

# Food Allergies – An Increasing Public Health Concern

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# Today's Presentation

- Quick overview of food allergy basics
- Public health aspects
- International impacts
- Labeling/Precautionary labeling
- Allergen control – good hygienic practice
- How clean is clean enough?

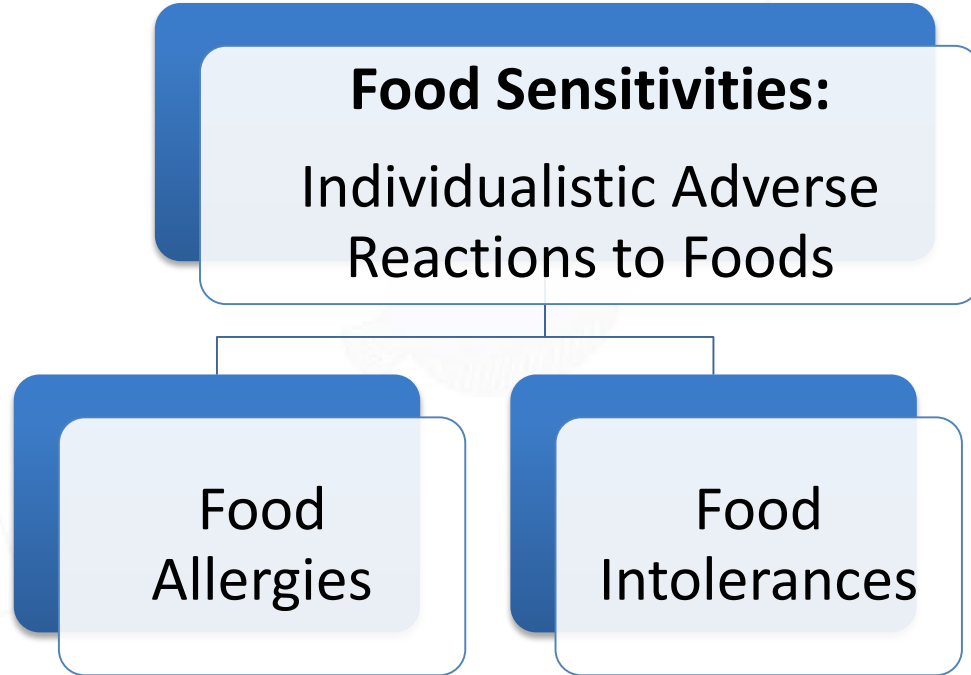
# Basics of Food Allergies & Intolerances

# Food Allergies & Intolerances

The food of one may be  
poison for another.

Lucretius  
*De Rerum Natura*

# Classification



# Types of Sensitivities to Foods

- Non-immunological – ex. lactose intolerance
- Immunological – ex. food allergy

# Codex Alimentarius Commission

- Guidance is focused on all food sensitivities (CODEX STAN 1-1985)
- But the major public health issues are food allergies and celiac disease
- Other issues such as sulfite sensitivity and lactose intolerance can be addressed by labeling strategies alone; carryover (cross contact) on shared equipment is not a big deal
- Food allergies and celiac disease can be provoked by rather low doses of the offending food; thus good hygienic practice is needed in addition to labeling

# Cross Contact

- The inadvertent, unintentional transfer of residues of an allergenic food into another food that is not intended to contain the allergen
- Can occur from common food industry practices
  - shared processing equipment
  - shared processing facilities
  - employee clothing, traffic patterns, etc.
- Occurs even more commonly in restaurants and other foodservice facilities
- Can also occur in homes of consumers



# Food Sensitivities



```
graph TD; A[Food Sensitivities] --> B[Food Allergies]; A --> C[Food Intolerances]; B --> D[IgE-Mediated]; B --> E[Cell-Mediated];
```

A hierarchical flowchart showing the classification of food sensitivities. The top level is 'Food Sensitivities', which branches into 'Food Allergies' and 'Food Intolerances'. 'Food Allergies' further branches into 'IgE-Mediated' and 'Cell-Mediated'. The boxes are blue with white text and are connected by thin black lines. Faint background images of a banana, a carton of milk, and a shrimp are visible.

