Food Allergies, Intolerances, Sensitivities, OH MY!

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“Adverse reactions to food are arguably some of the most confusing and misunderstood conditions in medical practice.”

- Joneja
These sandwiches are a tad disappointing...

Well, there's nothing on them!!

Really... how so??

That's odd! We did cater for everyone's dietary requirements...
Objectives

• Identify the underlying mechanisms of intolerances, food allergies, and sensitivities.

• Become familiar with symptoms associated with the different types of adverse food reactions.

• Describe the role of RDNs in identification and management of adverse food reactions.
Why are Adverse Food Reactions so confusing?

• Different ways to classify adverse food reactions.

• Not all mechanisms are known.

• Misconception that ‘food allergy’ is a distinct disease.
  ▫ Patient-specific – triggers, symptoms, dose

• Diagnostic methods vary.
Adverse Food Reactions

Non-Immunological Reactions (Intolerance)
- Metabolic (e.g. Enzyme deficiency)
- Pharmacological (e.g. Histamine sensitivity)
- Poorly-Defined Mechanism (e.g. MSG)

Immunological Reactions (Allergy/Hypersensitivity)
- IgE Mediated (e.g. Anaphylaxis)
- Mixed IgE & Non-IgE Mediated (e.g. Eosinophilic esophagitis)
- Non-IgE Mediated (e.g. Celiac)

Adapted from:
Adverse Reactions to Food
Stressful for Sufferers and Their Families

• Range of reactions:
  ▫ Not clinically visible – Anaphylaxis

• Social stigma

• Hypoallergenic diet does not exist
What contributes to the way a person’s body reacts to foods and chemicals?

- Inherited tendencies
- Previous medical history
- Response to other foods and nonfood factors
  - Airborne and environmental allergens
- Lifestyle
Non-Immuneological Adverse Reactions (Intolerances)
## Causes of Non-Immunological Adverse Reactions

<table>
<thead>
<tr>
<th>Intolerances</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzymatic deficiencies</td>
<td>Lactose intolerance</td>
</tr>
<tr>
<td></td>
<td>PKU</td>
</tr>
<tr>
<td></td>
<td>Fructose malabsorption</td>
</tr>
<tr>
<td>Maldigestion/Malabsorption</td>
<td>FODMAPS</td>
</tr>
<tr>
<td>Psychological / Neurological Reaction</td>
<td>Any food</td>
</tr>
<tr>
<td>Reactions to Pharmacological Agents*</td>
<td>Histamine</td>
</tr>
<tr>
<td></td>
<td>Salicylates</td>
</tr>
<tr>
<td>Reaction to Additives*</td>
<td>Nitrates</td>
</tr>
<tr>
<td></td>
<td>BHA, BHT</td>
</tr>
<tr>
<td></td>
<td>MSG</td>
</tr>
<tr>
<td></td>
<td>Sulfites</td>
</tr>
<tr>
<td></td>
<td>Tartrazine</td>
</tr>
</tbody>
</table>

* Reactions mimic classic IgE allergies.
Food Intolerances

- Symptoms suffered by 122 patients:
  - Abdominal pain (73%)
  - Diarrhea (60%)
  - Tiredness (42%)
  - Headaches (38%)
  - Constipation (23%)
  - Bloating (21%)
  - Fluid retention (20%)
Food Intolerances

• Symptoms that mimic classic IgE allergy:
  ▫ Asthma (with history)
  ▫ Angioedema
  ▫ Urticaria
  ▫ Nasal congestion
  ▫ CNS involvement
Immunological Adverse Reactions to Foods (Allergies)

IgE-Mediated Allergies
Immunological Reactions - Gut Immunology

- Intestinal tract is on the outside of your body.
- It is bombarded with countless chemicals, proteins, bacteria, and antigens on a daily basis.
- The GI tract is the most active immunologic organ in the body. (GALT)
- The ability to respond to antigens in the GI tract is an essential function of the immune system.
These eight foods account for the vast majority of all IgE-mediated food allergies in the US.
IgE Mediated Allergies

Clinical Manifestations of Classic Allergic Disorders

Immediate (< 2 hrs)

- Oral allergy syndrome
- Anaphylaxis
- Urticaria
- Angioedema
- Pruritus
- Rhinitis
- Asthma
- Reflux
- Vomiting
- Cramps
- Diarrhea
IgE Mediated Allergies

Oral Allergy Syndrome

• Most common (IgE) food allergy in adults.
• Mild contact allergy related to:
  ▫ Plant associated proteins (fruits, vegetables, nuts).
  ▫ Cross-reactivity: Food antigens structurally similar to those of pollen or latex.

