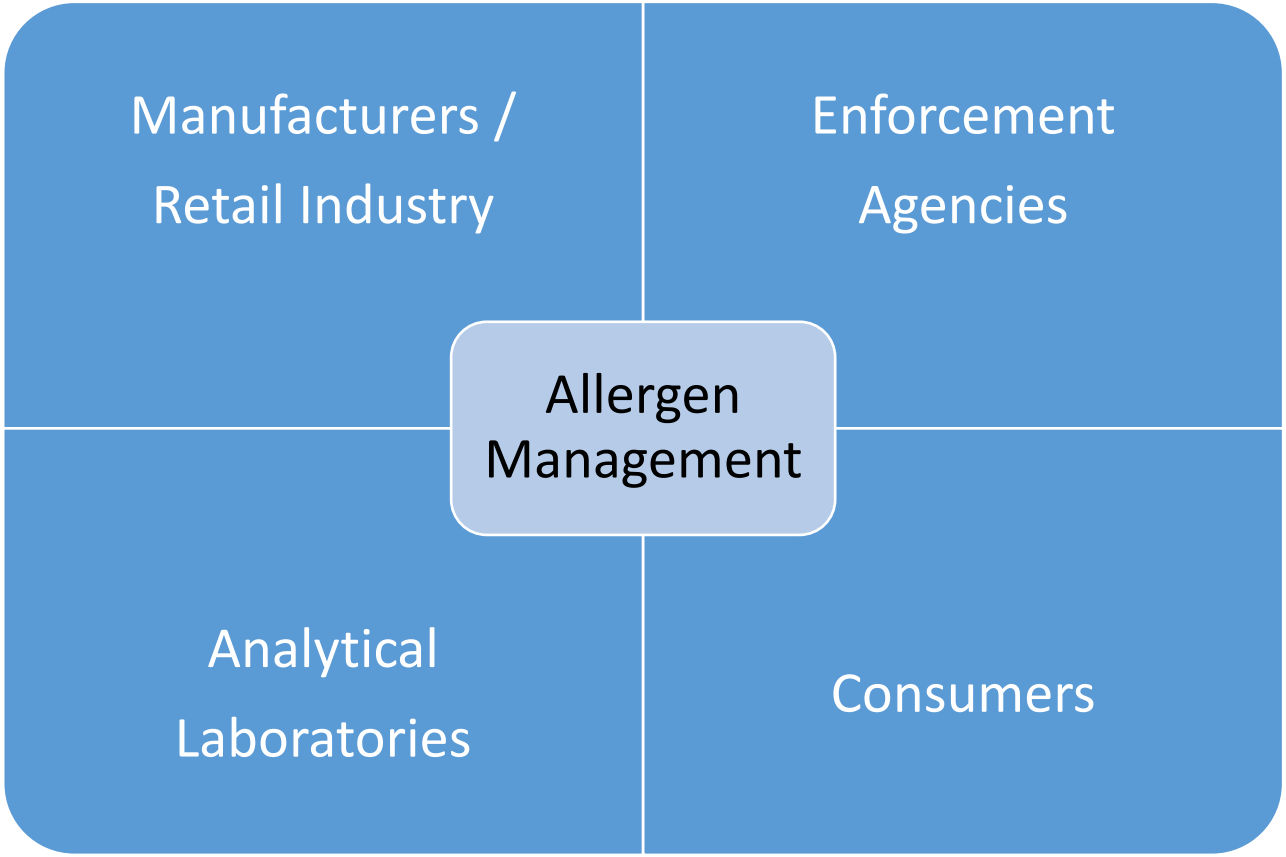
Management of food allergens involves:



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How do allergens get into our food:

1. Added as a deliberate ingredient with the manufacturer labelling the product
    I. Occasionally mistakes in mis-labelling causing recalls

2. Adventitious addition

    a. Unintentional addition: Cross-contamination or cross contact of ingredient through production lines or machinery in the factory
        I. Requires a risk assessment in production
        II. Concern for manufacturers and leads to the precautionary labelling of the products to "may contain" but this form of labelling is now meaningless to the consumer if on every product
        III. Generally low level contamination and only affects highly sensitive

    b. Intentional addition by adulteration – deliberate addition whereby products are substituted eg peanut substituted for almond powder as cheaper ingredient
        i. No labelling of the product
        ii. Poses a serious health threat as ingredient at potentially high levels

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Management of food allergies

Food Industry	Government	Analytical Laboratories	Consumer
Good risk management practices by primary producers and distributors	Food legislation / Enforcement	Suitable testing methods	Educated and knowledgeable public
Quality assurance and control measures for production of foods	Advice for Food Industry	Validation and Accreditation	Discriminative and selective consumers
Appropriate process and equipment considered in factory design	Consumer Education	Rapid Turnaround	Safefood practice in the home

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HACCP Plan for Allergen Management

Food-safety management is based on:

Hazard Analysis Critical Control Point (HACCP) – Regulation 2004/852/EC.

