

Food Intolerance and Metabolic Disorders

Food Toxicology
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Learning Objectives

- Understand a range of food intolerances and metabolic disorders related to food consumption.
- Explore the occurrence and manifestation of Celiac Disease.
- Understand the major classes of food sensitivity.
- Survey some examples of food sensitivity and metabolic intolerance.
- Examine idiosyncratic food sensitivity.

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Food Sensitivities: Major Classes

- Anaphylactoid Reactions
- Metabolic Food Disorders
- Idiosyncratic Reactions
- *Not due to protein as food allergy*
- Overlapping classes
 - Celiac disease?

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Celiac Disease

- Celiac sprue or gluten-sensitive enteropathy
- One of most common food allergies/sensitivities in world
- 1/3000 incidence
- Not IgE-mediated
 - Type IV DTH?
 - Delayed Type Hypersensitivity
 - 24-72 hrs post exposure
- Does involve abnormal immunity



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Celiac Disease

- Ingestion of wheat, barley, rye
- Proline-rich protein - gliadins
- Triggers immune damage to small intestine
- Impairs absorption of nutrients
- Diarrhea, bloating, wt loss, bone pain, anemia, chronic fatigue, weakness, muscle cramps

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Celiac Disease

- Inherited trait – Chromosome 6
- Better classification may be idiosyncratic reaction
- But involves immune component



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Anaphylactoid Reactions: Scombroid Poisoning Food Toxicology

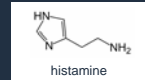
- Eating fish with high histamine levels
 - Tuna, mackrel, other
- Histamine from spoilage bacteria in fish
- Everyone is susceptible - allergy or just toxic???
- Same symptoms as food allergy but no IgE



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Scombrototoxicosis Food Toxicology

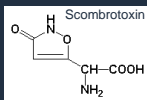
- Other factors besides histamine in fish that may exacerbate reaction
- Putrefactive amines - putrecine, cadaverine
- Histaminase inhibitors - aminoquanine, isoniazid
- Diamine oxidase inhibitors
- FDA histamine action level = 50mg/100g fish



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Scombrototoxicosis Food Toxicology

- In absence of high histamine
- Increased intake of biogenic amines
- Increased synthesis of biogenic amines by gut flora
- Diminished breakdown of biogenic amines by gut mucosa
- Increased release of histamine



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Case Study: Scombroid Fish Poisoning Pennsylvania, 1998 Food Toxicology

- On December 3, 1998, four adults became ill after eating tuna-spinach salad at the restaurant.
- Symptoms of illness included a burning sensation in the mouth, a metallic taste, facial flushing, nausea, diarrhea, sweating, and headache; symptoms occurred approximately 5 minutes to 2 hours after eating the salad.
- One patient was taken to the local emergency department and treated with diphenhydramine, cimetidine, and epinephrine. The other three patients were not examined by physicians and their symptoms resolved within a few hours. A presumptive diagnosis of scombroid fish poisoning was made based on clinical and epidemiologic features of the illness.



10 MMWR (2000) 49(18):398-400

Case Study: Scombroid Fish Poisoning Pennsylvania, 1998 Food Toxicology

- A sample of the remaining fish obtained from the restaurant was sent to PDOH for testing. The fish was positive for coliform and *Escherichia coli*, and tests were positive for histamine levels >50 ppm (fresh fish normally contain histamine levels of <10 ppm) using an enzyme-linked immunoabsorbent assay.
- The wholesale-to-retail chain of events involved transporting the fish across national, state, and municipal borders and involved five transporters and four processors. The tuna was from a 40–60 lb yellow-fin tuna caught by a commercial fishing boat in the Gulf of Mexico during late November 1998.
- The fish was caught using the long-line method, which uses a mainline up to 60 miles long with a series of suspended hook lines. The water temperature where the fish was caught was 78.5 F (25.8 C).



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Case Study: Scombroid Fish Poisoning Pennsylvania, 1998 Food Toxicology

- The catch of tuna was shipped from the fishing boat in iced vats by truck to a processor on November 24. The average temperature of the fish was 32 F–33 F (0 C–1 C). Of this catch, 785 lbs of tuna were shipped the same day to the wholesaler in Pennsylvania. The wholesaler received the shipment on November 27, and the average temperature of the fish was recorded as 36 F (2 C).
- Three of these fish were delivered to the retail supplier; two large filets, weighing 11.1 lbs each and noted to be in good physical appearance, were delivered to the restaurant on November 27. The fish was divided into 30 portions, kept in the freezer, and removed for thawing as needed for use. During November 28–December 4, 17 portions of the fish were served. The only four persons reporting illness ate the tuna-spinach salad on Dec 3.
- No deviations in HACCP procedures in the wholesale-to-retail distribution of the tuna could be identified.

