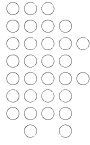
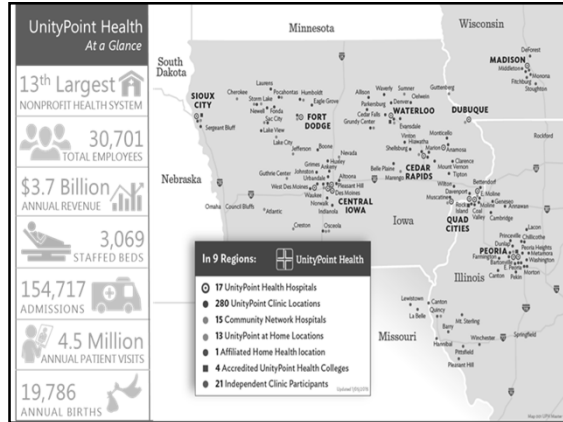


# Food Allergy in 2016


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Quincy, IL


## Objectives:

- Identify the foods most commonly associated with food allergy in pediatric and adult populations.
- Recognize the differences between food allergy and food intolerance, including the limitations of currently available testing modalities.
- Describe the atypical presentations of certain, clinically relevant food allergies



## Disclosures:


- No disclosures



## Question #1: Best Answer

7 year old boy presents to clinic with mom to discuss gradual failure to thrive, abdominal bloating, diarrhea and fatigue. What is the most like diagnosis?


- A. Colon cancer
- B. Gluten intolerance
- C. Irritable bowel syndrome
- D. Celiac disease



## Question #2:

40 yo man with seasonal allergies, complains of oral itching and tingling sensation when he eats fresh apples, cherries, kiwi and honeydew melon. What is the treatment of choice?

- A. Injectable epinephrine
- B. "Pre-medicate" with Benadryl
- C. Allergy shots will always help
- D. Avoidance is the only reliable way to prevent symptoms



**Question #3:**

35 yo woman with “irritable bowel syndrome” presents with abdominal bloating and alternating constipation/diarrhea. Upper and lower endoscopy were normal. What is the next best step in her care?

- A. Extensive allergy skin testing with airborne and food antigens
- B. IgG testing with a non-FDA approved panel of 200-250 foods at a cost of \$3700 (not covered by her insurance)
- C. Tissue transglutaminase (anti-TTG) IgA and total serum IgA blood test
- D. Reassurance only

**Question #4:**

16 yo male patient presents to ER with profound anaphylaxis after ingestion of shrimp cocktail. His blood pressure is not detectable. The best route of administration for epinephrine is:

- A. Intravenous
- B. Subcutaneous
- C. Intratracheal, following intubation
- D. Intramuscular

**Question #5:**

70 yo woman with repeated episodes of moderate-severe anaphylaxis to almonds, needs a refill on her injectable epinephrine device. The next best step is:

- A. Refill the device and ask the pharmacy staff to educate her on the proper use
- B. Personally instruct her on proper device usage, make sure she has a trainer device for practice and discuss purchase of a identification jewelry piece
- C. Give her a coupon for her co-pay
- D. Tell her to stop eating peanut butter sandwiches (she just had one for lunch today, no problems)

**Frequently Asked Questions!**

- “Why are food allergies increasing?”
- “Will I (or my child) outgrow the food allergy?”
- “Will the food allergy get worse?”
- “What about yeast allergy?”
- “Can’t I just be tested for all the foods?”
- “Can you test me for dairy?”
- “I have eaten \_\_\_\_\_ all my life, why am I allergic now?”

**Overview**

- Adverse Food Reactions (AFRs): Definitions and Overview
- Examples of atypical food anaphylaxis
- Treatment of food anaphylaxis
- Current injectable epinephrine options
- A cautionary word on diagnostics

*Practice parameter*

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**Food allergy: A practice parameter update—2014**

Hugh A. Sampson, MD, Seema Aceves, MD, PhD, S. Allan Bock, MD, John James, MD, Stacie Jones, MD, David Lang, MD, Kari Nadeau, MD, PhD, Anna Nowak-Wegrzyn, MD, John Oppenheimer, MD, Tamara T. Perry, MD, Christopher Randolph, MD, Scott H. Sicherer, MD, Ronald A. Simon, MD, Brian P. Vickery, MD, and Robert Wood, MD