**Symptoms**

- Oropharyngeal: lip/mouth/tongue edema/itching, papules, hoarseness, laryngeal edema/breathing obstruction
- Systemic: Urticaria, angioedema, rhinitis, asthma, anaphylaxis

**Management**

- Cooking food deactivates proteins/ prevents reaction
IgE Mediated Allergies
Reaction Patterns in Infants and Toddlers with Cow’s Milk Allergy...

<table>
<thead>
<tr>
<th></th>
<th>Immediate (27%)</th>
<th>Intermediate (53%)</th>
<th>Late (20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of onset</td>
<td>&lt; 2 hr</td>
<td>2-24 hrs</td>
<td>1-5 days</td>
</tr>
<tr>
<td>Milk dose</td>
<td>Smallest</td>
<td>Larger</td>
<td>Largest</td>
</tr>
<tr>
<td>Skin Symptoms</td>
<td>Urticaria, angioedema</td>
<td></td>
<td>Atopic eczema</td>
</tr>
<tr>
<td>Respiratory Symptoms</td>
<td>Rhinitis, asthma</td>
<td>Rhinitis, asthma</td>
<td>Rhinitis, asthma</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>V/D, colic, reflux</td>
<td>V/D/C, colic, reflux, FTT</td>
<td>D/C, reflux, FTT, other food intol</td>
</tr>
</tbody>
</table>
IgE Mediated Allergies

Other common symptoms:

- Pruritis
- Urticaria
- Gut symptoms
IgE Mediated Allergies
Anaphylaxis

- Food-induced generalized reactions account for 30-50%
- Most common triggers: Peanuts, tree nuts, shellfish
- Life threatening reactions include:
  - Respiratory failure
  - Hypotension
  - Cardiac failure
  - Shock
- Injection with epinephrine is often critical.

* Food-dependent, exercise-induced anaphylaxis
IgE Mediated Allergies

Diagnosis

• History usually identifies agent.

• Specific IgE test (skin, in vitro) may be useful in supporting diagnosis.

• Positive oral food challenge response is definitive.
  • Small dose can trigger reaction.
IgE Mediated Allergies
Diagnosis - Skin Tests

• Accurate for environmental IgE allergies.

• Not accurate for food allergies.

• Positive result is at most 50% predictive.

• Intradermal test may increase sensitivity by injecting antigen into the body.
IgE Mediated Allergies
Diagnosis – Blood Tests

- RAST - Radio Allergo Sorbent Test
- FAST – Flourescent Allergosorbent Test
- ELISA - Enzyme Linked Immuno Sorbent Assay
- About 60% accuracy (Many false positives and negatives)

Test does not always correlate with clinical symptoms.

2010 retrospective study:
- 125 children (1-19 years old)
- 84-93% of foods avoided as a result of positive skin and serum allergen-specific IgE test results did NOT trigger an allergic reaction when reintroduced by oral challenge. (Fleischer, Bock, Spears, et. al.)

Newer methods considered to be more sensitive:
- Phadebas
- ImmunoCAP
Immunological Adverse Reactions to Foods (Allergies)

Mixed IgE and Non-IgE Mediated Reactions
## Mixed IgE and Non-IgE Mediated Reactions

### Eosinophilic Gastrointestinal Diseases

- Distinct diseases involving localized eosinophilic inflammation

<table>
<thead>
<tr>
<th>Eosinophilic Esophagitis (EE)</th>
<th>Eosinophilic Gastroenteritis (EG)</th>
<th>Eosinophilic Colitis (EC)</th>
</tr>
</thead>
</table>

#### Symptoms:
- Localized – e.g., regurgitation, heartburn, abdominal pain, diarrhea, wasting

#### Diagnosis:
- Tests to exclude other causes of gastrointestinal disease
- Endoscopic biopsy showing localized eosinophils (most helpful in EE and EG)
- EC – bowel wall radiographs
- No evidence of IgE involvement
- EE - Eosinophil Count Resolution of symptoms and drop in eosinophil count upon elimination and recurrence of eosinophilia with reintroduction of suspect food

#### Management:
- Anti-allergy medications, corticosteroids, anti-acid approaches and avoidance of provocative foods
Immunological Adverse Reactions to Foods (Allergies)

Non-IgE Mediated Hypersensitivities
Non-IgE Mediated Hypersensitivities
Allergic disorders plus variable involvement of single or multiple organ systems