## Food Allergies

## Food Intolerances

IgE-  
Mediated

Cell-  
Mediated

# Cell-Mediated Allergy

(Delayed Hypersensitivity)

# Celiac Disease

- celiac sprue, non-tropical sprue
- gluten-sensitive enteropathy

# Celiac Disease

- 1 of every 133 individuals in U.S. has genetic predisposition to develop celiac disease but not all are symptomatic
- Associated with consumption of gluten fractions of wheat, rye, barley, triticale, and sometimes oats
- Symptoms associated with malabsorption (body wasting, anemia, diarrhea, bone pain, etc.)
- Treatment with avoidance diets (life-long)
- Tolerance for gluten is low – between 10-50 mg of gluten is sufficient to cause intestinal damage

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## Food Allergies

## Food Intolerances

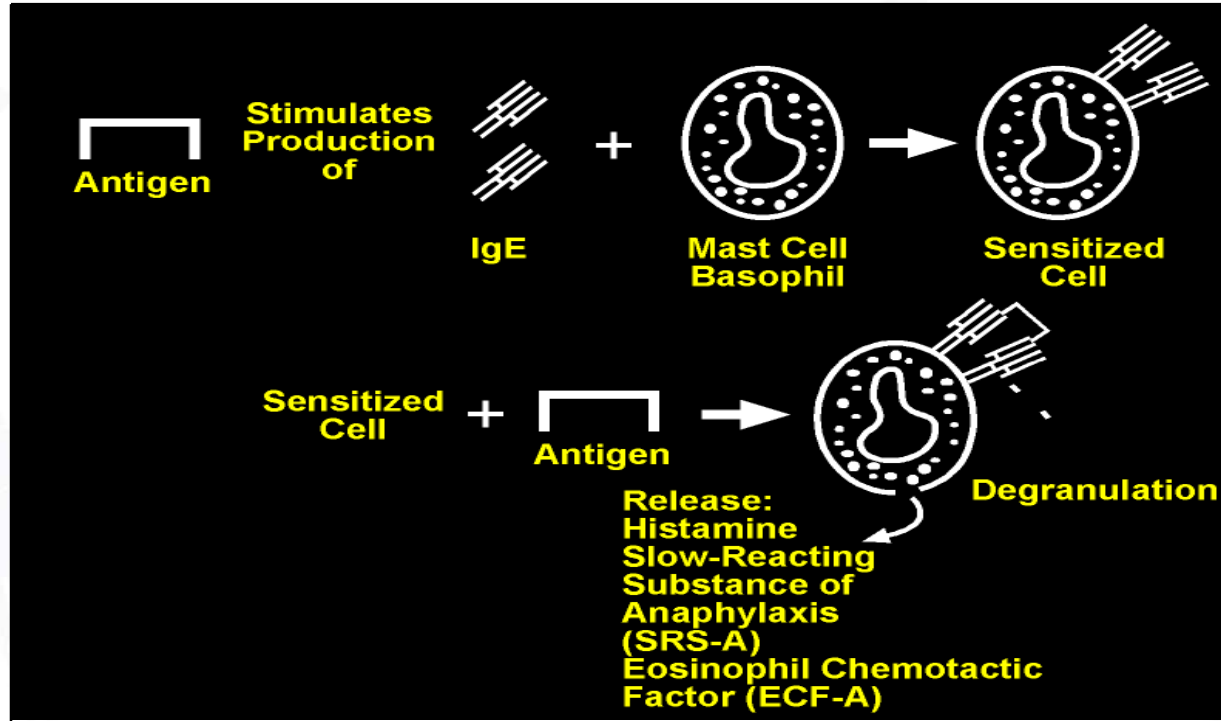
### IgE-Mediated

### Cell-Mediated

# IgE-Mediated Allergy

(Immediate Hypersensitivity)

# Mechanisms of Mediator Release



# IgE-Mediated Food Allergy

- Symptoms range from mild to severe and life-threatening; fatal reactions do occur
- Most foods can cause food allergies but >90% of all food allergies/ceeliac disease on a global basis are caused by 8 foods or food groups
- Allergens are proteins but most food proteins are not allergenic
- Treatment with avoidance diets (life-long)
- Tolerance for offending food is quite low, but not zero