- to be included in the process to reduce the risk
- pre-requisite programes e.g. sanitation have to be installed

Allergen HACCP

1. Approved supplier program
2. Raw material control for ingredients
3. Sanitation
    a. Separation
    b. Scheduling
4. Employee awareness and training
5. Labelling to be informative and accurate
6. Documentation of procedures

http://www.fooddrinkeurope.eu/uploads/press-releases_documents/temp_file_FINAL_Allergen_A4_web1.pdf

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Australia and New Zealand's Industry Tools

VITAL ® - *Voluntary Incidental Trace Allergen Labelling Risk assessment Tool*

http://www.allergenbureau.net

VITAL® allows food producers to assess the impact of allergen cross contact and provide appropriate precautionary allergen labelling on their products.

Food allergens may be present in a food due to intentional inclusion as part of a recipe, allergens but may also be present due to unintentional cross-contact eg raw materials; line-sharing; dusts (e.g. milk powder); use of common equipment and/or environment

Can occur at any point in the supply chain due to the type of ingredients used or through the use of shared equipment and processes during manufacture.

Even under conditions of Good Manufacturing Practice (GMP) cross-contact may be difficult to eliminate entirely, leading manufacturers to use precautionary advisory statements to advise allergic consumers.

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10 Steps of the VITAL Risk Assessment

1. Determination of relevant allergens
2. Identification of intentionally added allergens
3. Identification and quantification of cross contact allergens due to ingredients
4. Identification and quantification of cross contact allergens due to processing
5. Calculation of total cross contact allergen in the finished product
6. Determination of action levels – referring back to the reference dose
7. Review of labelling recommendations and source of cross-contact
8. Recording of assumptions
9. Validation of VITAL assessment
10. Ongoing monitoring

All of these steps rely heavily on the security of the manufacturers supply chain and good manufacturing practices and awareness of employees

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Food fraud: the dangerous allergens lurking in the supply chain

Replacing ingredients to cut costs can have deadly results if consumers are exposed to foods that cause an allergic reaction

Allergy sufferers are placed at risk when restaurant ingredients are substituted for alternatives or contaminated by suppliers. Photograph: Ray Tang / Rex Features Ray Tang / Rex Features/Ray Tang / Rex Features

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Food fraud: Deadly peanuts may be lurking in your high street takeaway

UNDERCOVER investigators prevented a peanut allergy disaster when they exposed a high street food fraud.

By: Stuart Winter
Published: Sun, February 17, 2013

Tragic victim, student Emma Egerton

Harmful peanuts had been swapped for more expensive almonds in Indian restaurant dishes

FOOD SAFETY ISSUE

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Peanut curry death: Restaurant owner Mohammed Zaman jailed

23 May 2016 | England

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Analytical testing in allergen analysis

- Monitor ingredients
  - Ensure raw material allergen profile is as specified
  - Demonstrate appropriate handling and storage.
- Investigate and validate cleaning procedures
  - Target analysis of problem pieces of processing equipment
  - Environmental swabs and sampling in production to determine effectiveness of cleaning protocols
- End product analysis
  - Verify effectiveness of and adherence to control procedures
  - Investigate complaints related to undeclared allergens
  - Monitoring of change impact in formulations
  - Confirm assumptions made during risk assessment process
  - Monitor 'free from' and 'very low' labelling
  - To show regulatory compliance

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Current Techniques for routine analysis

- Non-specific methods
  - Adenosine triphosphate (ATP)- bioluminescence
  - Protein tests – biuret method

- Specific methods -Target either the allergen itself or a biomarker that indicates the presence of the allergenic food.

  - **Enzyme linked immunosorbent assay (ELISA)**
    - **Sandwich ELISA**
    - **Competition ELISA**
  - **Lateral Flow Device (LFD)**

  - **Polymerase Chain Reaction – DNA analysis**

  - Mass spectrometry – new tool

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Some considerations for Analysis

Discuss the following questions and rank in order of importance?