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Anaphylactoid Reactions: Strawberry Allergy Food Toxicology

- Urticaria and anaphylactoid
- No allergen identified
- Strawberries do not contain histamine
- Release of endogenous histamine
- Not IgE-mediated



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Food Sensitivities: Metabolic Food Disorders Food Toxicology

- Two best known
 - Lactose intolerance
 - Favism



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Food Sensitivities: Metabolic Food Disorders Food Toxicology

- Genetically determined disorders
- Affects host ability to metabolize food
 - Lactose intolerance
- Alters metabolic patterns that enhances host sensitivity to chemical
 - Favism
- Celiac disease could also be classified as a MFD

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Metabolic Food Disorders: Lactose Intolerance Food Toxicology

- Lack B-galactosidase (lactase)
- Metabolizes lactose to glucose and galactose in intestinal mucosa
- Lactose cannot be metabolized
- Bacteria in colon break down into CO₂, H₂, H₂O
- Abdominal cramping, flatulence, frothy diarrhea



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Lactose Intolerance: Occurrence Food Toxicology

- 6-12% Caucasians
- 60-90% Arabs, Greeks, Jews, Black Americans, Hispanics and Japanese
- Can occur in children but more common in adults
- More severe in adults
- Lactase in gut at birth
 - Decreases with age in susceptible people

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Secondary Lactose Intolerance Food Toxicology

- Caused by other intestinal problems
- Failure to absorb lactose
- Viral gastroenteritis
- Intestinal damage
- Disappears when gut heals



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Lactose Tolerance Test (LTT)

- Oral administration of 50 g lactose to fasting person
- Measure blood glucose or breath H_2
- Monitor GIT symptoms

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Lactose Tolerance Test: Problems

- 50 g = liter of milk = high dose
- Many people can handle smaller dose
- More recent tests use smaller dose or gradually increasing doses
- Some people have normal lactase levels - still intolerant

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Treatment of Lactose Intolerance

- Avoidance of dairy products
- Complete avoidance not needed
- Small divided doses of milk
- lactose-hydrolyzed milk
- Add lactase to milk
- Yogurt and acidophilus milk have some lactase

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Metabolic Food Disorders: Favism

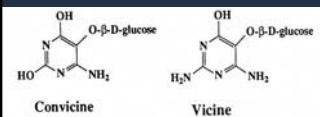
- Inherited deficiency of glucose-6 phosphate dehydrogenase enzyme (G6PDH) in red blood cells
- Ingestion of fava beans (broad beans) or breathing pollen causes hemolytic anemia
- Other symptoms - pallor, fatigue, shortness of breath, nausea, abdominal pain, fever



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Favism

- Contain oxidants - vicine, convicine
- G6PDH critical to rbc's
- Helps maintain adequate levels of glutathione and NADPH which prevent oxidative damage to rbc's



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Favism - Occurrence


- Most common enzyme defect
- 100 million people
- Asians, Jews, Sardinians, Cypriot Greeks, African Blacks most susceptible
- Absent in Caucasians, American Indians and Eskimos
- More common in males than females
- More severe in infants and children

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Other Metabolic Disorders

- Asparagus - sulfur-smelling urine
 - Inability to metabolize methanliol, excreted in urine
- Red wine - sneezing, itch, flush, headache, dyspnea
 - Impaired histamine degradation, possible diamine oxidase deficiency




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Other Metabolic Disorders

- Beets/Beeturia - red urine
 - Excretion of betanin in urine
- Chocolate - migraine headaches
 - Phenylethylamine metabolism
- Fructose intolerance - GIT problems and hypoglycemia
 - Reduced hepatic aldolase



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Food Sensitivities: Idiosyncratic Reactions

- Mechanisms unknown
- Some well documented
 - Sulfite sensitivity
- Some anecdotal - weak evidence
 - Yellow dye, MSG
- Some disproved but still popular belief
 - Some food coloring

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Idiosyncratic Reactions: Proven

- Sulfites - asthma
- Celiac disease - cereal products
- Aspartame - urticaria

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Idiosyncratic Reactions: Unproven


- Chronic urticaria - BHA/BHT, benzoates
- Asthma, urticaria - tartrazine
 - FD&C Yellow dye #5
- Migraine headache - aspartame
- Aggressive behavior - sugar
- Chinese Restaurant Syndrome and asthma- MSG

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Idiosyncratic Reactions: Disproved

- Hyperkinesis in children - food coloring agents



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Sulfite Food Additives

- Prevent enzymatic and non-enzymatic browning of food
 - Salad bars
- Antimicrobial, antioxidant
- Dough conditioner
- Bleaching agent
 - Maraschino cherries and hominy

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Sulfite-Induced Asthma

- Triggered by exposure to sulfites
- Acute onset - minutes
- Can be severe - 20 deaths
- Prevalence low - 1-2% asthmatics
- Use on salad bars banned
- Lettuce problem
 - High free sulfite
- Natural levels are quite low

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Sulfite Additives in Foods (ppm)

- Dried raisins/prunes - 500-2000
- Lemon/lime juices - 150-800
- Grape juices - 50-250
- Wine - 20-350
- Molasses - 125
- Shrimp - 10-100
- Must label if >10 PPM

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Sulfite Asthma: Mechanism

- Spans anaphylactoid, metabolic and idiosyncratic
- Some IgE-mediated
- Some sulfite oxidase deficiency
- Hypersensitivity to inhaled SO₂
- Individual tolerance vary
 - 3-130 mg

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Tartrazine-Induced Asthma and Urticaria

- Tartrazine = FD&C Yellow Dye #5
- Reports of asthma and urticaria in children
- FDA required labeling in 1979
- Failure to list on label is most frequent cause of recalls today



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Tartrazine-Induced Asthma and Urticaria

- Problems with studies
- No effects on double-blind studies
- Withholding medications - bronchioinhalers, antihistamines
- Similar problems with other food additive studies and urticaria - flawed designs

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Food Additives and Chronic Urticaria

- FD&C Yellow dye # 5
- Sunset Yellow FD&C #6
- Sodium benzoate, benzoic acid
- Parabens
- BHA/BHT
- Evidence for effects
very suspect