# The Big 8

## Most Common Causes of Food Allergy (IgE-Mediated + Celiac Disease)

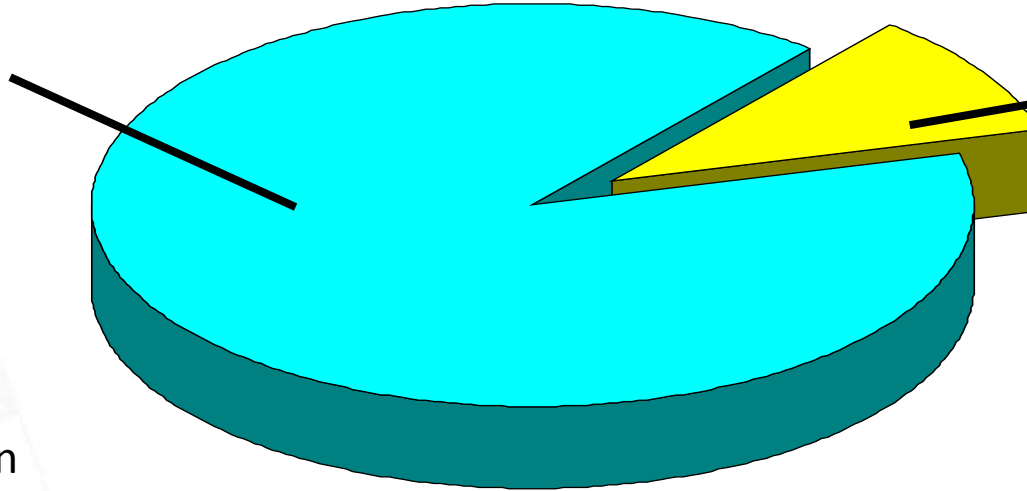
### CODEX STAN 1-1985

- Cows' milk
- Egg
- Crustacea
- Fish
- Peanut
- Soybean
- Tree nuts
- Cereal sources of gluten

# Food Allergies Prevalence - Codex List



90%  
Peanut  
Tree nuts  
Milk  
Egg  
Soy  
Fish  
Crustacean  
Shellfish  
Cereal Sources  
of Gluten



10%  
Hundreds  
of others

# Additional Listed Allergenic Foods in Countries Other than USA

Food	Country
Sesame seed	Canada, EU, Australia/New Zealand
Mustard	EU, Canada
Celery	EU
Buckwheat	Japan, Korea
Molluscan shellfish	EU, Canada
Mango	Taiwan
Lupine	EU
Peach, Pork, Tomato	Korea
Bee Pollen, Propolis, Royal Jelly	Australia/New Zealand

# Public Health Impact of Food Allergies & Celiac Disease

# Food Allergy Facts – U.S.

- CDC reports that food allergies result in 300,000+ ambulatory-care visits a year among children under the age of 18.
- Every 3 minutes a food allergy reaction sends someone to the emergency department— approx. 200,000 visits PY; once every 6 minutes the reaction is anaphylaxis.
- From 2004 to 2006, there were approximately 9,500 hospital discharges per year with a diagnosis related to food allergy among children under age 18 years.
- Food allergy is the leading cause of anaphylaxis outside the hospital setting.
- Teenagers and young adults with food allergies are at the highest risk of fatal food-induced anaphylaxis.
- More than 15% of school aged children with food allergies have had a reaction in school.

# Food Allergy Facts – U.S.

- Prevalence of food allergy in children has doubled over past 10 years
- Severity of cases also seems to be increasing
- Percentage of children with multiple food allergies is increasing
- Reasons are unclear but likely related to cesarean births, weaning practices, hygiene hypothesis, etc.

# Impact of Celiac Disease and Gluten Sensitivity

- Another 1% of the population has celiac disease or other form of gluten sensitivity
- An unknown % of the population are afflicted by other forms of gluten sensitivity
- Celiac is not fatal but untreated leads to very serious nutritional issues
- Celiac disease and gluten sensitivity have led to a nationwide marketing trend for gluten-free foods

# International Impact of Food Allergies and Celiac Disease

- Clinical data on prevalence and severity of IgE-mediated food allergy are sparse
- Impacts seem similar to U.S. in Canada, EU (although variable), Japan, Korea, Australia, New Zealand)
- Emerging impact information in China, India, Mexico
- IgE-mediated food allergy could be lower in countries with parasitic disease but uncertain
- Celiac disease prevalence globally is variable but similar in other countries where gluten-containing grains are widely consumed (EU, Australia, Canada)