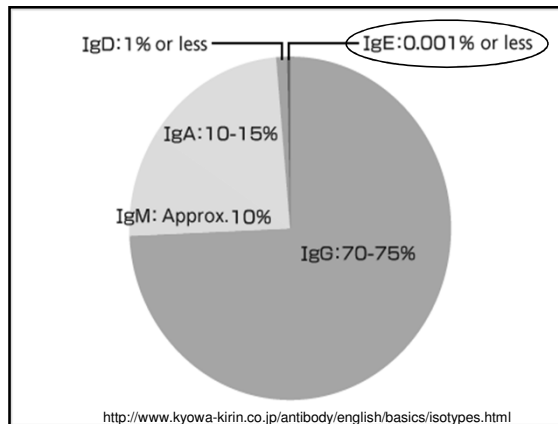
*Chief Editors:* Hugh A. Sampson, MD, and Christopher Randolph, MD

J Allergy Clin Immunol 2014;134:1016-25

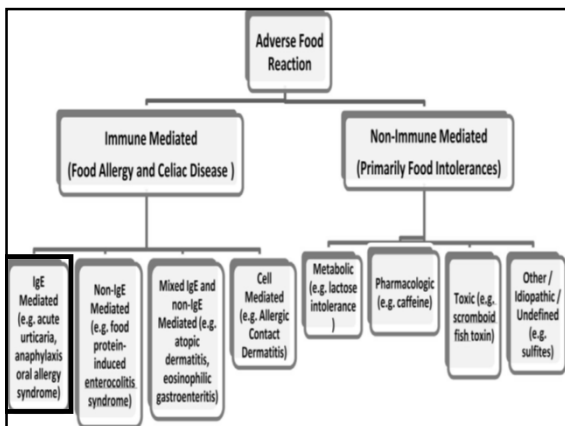
## Adverse Food Reactions (AFRs) : Rules of Engagement

- **Food allergy:** “an adverse health effect arising from a specific immune response, occurring reproducibly on exposure to a given food”
- **Food intolerance:** “Non-immunologic reaction (metabolic, pharmacologic, toxic and/or undefined/unknown mechanism) on exposure to a given food”

Sampson et al., Food allergy: A practice parameter update—2014. J Allergy Clin Immunol 2014;134:1016-25.

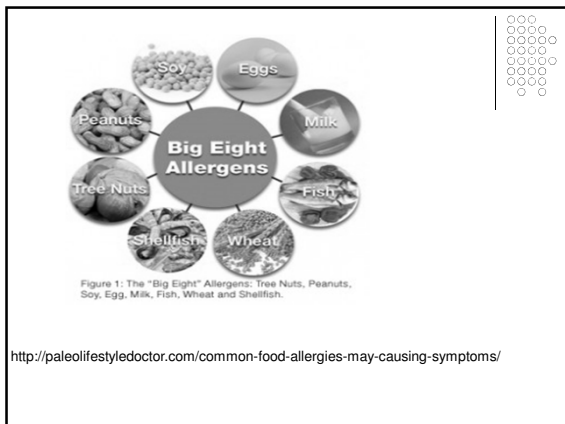


<http://www.kyowa-kirin.co.jp/antibody/english/basics/isotypes.html>



## IgE Mediated AFRs

- IgE – “the allergic antibody”
- Evolutionary purpose = protection against parasites
- Developed countries = atopic (allergic) conditions
- “Sensitive” or “Sensitized” – antibody present (by skin or blood test), but no clinical reaction
- “Allergic” – antibody present *and* a potentially life-threatening clinical reaction with each subsequent ingestion



If Allergic to:	Risk of Reaction to at Least One:	Risk:
A legume* peanut	Other legumes peas, lentils, beans	5%
A tree nut walnut	Other tree nuts cashew, hazelnut, almond, pistachio	37%
A fish* salmon	Other fish cod, haddock, sea bream	50%
A shellfish shrimp	Other shellfish crab, lobster, scallop	75%
A grain* wheat	Other grains barley, rye	20%
Cow's milk* cheese	Beef hamburger	10%
Cow's milk* cheese	Goat's milk goat	92%
Cow's milk* cheese	Mare's milk horse	4%
Pollen* birch	Fruits/Vegetables apple, peach, kiwi, raspberry	55%
Peach* peach	Other Rosaceae apple, cherry, strawberry	55%
Melon* cantaloupe	Other fruits watermelon, banana, avocado	92%
Latex* latex glove	Fruits kiwi, banana, avocado	35%
Fruits banana, kiwi	Latex latex glove	11%