What laboratory
What method
What calibrator
What matrix
Reference materials and proficiencies
Company pedigree and available information
External publication and approvals
Sensitivity, cross-reactivity and related products

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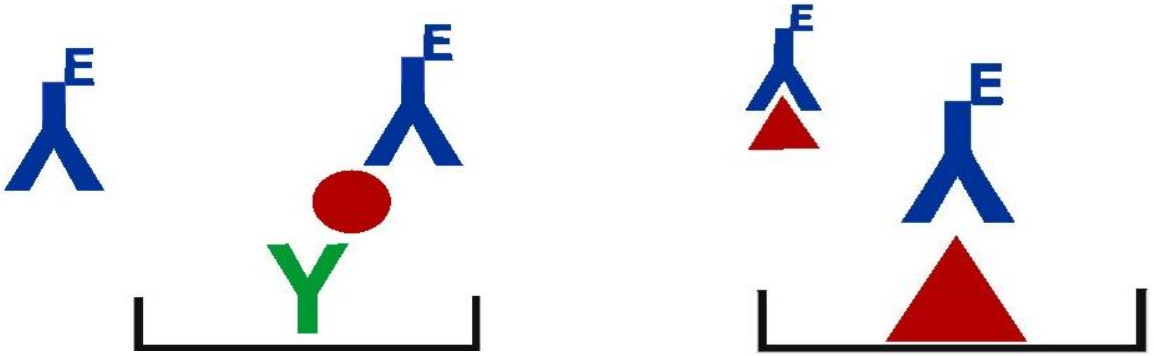
ELISA

- Based on specific antibodies as detector
- Enzyme is linked to the antibody to detect the antigen (allergenic protein)
- Enzyme converts a colorless substrate (chromogen) to a colored product
- Reaction is stopped by sulphuric acid – color changes to final product – measured at 450 nm with an ELISA reader

Two principles: **Sandwich ELISA** **Competition ELISA**



Dip Sticks / Lateral Flow Devices

- antibody based technology
- Qualitative or semi-quantitative

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Sandwich ELISA – Advantages

- Limits of detection or quantification at low mg/kg level
- Large numbers of samples can be tested per run
- Rapid, sensitive, selective, cost effective
- Widely used in food industry labs and by official control bodies
- Almost all commercial allergen ELISAs are using this technique

Competitive ELISA – Advantages

- Limits of detection or quantification at low mg/kg level
- Large numbers of samples can be tested per run
- Rapid, sensitive, selective, cost effective
- Can be used to detect smaller target molecules (e.g. haptens) or protein fragments

LFD – Advantages

Suitable for field testing, single sample testing and hygiene monitoring (HACCP)*

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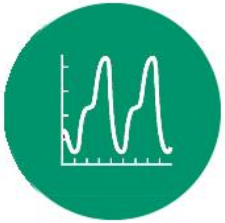
Polymease Chain Reaction Method

PCR Analysis comprises three steps:

- DNA extraction and purification
- Amplification of a specific DNA sequence
- Detection of the amplified PCR products

1. **DNA-Preparation**



2. **Amplification**

3. **Detection**

Advantages

- Detects the presence of the allergenic food species
- Tool to indicate presence/absence of an allergenic food commodity if no suitable ELISA is available
- Confimatory analysis to ELISA
- Highly species specific

Disadvantages

- Inteference in the test can be caused by remaining metal ions, lipids or proteins
- Short DNA sequences may be detectable in processed food whereas the protein may no longer be present
- Too low DNA concentation in products such as egg or milk
- No differentiation between products coming from the same species like cow‘s milk and beef or egg and chicken
- Species related products e.g. celery or other closely related plant species

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Allergen analysis – raw, cooked, processed?

Sample Preparation

Many different matrixes require different extraction methods for method of choice