# Public Health Responses

# Treatment for True Food Allergies

## Specific Avoidance Diets



# Public Health Responses

- Labeling is critical to successful implementation of avoidance diets
- Foods on country allergen lists and ingredients derived from those foods must be labeled by source
- Source labeling exemptions exist for some ingredients derived from priority allergenic foods in some countries but are variable between countries

# Public Health Responses

- Clinical evidence on the prevalence of overall and specific food allergies is lacking in many countries
- Very few countries collect data on severe and/or fatal allergic reactions to foods
- Only two countries (Switzerland and Japan) have established thresholds for allergen residues

# Good Hygienic Practices

# Food Manufacturing Facts

- Shared equipment is widely used between formulations with Big 8 allergens and formulations without
- Shared facilities even more widely used
- Companies must develop preventive allergen controls to avoid cross contact
- How clean is clean enough?

# Exquisite Sensitivity of Some Food-Allergic Individuals

- Trace amounts of the offending food will trigger reactions

# How Much is Too Much?

Milligram amounts!  
(ppm concentrations)



# FARRP-TNO Food Allergen Threshold Database

Allergenic Source	Included in 2012 VITAL Analysis	New Published or Clinic Threshold Data	Total
Peanut	750	452	1202
Milk	351	100	451
Egg	206	176	382
Hazelnut	202	209	411
Soy Flour	51	3	54
Soy Milk	29	4	33
Wheat	40	57	97
Cashew	31	214	245
Mustard	33	0	33
Lupine	24	1	25
Sesame	21	19	40
Shrimp	48	27	75
Celeriac*	39	43	82
Fish*	19	29	48
Buckwheat**		26	26
Walnut**		74	74
<b>Total</b>	<b>1844</b>	<b>1434</b>	<b>3278</b>

# Peanut Allergic Patients Present with Different Levels of Sensitivity



Ballmer-Weber and Hourihane

0.2 mg  
(0.05 mg)

0.4 mg  
(0.1 mg)

1.0 mg  
(0.25 mg)

5.0 mg  
(1.25 mg)

25 mg  
(6.25 mg)

100 mg  
(25 mg)

400 mg  
(100 mg peanut protein )

\*0.4 mg peanut (0.1 mg peanut protein) is the eliciting dose of the most sensitive peanut-allergic patient reported in the published clinical literature

# Good Hygienic Practice: A Validated Allergen Control Program

- Clean shared equipment
- Design/select equipment that can be cleaned
- Develop effective sanitation standard operating procedures
- Develop cleaning validation procedures (on-site testing)
- Develop procedures to verify use of appropriate cleaning
- Frequently monitor compliance; keep records

# Allergen Control Program

- Cannot and should not focus only on good hygienic practice and prevention of cross contact
- Packaging and labeling errors contribute to undeclared allergens as well; most common cause of recalls in U.S.
- Allergen Control Program should be comprehensive with the aim of assuring that food-allergic consumers are not exposed to hazardous levels of undeclared allergen residues
- Requires establishment of Reference Doses
  - How much is too much?
  - How clean is clean enough?

# Entrenched Zero Threshold Concept

- Physicians recommended complete avoidance
- Food-allergic consumers attempt to practice complete avoidance
- Labeling laws and regulations in many countries (e.g. FALCPA in USA) based on zero threshold (no protein) approach
- Food industry adopts zero threshold in many situations and advisory labeling abounds

# Disadvantages of Zero Threshold Approach

- Food-allergic consumers have diminished quality of life due to limited food choices
- FDA and other public health authorities spend time chasing zero
- Physicians deal with scared and frustrated patients – if you treat all of them the same, then they will all believe that they are the most sensitive
- Food industry focuses attention on zero and sometimes misses forest for trees
- Zero keeps getting less

# Precautionary Allergen Labeling (PAL)

- Voluntary, NOT required
- Must be truthful and not misleading
- Cannot be used as a substitute for GMP
- Many different statement formats

# Precautionary Labeling for Allergenic Foods: Use and interpretation by various stakeholders?





Carnauba wax.