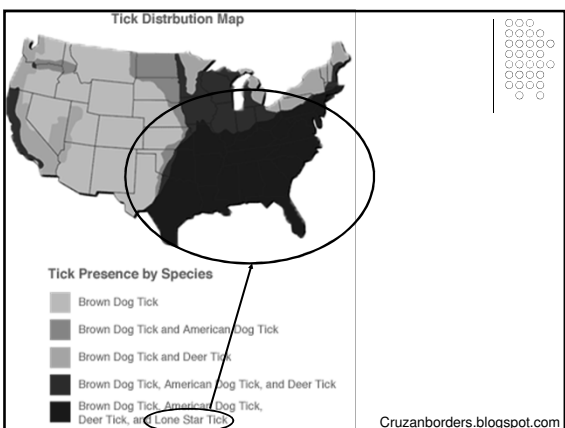
[www.gordonmedical.com](http://www.gordonmedical.com)

### Anaphylaxis: A Multi-Organ Concern

SKIN	RESPIRATORY	GASTROINTESTINAL	CARDIOVASCULAR	NEUROLOGICAL
hives, swelling, itching, warmth, redness	coughing, wheezing, shortness of breath, chest pain or tightness, throat tightness, trouble swallowing, hoarse voice, nasal congestion or hay fever-like symptoms. (sneezing or runny or itchy nose; red, itchy or watery eyes)	nausea, stomach pain or cramps, vomiting, diarrhea	dizziness/ lightheadedness, pale/blue colour, weak pulse, fainting, shock, loss of consciousness	anxiety, feeling of "impending doom" (feeling that something really bad is about to happen), headache
				OTHER <sup>2,3</sup> uterine cramps

### Alpha Gal Allergy

The diagram illustrates the process of Alpha Gal Allergy. It shows a Lone Star Tick (Ixodes scapularis) on the left, followed by a plus sign and a piece of meat. This combination leads to a starburst shape containing the text "ANAPHYLAXIS!!!". Below the tick image, there are small illustrations of the tick's life stages: Female, Male, Nymph, and Embryonated Analeth Stage.



### Alpha Gal Allergy

- IgE-mediated allergic reaction to galactose-alpha-1,3-galactose – *a sugar*
- Alpha-gal is found on cells and tissues of non-primate mammals
- History of tick bites (usually multiple)
- Mammalian red meats (eg, beef, pork, lamb, and venison) have a similar alpha-gal to that found in tick saliva
- Delayed anaphylaxis (3-6 hours) following ingestion of red meat, pork, lamb especially
- Can have *negative, initial allergy testing* to the meats!

Commins et al., 2009

### Food Dependent, Exercise Induced Anaphylaxis

- Anaphylaxis which occurs during significant physical exertion, hours following ingestion of particular foods
- Digestive mechanism, prognosis unclear
- Culpable foods (depends on part of the world) in U.S. include:
  - Wheat, shellfish, celery, lentils, peaches, apples, grapes, hazelnuts, cheeses, beef, pork, corn and many others!
- Skin testing for foods can be very helpful !!!
- Exercising first thing in the morning is encouraged – injectable epinephrine is mandatory

Shattuck et al. 1999

### Food Dependent, Exercise Induced Anaphylaxis

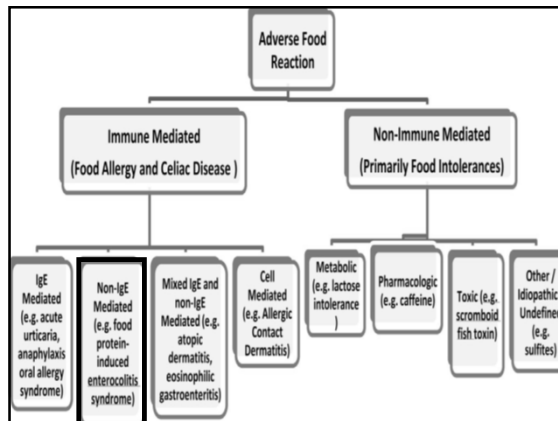
The diagram illustrates Food Dependent, Exercise Induced Anaphylaxis. It shows three scenarios:

- Celery + Rest = No Problem !!!
- No Celery + Exercise = No Problem !!!
- Celery + Exercise = ANAPHYLAXIS!!!

