Chivensity or Idaho

Food Allergy

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Learning Objectives

- Understand the types of adverse food reactions.
- Differentiate food allergy and food sensitivity.
- Understand the role of IgE (Immunoglobulin E) in allergic reaction.
- Explore the types of IgE and non-IgE mediated food allergy.
- Summarize the series of events in allergic reaction.

Learning Objectives

- Examine symptoms of allergic reaction including local and systemic anaphylaxis.
- Summarize the approach to food allergy diagnosis.
- Survey common food allergens.

Adverse Reactions to Food

- 30% of population report family member with food "allergy"
- Actual % estimates vary <1-7%
- Subpopulations/ethnic groups differ markedly

Most Common Allergic Foods/Groups

- Cows milk
- Crustacea
- Eggs
- Fish
- Peanuts
- Soybean
- Tree nut
- Wheat

Adverse Food Reactions Allergy – Sensitivity - Intolerance

General terms that can be applied to any clinically abnormal response to food or food additives.
Many symptoms are similar.

Types of Adverse Food Reactions

• Allergy

• Pharmacological (drug interaction) Toxicity Non-immune anaphylaxis

- (anaphylactoid)
- Intolerance
- Metabolic
- Idiosyncrasy

Types of Food Sensitivities and Allergies

True food allergy

- Food sensitivities
 - Anaphylactoid reactions
 - Metabolic food disorders
 - Idiosyncratic reactions

Some in several classes

Food aversions

- Mimic sensitivity but no blinded response

Food Allergy: Hypersensitivity

- Immune-mediated reaction
- · Can be triggered by very small amounts of food
- Occurs on second exposure or to a cross reacting antigen
- · Anaphylaxis and cutaneous reactions most common

Food Allergies: History

- Observed since early Greeks and Romans
- Hippocrates documents milk sensitivity Injected normal person with fish extract - no
- effect (1921) - Injected serum of sensitive person, then fish extract allergic reaction
- Researchers discovered IgE (Immunoglobulin E, antibody subclass) in serum was cause (1966)

Food Allergy Epidemiology

• Affect ~ 6% of children < 3 years old – Milk & soy

• Cow's milk: 2.5% Over 80% tolerant by 5th birthday

- Egg allergy: 1.5%
 - Over 85% tolerant by 3rd birthday
- Peanut allergy: 0.5%
 - Clinical tolerance reached in a minority
 - Prevalence may be
 - increasing in children

Epidemiology

• Small subpopulation at risk <1%

- 65% of susceptible people have close relative with allergy
- Increased intestinal permeability to macromolecules predisposes
 - Viral gastroenteritis, premature birth, cystic fibrosis
- Leaky gut syndrome (LGS)

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Epidemiology

- Higher in children with other atopic disorders

 35% of children with moderate to severe atopic dermatitis (eczema)
 - 6% of asthmatic children
- Adverse reactions to food additives 0.5-1% of children

Pathophysiology

- GI tract forms a barrier to outside environment
- GALT inhibits responses to non-dangerous antigens while mounting responses to pathogens

 Gut-Associated Lymphoid Tissue
- Oral tolerance = unresponsiveness
- Intact food antigens may penetrate the GI tract but not cause clinical symptoms
- Develop in genetically predisposed individuals when oral tolerance fails
- 14 Freik

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Types of Hypersensitivity

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

Type I: Immediate hypersensitvity

- Failure in oral tolerance leads to excessive food-specific IgE antibodies
- These bind receptors on many cells (esp basophils and mast cells)
- Food allergens penetrate mucosal barrier and bind these IgE antibodies
- Cellular mediator release

IgE Mediated e erance leads to pecific IgE

– Foto mucc these – Cellu

Food Toxicology IgE Mediated Cutaneous Urticaria (hives) Angioedema (welts) Morbilliform rashes Flushing Gastrointestinal Lip, tongue, and palatal

- pruritis and swelling
- Laryngeal edema
- Vomiting and diarrhea

17 Freile



Non-IgE Mediated

- Type II: Antibody dependent cytotoxicity
 - Specific antibody binds to a surface tissue antigen and induces complement activation (system of serum immunoproteins which interact in a cascade)
 - Complement \rightarrow inflammatory mediators \rightarrow tissue damage
 - Milk-induced thrombocytopenia

Non-IgE Mediated

- Type III: Antigen-antibody complex mediated
 - Complement activation
 - Has been implicated in food related complaints
 - Can be found in sera of normal patients
 - IgE-food antigen complexes are more commonly found in patients with food hypersensitivity
 - Little support for causing disease

20 Freiler

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Non-IgE Mediated

• Type IV: Cell-mediated hypersensitivity

- Mediated by sensitized CD4+ T lymphocytes which process antigens and release lymphokines.
- The lymphokines promote a reaction mediated through macrophages beginning in hrs
- but reaching a peak in 2 to 3 days.
 Implicated in foods with <u>delayed</u> onset of sx
- Likely to contribute to a number of GI disorders
- Ingestion of sensitizing antigen may cause mucosal lesions

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Non-IgE Mediated

• Cell Mediated Hypersensitivity

- Cutaneous
- Contact dermatitis
- Dermatitis herpetiformis

Gastrointestinal

- Food protein-induced enterocolitis
- Food protein-induced proctocolitis
- Food protein-induced enteropathy syndromes
- Celiac disease

Respiratory

- Food-induced pulmonary
- hemosiderosis (Heiner syndrome)