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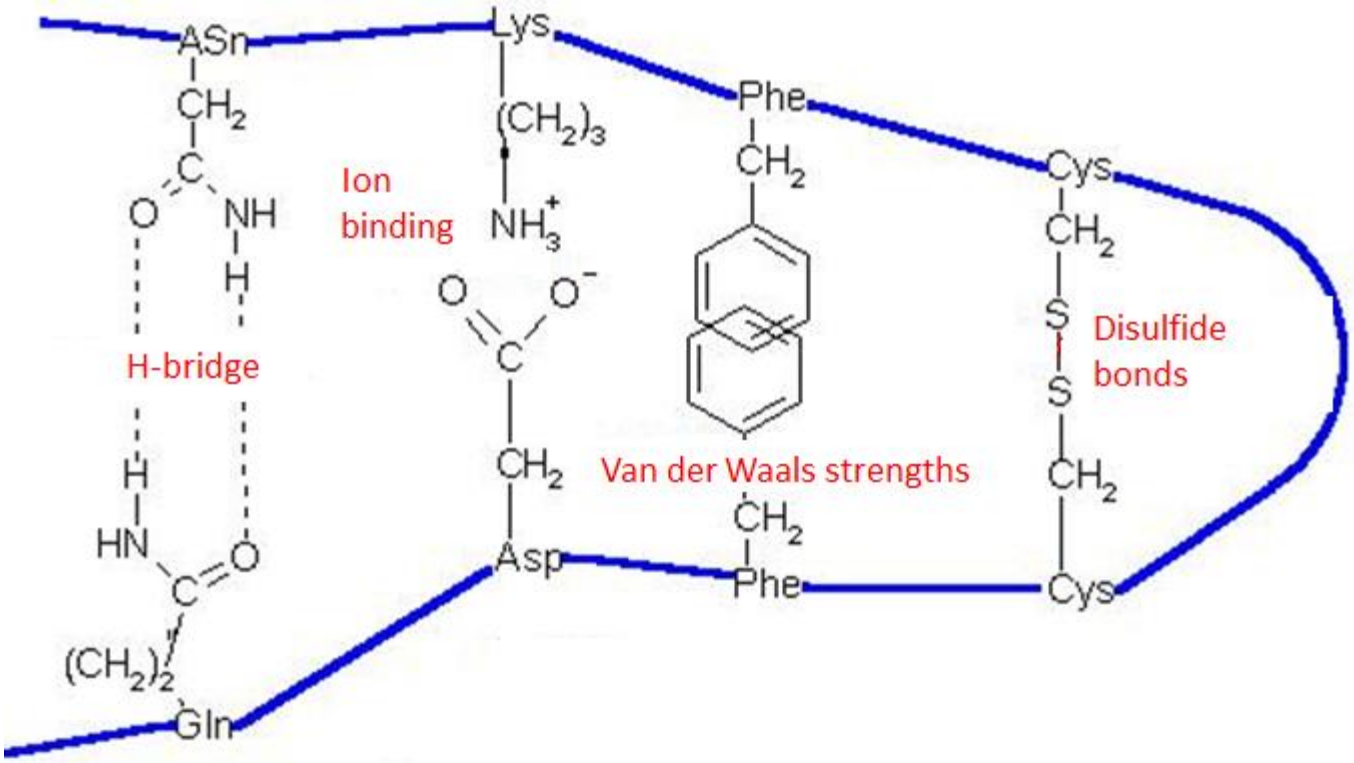
Sample preparation

Food processing has an influence on the structure of proteins

Question: How might this affect different methods of detection ?



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Allergen analysis

- **Analytical methods have to fulfill requirements for**
  - HACCP and risk management in industries
  - To support the work of enforcement authorities
  - Validation/verification of cleaning protocols
  - Fit for purpose – cost effective yet reliable

- **Developments**
  - Overall increase in analysis
  - Increase in risk based analysis
  - Increase in lateral flow or strip based tests for in situ testing

- **Still missing:**
  - Few validated analytical methods
  - No universally recognized reference materials
  - No Certified standards
  - No harmonized validation protocols on an international level or limits of detection

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Learning Outcomes

- **Provide an Introduction to adverse food reactions**
- **Examine the individual factors for predisposition**
- **Aware of the legislation governing key allergenic foods**
- **Develop an ability to define and classify allergens**
- **Knowledge of control measures that are implemented to prevent allergens entering into the food chain**
- **Identify emerging issues in food security from allergens and their implications to human health**
- **Recognise bioanalytical approaches used to monitor the presence of allergens in order to protect human health.**

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References

International Life Sciences Institute (ILSI)
http://www.ilsi.org
Chung et al., 2012 Application of scientific criteria to food allergens of public health importance. Regulatory Toxicology and Pharmacology 64, 315–323

FARE – Food Allergy Research and Education
www.foodallergy.org

ALLERGY UK
http://www.allergyuk.org

Allergen Bureau – Informing the Industry
http://allergenbureau.net/

Allergen Management in the Food Industry
Edited by Joyce Boye and Samuel Benrejeb Godefrey

Food Allergy Information
http://www.foodallergens.info/

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Reading Materials

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In 2011, a series of systematic reviews of the literature was conducted

1. to collate the available scientific data on the prevalence of each food allergy in European and non-European countries,
2. to derive threshold concentrations for each allergen in foods when possible, and
3. to review the analytical methods available for the detection/quantification of food allergens.

Please download and read the following articles

14 allergens coming to a food label near you
http://www.totalfoodservice.co.uk/data/ckeditor/Pdfs/14-Allergens.pdf

Literature searches and reviews related to the prevalence of food allergy in Europe
https://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/506e.pdf
EFSA supporting publication 2013:EN-506

Scientific Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes
https://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3894.pdf
EFSA Journal 2014;12(11):3894

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Thank you

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