## Food Allergy: Management

- Injectable epinephrine (administered into the middle, upper/outer thigh muscle) is the ONLY life-saving treatment for an allergic reaction!
- Avoidance!
- Education, including a clear anaphylaxis action plan
- Identifying high-risk settings (buffets, bakeries, etc)
- Transition to self-care in adolescence
- Identification jewelry strongly encouraged
- Support at school (eg. zero tolerance for bullying)
- Identifying anaphylaxis, and not denying that symptoms are anaphylaxis!

Sampson et al., Food allergy: A practice parameter update—2014. J Allergy Clin Immunol 2014;134:1016-25.



## FPIES: Food Protein-Induced Enterocolitis Syndrome

- ~1/300 in first year of life
- Recurrent vomiting, poor weight gain, bloody stools (possibly diarrhea, lethargy) up to 4 hours following ingestion, can present with sepsis-like picture
- Mean age at presentation about 6 months, presents with increased white blood count, dehydration, hypothermia
- Common foods in the order of occurrence: Cow milk, soy, rice, other (i.e. sweet potato is most common vegetable)
- Mediated by non-IgE mechanism (Ag-specific T cells, pro-inflammatory cytokines)

Jarvinen KM. J Allergy Clin Immunol Pract. 2013;1:317-22.  
Ruffner MA. J Allergy Clin Immunol Pract. 2013;1(4):343-9.

## Gluten Intolerance: Celiac Disease

- 1% of U.S. population
- Abnormal immune response to gluten (storage protein) in wheat, barley and rye
- Chronic inflammation of the proximal small intestine resulting in malabsorption
- Children: diarrhea, failure to thrive, abdominal pain, distention
- Adults: diarrhea, anemia, bone pain, severe skin rash called dermatitis herpetiformis
- Most specific blood test is tissue transglutaminase (tTG-IgA)
- HLA typing may be useful to exclude CD or assess genetic susceptibility (DQ2, DQ8)
- Treatment = gluten free diet



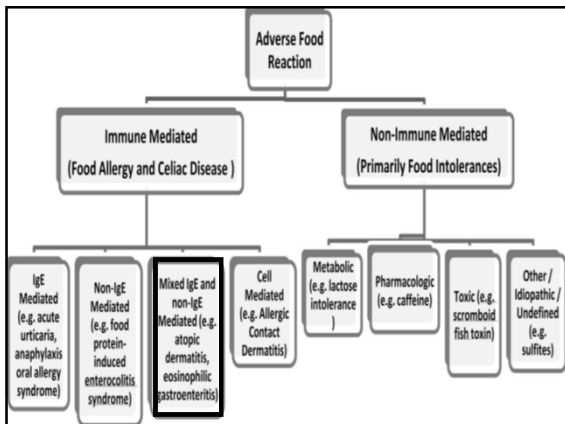
Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine, 17th Edition: <http://www.accessmedicine.com>. Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

**Dermatitis herpetiformis** manifested by pruritic, grouped vesicles in a typical location. The vesicles are often excoriated and may occur on knees, buttocks, and posterior scalp.

## Gluten Intolerance: Non-celiac gluten sensitivity

- Symptoms: abdominal pain, bloating, diarrhea/constipation, "foggy mind", headache, fatigue, joint and muscle pain, leg or arm numbness, dermatitis, depression, anemia (others?)
- Mechanism unknown
- No standardized diagnostic testing available – skin testing to multiple foods often returns negative
- Can be difficult to assess strict gluten-free diet adherence (i.e. 'allergen' exposure)
- No major complication of untreated NCGS has so far been described