 Intra-alveolar bleeding

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Mixed IgE and Cell Mediated

Cutaneous

- Atopic dermatitis
- Gastrointestinal inflammation
 - Allergic eosinophilic esophagitis
 - Allergic eosinophilic gastroenteritis
- Respiratory
 - Asthma

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Allergic Response Type I Hypersensitivity

- 1) The food is eaten.
- 2) Reaches the stomach and small intestine where the proteins are not digested correctly
- Intact proteins cross the small intestine and reach the blood and lymph system.
- 4) The immune system makes antibodies against the proteins
- Allergic people make Immuglobulin E (IgE) which non allergic people don't.
- IgE binds to the surface of mast cells or basophils which sensitizes them.
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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 two to IgE antibodies.
- 4) Causes the mast cell or basophil to degranulate.
- 5) Granules contain 40 different substances that cause allergic reactions.
 - Histamine, prostaglandins, leukotrienes

IgE Mediated Food Allergy Summary

- Production of IgE antibodies
- IgE bind to surface of mast cells or basophils
- Second exposure to allergen
- Allergen cross-links IgE on surface
 Release of histamine, bradykinin, leukotrienes, TNF
- Inflammation and swelling via capillary leakage and wbc
- Allergic reaction
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Food Allergy: Symptoms

- Respiratory = asthma, wheezing, bronchiospasms, dyspnea (shortness of breath)
- Cutaneous = urticaria (hives), eczema, rash, pruritis
- Gastrointestinal = vomiting, diarrhea, abdominal pain
- Inflammation, vasoconstriction, hypotension, chest pain, nausea

Food Allergy: Symptoms

- Other = anaphylaxis
- Mild and annoying to fatal
- Depend on amount ingested and length of time from initial exposure
- Not all symptoms in all people





Food Allergens

- · Almost all natural food proteins
- Papain only known additive meat tenderizer additive - enzyme
- · Penicillin contaminants in meat and dairy products are potential hazard



Local Anaphylaxis (atopy)

• About 10% of people have "atopy" (atopic syndrome) and are easily sensitized to allergens that cause a localized reaction when inhaled or ingested.

- This can produce hay fever, hives, asthma, etc.

Generalized Systemic Anaphylaxis

- Accounts for 1/3 of all anaphylaxis seen in emergency rooms
- Symptoms
 - Skin urticaria / angioedema
 - Respiratory rhinitis, bronchial hyperreactivity
 - Cardiac hypotension,
 - arrhythmias, vascular collapse - GI - nausea, vomiting, abdominal
 - cramping, diarrhea
- Dx by history and demonstration of food specific IgE
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Fatal Food-Induced Anaphylaxis (32 cases)

- 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 (EIA)

• Rare form occurring when patient exercises 2-4 hrs after ingestion of specific food

• Without exercise, food no problem

Most common in women 15-35 y.o.



Diagnosis of Food Allergy

- · Self/parental often erroneous
- Food diary-when/what/how much
- Double-blind food challenge(DBFC)
 - Neither patient nor doctor know if placebo or allergen (crossover)
- Skin prick test
- RAST •

prior to menstruation - Dx based on history and evidence of specific IgE

- Sx more pronounced just

· Common offenders: wheat, celery, shellfish, fish, fruits, milk

Skin Prick Test

- To determine if IgE involved
- Usually preliminary test
- Apply allergen extract to skin



- Inflammation results from release of histamine, edema and swelling
- Positive control = histamine
- Result in ~ 20 min

Radio-Allergosorbent Test (RAST)

- Also test for IgE
- Apply crude extract of allergen to solid phase (tissue culture plate)
- Add patient serum
- IgE (if present) binds allergen
 Add anti-IgE radiolabeled
- antibody
- Measure binding

Common Allergenic Foods: Infants/Children

- Cow's milk most common
- Eggs
- Legumes
 - peanuts
 - soybean
- Wheat



Common Allergenic Food: Adults

- Legumes peanuts, soybean
- Crustacea shrimp, crab, lobster
- Molluscs clams, oyster, scallop
- Fish
- Tree nuts
- Eggs
- Wheat

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Food Allergens

Most food allergens contain multiple proteins
 which are allergenic



Protein Allergens Milk - casein, lactoglobulins, lactoalbumins No reduction by pasteurization, condensation, evaporation, and drying Eggs - ovalbumin, conalbumin, lipoprotein Egg white more allergenic No reduction by cooking Peanuts - arachin, lectin-reactive glycoprotein, Peanut I Very heat stable, trace sensitivity

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Allergen M

- Common protein allergen in fish
- Muscle protein parvalbumin
- These proteins are conserved in fish species
- Very cross-reactive
- Very stable in processing



Allergenic Proteins

- Not many specific allergens have been identified
 Peanuts 30% protein
- Soybeans 42% protein
- Difficult to isolate specific moieties
- Groups albumins, lipoproteins, globulins, glycoproteins,
 - S-fractions

Food Allergen Proteins

> Lipoprotein

≻ Albumin

> Peanut I + others

Glycinin + othersAllergen M

Glutelin/globulins

➢ Glycoproteins

- Cow milk > β-lactoglobulin
- Egg yolk
- Peanuts
- Soybeans
- Codfish
- Green peas
- Rice
- Tomatoes

Food Allergens

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



Treatment of Food Allergy

- Total avoidance of specific allergen
- No level is safe
- Very small doses can elicit
 - Distinguishes from other food sensitivities
- Cross reactivity is constant worry