**Clinical Manifestations**

<table>
<thead>
<tr>
<th>Delayed (&gt; 2 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Atopic dermatitis</td>
</tr>
<tr>
<td>• Abdominal pain</td>
</tr>
<tr>
<td>• Heartburn</td>
</tr>
<tr>
<td>• Arthralgias</td>
</tr>
<tr>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Hyperactivity</td>
</tr>
<tr>
<td>• Headaches / Migraines</td>
</tr>
<tr>
<td>• Lack of concentration</td>
</tr>
</tbody>
</table>
Non-IgE Mediated Hypersensitivities

**Diagnostic Points**

**Delayed (> 2 hr)**

- History is of limited use.
- Specific IgE test results usually negative.
- Many in vitro test results unreliable.
- Positive oral food challenge response definitive.
- Large doses often required.
Non-IgE Mediated Hypersensitivities
Type IV Hypersensitivity Reaction

- Foods and food additives can trigger leukocytes to release mediators within 4-72 hours.

- Mediators:
  - Histamine
  - Serotonin
  - Prostaglandins
  - Leukotrienes
  - Cytokines
  - Dopamine
  - Others
Non-IgE Mediated Hypersensitivities
Inflammatory Mediators Can Affect the CNS.

• Some mediators can open and/or cross the blood brain barrier.

• Systemic cytokines can alter neurologic functions influencing:
  ▫ food intake.
  ▫ temperature.

• Cytokines are potent regulators of the neuroendocrine system that regulates the body’s response to stress.
Non-IgE Mediated Hypersensitivities

Diagnostic Tests

• Many test for IgG as an indicator.

  ▫ Limitation: positive test only indicates exposure. Can’t determine allergic sensitization

  ▫ Clinical usefulness is questionable.

  ▫ May indicate only an increase in intestinal permeability
Non-IgE Mediated Hypersensitivity Reaction

<table>
<thead>
<tr>
<th>Physiologic effects of released pro-inflammatory and pro-algesic mediators</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IBS:</strong></td>
</tr>
<tr>
<td>• Inflammation</td>
</tr>
<tr>
<td>• Smooth muscle contraction</td>
</tr>
<tr>
<td>• Diarrhea</td>
</tr>
<tr>
<td>• Cramping</td>
</tr>
<tr>
<td>• Visceral hypersensitivity</td>
</tr>
<tr>
<td><strong>Migraine:</strong></td>
</tr>
<tr>
<td>• Changes in blood flow (vasoconstriction or vasodilatation)</td>
</tr>
<tr>
<td>• Inflammation</td>
</tr>
<tr>
<td>• WBC activation</td>
</tr>
<tr>
<td>• Pain receptor activation</td>
</tr>
<tr>
<td><strong>Other Physiological Effects:</strong></td>
</tr>
<tr>
<td>• Hives, Eczema, Angioedema</td>
</tr>
<tr>
<td>• Reflux</td>
</tr>
<tr>
<td>• Muscle and joint aches and pain</td>
</tr>
<tr>
<td>• Rhinitis/Sinusitis</td>
</tr>
<tr>
<td>• Insomnia</td>
</tr>
<tr>
<td>• Fatigue, Brain fog</td>
</tr>
<tr>
<td>• Food cravings</td>
</tr>
<tr>
<td>• Anxiety, Depression, Mood swings</td>
</tr>
</tbody>
</table>
Non-IgE Mediated Hypersensitivities Diagnostic Tests

- ALCAT and MRT
  - Indirect measurement of the presence of cytokines released from leukocytes in the presence of antigen
  - Measures volume change of leukocytes via automated computer analysis
Case Study - Tom

- 54 yr male, hx of diarrhea for 30 years, undergoing biofeedback for pelvic floor retraining with PT for 18 months, hyperlipidemia, hypogonadism, bacterial growth overgrowth, hypertension

- Diarrhea: for 20 years pure liquid BMs, 8-10 yrs ago started on colestipol, ‘firmed him up’, but off it, liquid BM’s, added Questran and Lomotil. Advised to change his diet to improve his TG’s, added more fruits and vegetables pure liquid BM’s in spite of taking the colestipol, probiotics, and other anti-diarrheal meds

- Meds: Colestipol, Lomotil, Imodium, Pamine Forte, Bentyl, Levsin, Wellbutrin, Losartan/HCTZ, Bystolic, Finasteride, Prilosec, Baby aspirin, Align Probiotic, Fish oil, Testosterone inj, Cialis, Clorzepate Dipotassium, Proventil, Xifaxan, Flonase