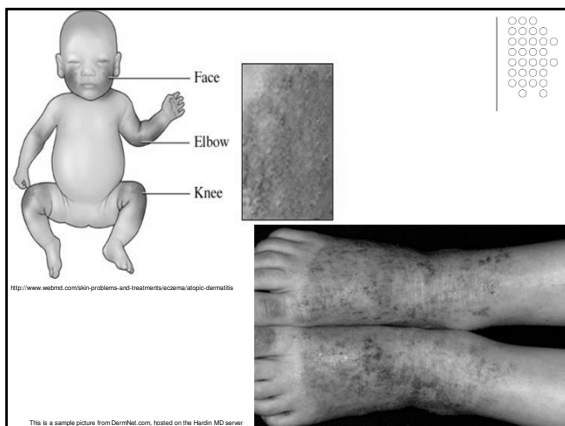
Catassi C. Non-Celiac Gluten Sensitivity: The New Frontier of Gluten Related Disorders. *Nutrients* 2013, 5, 3839-3853



### Atopic Dermatitis

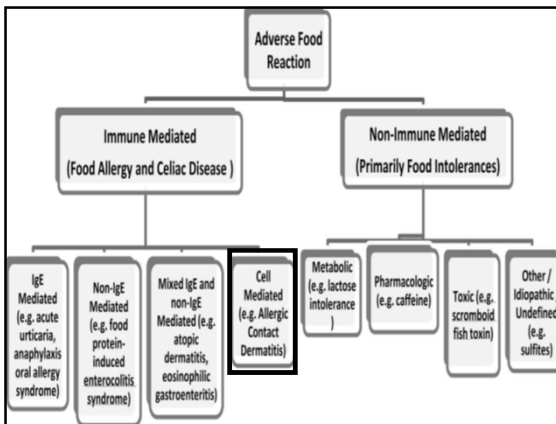
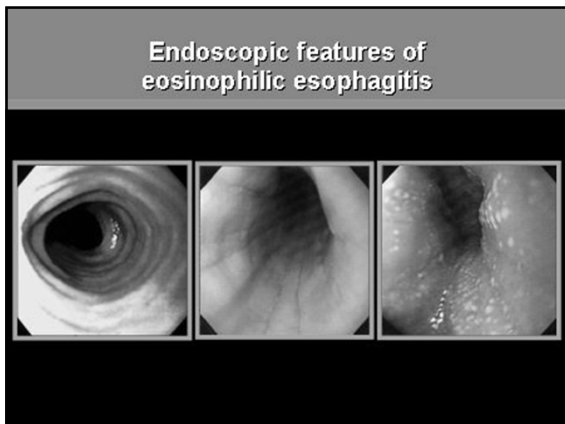
- Most common chronic inflammatory skin disease
- Of moderate-severe AD patients, about 1/3 have related food allergies
  - Milk, hen's egg, wheat, soy, peanut, fish, tree nuts account for >90%
- Abnormal skin barrier, dry skin, itch-scratch cycle
- Predisposed to colonization or infection by pathogenic microbes, most notably *Staphylococcus aureus* and herpes simplex virus
- Basic, initial therapy includes skin hydrations measures, topical steroids, topical calcineurin inhibitors etc.
- Refractory cases treated with cyclosporine, methotrexate, azathioprine, IL-6 blockade, dust mite immunotherapy (when indicated), wet wrap therapy, and UV light