**ALLERGY INFORMATION:**

**Consumers with food allergies or other sensitivities, please review the ingredients carefully.**

All ingredients are wheat free, gluten free, nut free, peanut free, and trans-fat free. All mixes are packaged on equipment that process wheat, milk, egg, soy, and sulfiting agents. May contain traces of peanuts and tree nuts.

Major allergens: milk and egg.

May contain soy.

# Food Allergies (and Intolerances): Conclusions

- Food allergies represent a growing public health risk in many countries
- Public health agencies could do more to protect food-allergic consumers
  - Sensible, risk-based good hygienic practices
  - Sensible, risk-based labeling practices



[www.farrp.org](http://www.farrp.org)

# Eliciting Doses for Food Allergens: Reported in mg Protein

Allergen	Total No. of Subjects with Objective Symptoms	ED10 (lower, upper 95% CI) mg protein	ED05 (lower, upper 95% CI) mg protein	ED01 (lower, upper 95% CI) mg protein
Peanut	750	<b>3.8</b> (3.0, 5.0)	<b>1.5</b> (1.1, 2.1)	<b>0.28</b> (0.19, 0.4)
Milk	351	<b>4.8</b> (3.1, 7.2)	<b>1.9</b> (1.2, 3.1)	<b>0.34</b> (0.18, 0.62)
Egg	206	<b>1.3</b> (0.71, 2.5)	<b>0.44</b> (0.21, 0.91)	<b>0.056</b> (0.022, 0.14)
Hazelnut	202	<b>7.0</b> (4.1, 12.1)	<b>2.6</b> (1.4, 5.0)	<b>0.42</b> (0.18, 0.96)
Soybean	80	<b>63.4</b> (19.4, 207)	<b>22.2</b> (5.5, 89.5)	
Wheat	40	<b>8.7</b> (3.4, 22.5)	<b>4.2</b> (1.4, 12.6)	
Cashew	31	<b>16.8</b> (6.5, 43.5)	<b>9.0</b> (3.0, 27)	
Mustard	33	<b>1.0</b> (0.33, 3.1)	<b>0.45</b> (0.12, 1.7)	
Lupin	24	<b>31.3</b> (11.0, 89.2)	<b>16.1</b> (4.5, 57.5)	
Sesame	21	<b>8.0</b> (1.8, 35.6)	<b>3.4</b> (0.61, 18.6)	
Shrimp	48	<b>284</b> (63.1, 1278)	<b>73.6</b> (12.1, 446)	

\*Based on the LogNormal distribution generated from the cumulative data of each allergen.

# Allergen Bureau of Australia/New Zealand VITAL Reference Doses

Allergen	mg Protein Level
Peanut	0.2
Milk	0.1
Egg	0.03
Hazelnut	0.1
Soy	1.0
Wheat	1.0
Other Tree Nuts	0.1
Sesame	0.2
Crustacea	10.0
Fish	0.1

# Causes of Food Allergen Recalls – U.S.

Cause	Number of Recalls
Wrong package/label	86
Terminology	59
Failure to carry forward information from an ingredient to the final label	41
Cross-contact	28
Ingredient mislabeled by supplier	21

Gendel, S.M., J. Zhu, N. Nolan, and K. Gombas. 2014. Learning from FDA Food Allergen Recalls and Reportable Foods. Food Safety Magazine

April/May

# Tenth Workshop on Food Allergen Methodologies

May 7 – 9, 2018

DoubleTree Downtown, Toronto Canada

<https://farrp.unl.edu/10thmethodologies>

## Highlights

**Day 1** – Consumer Impacts of Food Allergies, Analytical Updates, and European Government iFAAM grant.

**Day 2** – Scientific Presentations by Mass Spectrometry and ELISA Companies, Reception and Product Demonstrations

**Day 3** – Food Industry Day with talks on Risk Assessments and Government Regulations

*1, 2 and 3 day registrations available*

# FARRP Workshop: Effective Food Allergen Management

March 21-23, 2018

Hyatt Regency O'Hare, Chicago, IL



<https://farrp.unl.edu/effective-food-allergen-management>

## Highlights

- The science behind food allergies
- Food allergens and FSMA
- Allergen labeling laws
- Practical strategies for food allergen management
- Hands-on experience developing an allergen control program
- ELISA kit companies product demonstrations

*Registration is now open.*