- TG 396, HDL 39
<table>
<thead>
<tr>
<th>Visit #1 – 10/19</th>
<th>Visit #2 - 11/14</th>
<th>Visit #3 - 12/19</th>
<th>Visit #4 - 1/9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Symptom Score (MSQ): 64</td>
<td></td>
<td></td>
<td>MSQ: 50</td>
</tr>
<tr>
<td><strong>Initial Assessment</strong></td>
<td><strong>Gas and borborygmi somewhat improved</strong></td>
<td><strong>MRT results</strong></td>
<td><strong>Getting over a cold, taking Nyquil, Mucinex</strong></td>
</tr>
<tr>
<td>Heart healthy modifications</td>
<td>No change in diarrhea</td>
<td>Reactive to: sodium sulfite, tomato, amaranth, buckwheat, beef, cola, sodium metabisulfite, FD&amp;C yellow #5 + red # 4 caffeine, cheddar cheese, American cheese, cocoa, honey, mustard, cayenne pepper, vanilla, banana, watermelon, pear, apricot, apple honeydew melon, raspberry, peach, green pepper, sweet potato, cauliflower, yellow squash, turkey, hops, soybean, garbanzo bean, hazelnut</td>
<td>No improvement on fatigue, anxiety, &amp; focus</td>
</tr>
<tr>
<td>Non-irritating to gut</td>
<td><strong>Diet and supplement modifications</strong></td>
<td><strong>Discussed LEAP/MRT</strong></td>
<td><strong>Improvements in:</strong> Joint/muscle pain and stiffness 10=&gt;0</td>
</tr>
<tr>
<td>On antibiotic for SIBO</td>
<td><strong>Built personalized meal pattern (low fructose)</strong></td>
<td><strong>MRT results</strong></td>
<td>Digestive sx 13=&gt;10</td>
</tr>
<tr>
<td>Counseling, goal setting, self-monitoring, healthy relationship with food</td>
<td><strong>Discussed LEAP/MRT</strong></td>
<td>Reactive to: sodium sulfite, tomato, amaranth, buckwheat, beef, cola, sodium metabisulfite, FD&amp;C yellow #5 + red # 4 caffeine, cheddar cheese, American cheese, cocoa, honey, mustard, cayenne pepper, vanilla, banana, watermelon, pear, apricot, apple honeydew melon, raspberry, peach, green pepper, sweet potato, cauliflower, yellow squash, turkey, hops, soybean, garbanzo bean, hazelnut</td>
<td>Diarrhea - better consistency</td>
</tr>
<tr>
<td><strong>Symptoms:</strong> fatigue, restlessness, sleepiness during the day, anxiety, forgetfulness, concentration/focus problems, eczema, itching, minor post nasal drip + stuffy nose, gagging, SOB, joint &amp; muscle aches, stiff joints =&gt;10</td>
<td><strong>Diarrhea - better consistency</strong></td>
<td><strong>Reflux ‘lowest it’s been in years’</strong></td>
<td>Reflux ‘lowest it’s been in years’</td>
</tr>
<tr>
<td>diarrhea, gas, bloating, reflux =&gt;13 binge drinking</td>
<td><strong>Weight:</strong> 230 lbs</td>
<td><strong>Weight:</strong> 220 lbs</td>
<td><strong>Weight:</strong> 220 lbs</td>
</tr>
</tbody>
</table>