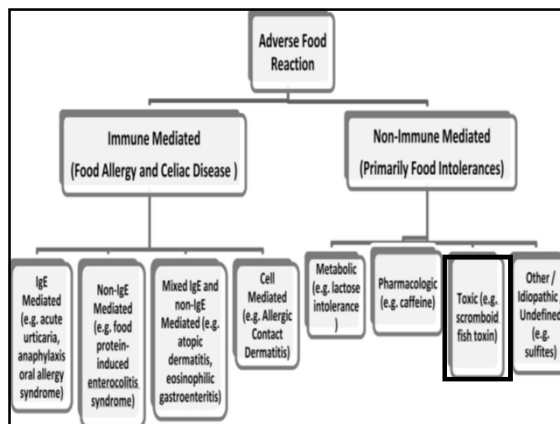
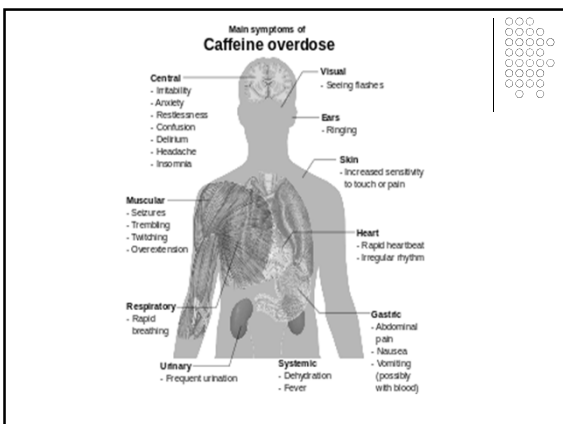
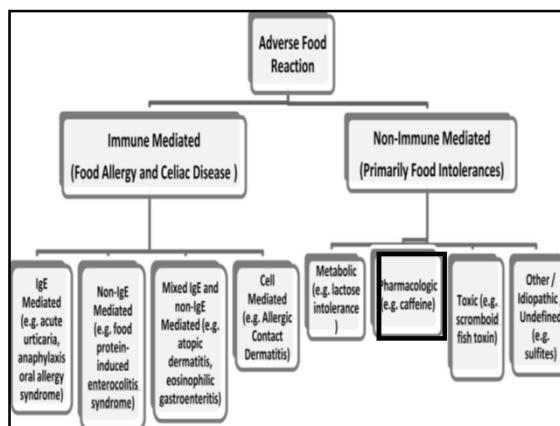
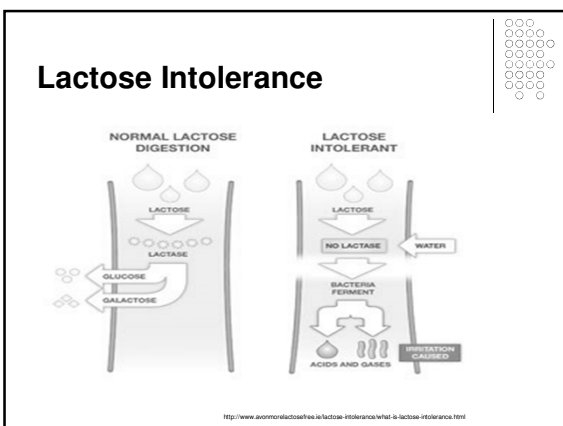
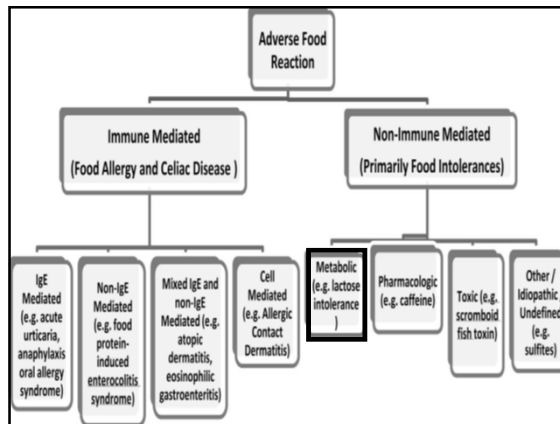
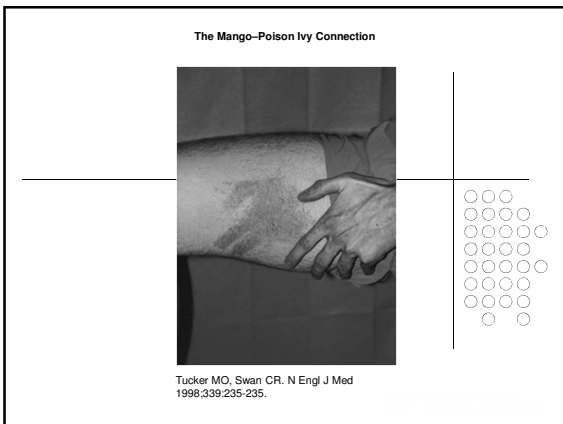
J Allergy Clin Immunol 2014;134:769-79  
J Allergy Clin Immunol: In Practice 2013;1:22-8



### Eosinophilic Esophagitis

- Increasingly recognized cause of vomiting, dysphagia and food impaction over the last 20-30 years, especially in younger male patients
- Normal esophageal mucosa does not contain eosinophils
- Definitive method of skin or serum testing for food allergies has not been defined
- Empiric avoidance of egg, milk, wheat, soy, peanut, tree nut, fish and shellfish has led to symptomatic improvement in 53-82% of patients.





## Scombroid Fish Poisoning

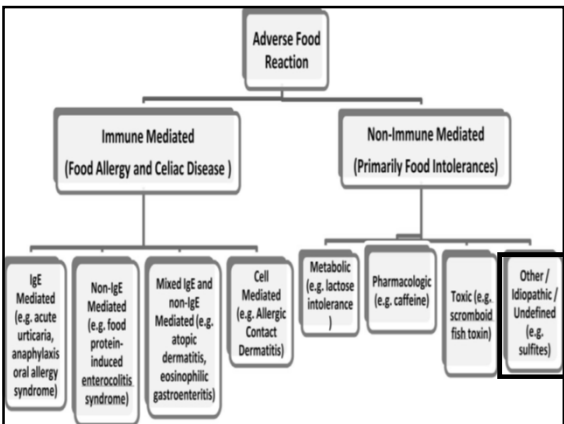
- Illness caused by eating spoiled fish
  - Especially with mackerel, tuna, bluefish, mahi-mahi, bonito, sardines, anchovies, others
- At temperatures above 60F, histidine enzymatically converted to histamine (not deactivated by cooking)
- Pseudo-allergic reaction can result:
  - Symptoms consist of skin flushing, throbbing headache, oral burning, abdominal cramps, nausea, diarrhea, palpitations, a sense of unease

Scombroid food poisoning  
From Wikipedia, the free encyclopedia

## Scombroid Fish Poisoning



At least 26 people were sickened with scombroid fish poisoning after eating stale mackerel, according to a Shenzhen Post report Friday.



## Sulfite Use in Foods

*Table 24-4. Technical Attributes of Sulfites in Foods*

Technical Attribute	Examples of Specific Food Applications
Inhibition of enzymatic browning	Fresh fruits and vegetables* Guacamole* Pre-peeled raw potatoes Salads* Shrimp (black spot formation)
Inhibition of non-enzymatic browning	Dehydrated potatoes Dried fruits Other dehydrated vegetables
Antimicrobial actions	Corn wet milling to make corn-starch and corn syrup Wines
Dough conditioning	Frozen pie crust Frozen pizza crust
Antioxidant action Bleaching effect	No major US applications Honey Maraschino cherries

\*No longer allowed by US FDA.

Food Allergy: Adverse Reactions to Food and Food Additives, 2003, Blackwell Science, Metcalfe et al. 2003 p. 332

## Sulfites and Asthma Attacks

- Adverse reactions with sulfites have been best established in asthma
  - Sulfur dioxide, sodium metabisulfite, potassium metabisulfite etc...
  - Less than 5% of all asthmatics
  - Oral, IV, ocular drops, inhalation routes all may apply
- Severe, steroid-dependent asthmatics seem to be at highest risk of fatal reactions from sulfites

Food Allergy: Adverse Reactions to Food and Food Additives, 2003, Blackwell Science, Metcalfe et al. 2003 "Sulfites"

## Food Allergy vs. Food Intolerance

- **Food Allergy:**
  - Usually comes on suddenly
  - Small amount of food can trigger
  - Happens every time you eat the food
  - Can be life-threatening
- **Food Intolerance:**
  - Usually comes on gradually
  - May only happen when you eat a lot of the food
  - May only happen if you eat the food often
  - Is not life-threatening

<http://www.webmd.com/allergies/foods-allergy-intolerance>



### Limitations of Modern Food “Allergy” Testing

- “IgG” or “IgG4” – suggests past exposure, only – NOT an Adverse Food Reaction
- “Shotgun” food allergy testing carries a false positive rate approaching 50% (coin flip)
- Currently-available testing modalities cannot accurately predict or diagnose food intolerance
  - Hydrogen breath test can *suggest* lactose intolerance in high pre-test probability patients – need a trial of lactose free diet to confirm

### So... How IS a Food Allergy Diagnosed?

Clinical history is the most important tool!!!

.....


Diagnostic testing is not a crystal ball – it should ONLY be used to confirm clinical suspicion !!!

### Treatment of Life-Threatening Food Allergy

- Avoidance of offending food!
- Know how to use injectable epinephrine device
- Keep injectable epinephrine immediately available always
- Recognize early signs/symptoms of anaphylaxis
- Administer injectable epinephrine early, without delay!

### Options for Injectable Epinephrine: 2016

- AdrenaClick
- EpiPen
- Auvi-Q



### Fatal Anaphylaxis in the United States

- National Mortality Database in the United States between 1999 and 2010 (Anaphylaxis ICD-10 Coding)
- 2458 fatal anaphylaxis cases in U.S.
- 4 categories:
  - Drug or serum = 58.8%
  - Unspecified = 19.3%
  - Venom = 15.2%
  - Food = 6.7%

Jerschow et al. J Allergy Clin Immunol 2014;134:1318-28.

### New Advances in Peanut Allergy Diagnostics

- Peanut (*Arachis hypogaea*)
  - Most common food associated with *fatal anaphylaxis* in westernized countries
  - Numerous allergens identified, but 6 allergens stand out:
    - Ara h 1, 2, 3, 6, 8 and 9
  - Ara h 1, 2 and 3 (especially Ara h 2) associated with severe peanut allergy
  - Commercially available testing and even skin testing can be falsely positive up to 77% of the time!!!
  - Clinical correlation is essential before settling on the diagnosis of peanut allergy, proper

Nischkau N, Pfoordtshen M, Murray C, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. J Allergy Clin Immunol 2010;125:191-197. 81-13

## New Advances in Peanut Allergy Diagnostics

- Swedish study: component-resolved diagnostics
- 144 children with peanut sensitization from two databases (Ara h 8, but NOT Ara h 1, 2 or 3)
- 82 tolerated peanut already, so were excluded
- 62 were invited for observed food challenge
  - 47 passed challenge – no symptoms
  - 14 had localized oral cavity symptoms, only
  - 1 reacted (found to have Ara h 6)
- Isolated Ara h 8 sensitization seems to indicate peanut tolerance. Peanuts can be carefully introduced at home in children with such sensitization.

ASARNOJ ET AL JACI 2012

## A Word On The Title

- Much is unknown regarding adverse food reactions
- Clinical history is important, as is patient recall and provider interpretation
- Genetics plays a role in both food intolerance and food allergy
- Diagnostic testing in 2015 is quite limited and is by no means a "crystal ball"
- Not all unusual symptoms (real *and* perceived) can be explained by adverse food reactions!

## Question #1: Best Answer

- 7 year old boy presents to clinic with mom to discuss gradual failure to thrive, abdominal bloating, diarrhea and fatigue. What is the most like diagnosis?
  - A. Colon cancer
  - B. Gluten intolerance
  - C. Irritable bowel syndrome
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## Question #2:

- 40 yo man with seasonal allergies, complains of oral itching and tingling sensation when he eats fresh apples, cherries, kiwi and honeydew melon. What is the treatment of choice?
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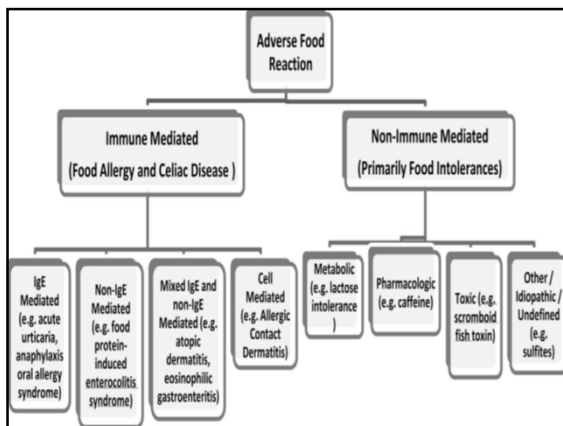
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### Summary

- Identify the foods most commonly associated with food allergy in pediatric and adult populations.
- Recognize the differences between food allergy and food intolerance, including the limitations of currently available testing modalities.
- Describe the atypical presentations of certain, clinically relevant food allergies



## Thank You For Your Attention!

Call or email me with questions!  
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[jknuffman@gmail.com](mailto:jknuffman@gmail.com)