**Weight:** 230 lbs
<table>
<thead>
<tr>
<th>Visit #5 – 1/31</th>
<th>Visit #6 – 2/15</th>
<th>Visit #7 – 3/1</th>
<th>Visit #8 – 3/21</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSQ: 31</td>
<td>MSQ: 15</td>
<td>MSQ: 7</td>
<td>MSQ: 3</td>
</tr>
<tr>
<td>Mino fatigue, daytime sleepiness 12=&gt;5</td>
<td>Minor fatigue, hyperactivity, restlessness, daytime sleepiness</td>
<td>3/1/13- 7th visit</td>
<td>Diarrhea and borborygmi completely resolved. Continue gut healing supplements</td>
</tr>
<tr>
<td>Lack of concentration and focus significantly improved</td>
<td>Anxiety much improved, sharp mind 7=&gt;3</td>
<td>MSQ: 7</td>
<td>Rotation diet, healthy diet, challenge with some of the reactive foods</td>
</tr>
<tr>
<td>No eczema, itching or nasal congestion</td>
<td>No skin, nasal, mouth, lung, GU, musculoskeletal complaints, minor dark circles; digestive: 6=&gt;4 no reflux, stomach ache, diarrhea still frequent but better consistency, not severe, minor gas and bloating, still borborygmy</td>
<td>Started on nutritional supplements to support gut healing: glutamine, switched probiotic, zinc carnosine; continue challenge phase</td>
<td></td>
</tr>
<tr>
<td>Minor joint pain and stiffness</td>
<td>Minor diarrhea, bloating and gas 13=&gt;6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor diarrhea, bloating and gas 13=&gt;6</td>
<td>Weight: 214 lbs</td>
<td></td>
<td>Weight: 214 lbs</td>
</tr>
<tr>
<td><strong>Weight: 214 lbs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Elimination Diet (Duration)</td>
<td>Appropriate for</td>
<td>Specific Food Restrictions</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Selective</strong> (4-6 weeks)</td>
<td>Acute reaction indicative of IgE mediated Known or suspected food Identify food triggers in chronic allergic disease</td>
<td>Top 8 allergenic foods Sulfites, Benzoates Artificial colors Nickel, MSG</td>
<td></td>
</tr>
<tr>
<td><strong>Few Foods or Oligoantigenic</strong></td>
<td>Multiple symptoms, no pattern No indicators of food additive intolerance or sensitivity Chronic allergic conditions</td>
<td>May start with sample diet Individualized Psychological and practical preparation</td>
<td></td>
</tr>
<tr>
<td>(14 days; 7-10 days for children &lt; 7 y.o.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Elemental</strong> (Temporary)</td>
<td>Suspected allergy to multiple foods Failed selective or Few Foods protocols</td>
<td>Elemental formula</td>
<td></td>
</tr>
<tr>
<td><strong>Therapeutic</strong> (Lifelong)</td>
<td>Cause identified as food – celiac, EE, EG Errors of metabolism Intolerances Malabsorption – ie, fructose intolerance Clinical condition – experimental in idiopathic urticaria and angioedema, IBS, migraines, infant eczema</td>
<td>Dietary histamine restricted FODMAPS Tyramine &amp; phenylethylamine restricted Artificial colors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intolerance</td>
<td>Allergy Type 1 Hypersensitivity</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>----------------</td>
<td>------------------------------</td>
<td>---------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>Non-Immunological</td>
<td>Immunological</td>
<td>Immunological</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IgE - Mediated</td>
<td>Non IgE-Mediated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IgG, IgM, Complexes, T-Cells</td>
</tr>
<tr>
<td><strong>Cells Involved</strong></td>
<td>N/A</td>
<td>Mast Cells (primarily)</td>
<td>Leukocytes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(7 different types)</td>
</tr>
<tr>
<td><strong>Mediators</strong></td>
<td>N/A</td>
<td>Histamine &amp; others</td>
<td>~100 possibilities</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Cytokines, Histamine, Prostaglandins, etc.)</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Delayed</td>
<td>Immediate (&lt; 2 hour)</td>
<td>Delayed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delayed (&gt; 2 hours)</td>
<td>(&gt; 2 hours-5 days)</td>
</tr>
<tr>
<td><strong>Possible Symptoms</strong></td>
<td>Constipation, Bloating, Gas, Pain, Diarrhea</td>
<td>Anaphylaxis Urticaria, Angioedema</td>
<td>Diarrhea, Headache, Pain, Excess Mucus, Malaise, Fatigue...</td>
</tr>
<tr>
<td><strong>Conditions</strong></td>
<td>IBS, Lactose Intolerance, FODMAPS Malabsorption, Gallbladder disease, etc.</td>
<td>Atopy Allergic Rhinitis</td>
<td>Migraines RA IBS GERD Fibromyalgia</td>
</tr>
</tbody>
</table>
I keep getting stomach cramps after eating.

You're probably intolerant to certain foods.

Can you test for that?

Yes, just eat things one by one and see what makes you ill.

Won't that be slow and painful?

Fingers crossed.
Role of RDNs
Role of RDN

• The primary treatment is elimination of all, or most of, the major foodstuff offenders, so that the patient can be essentially free of symptoms

• Keeping accurate food and symptom journal is key.

• It is essential for all health care providers to recognize possible adverse food reactions and encourage patient to seek guidance
Role of RDN

- **Step One:** Appreciate the diversity of reactions to foods or additives.

- **Step Two:** Determine which foodstuffs are likely to cause symptoms/disease.
  - Obtain detailed history of probable reactions following ingestion of specific foodstuffs.
  - If indicated, obtain appropriate in vitro tests.
  - Do food elimination and challenge.

- **Step Three:** Develop nutritionally sound maintenance diet.
Role of RDN

• Early Diet and Immunomodulatory Factors
  ▫ Probiotics
  ▫ Polyunsaturated Fatty Acids
  ▫ Vitamin D
  ▫ Antioxidants

• Therapeutic potential of probiotics in food allergies and intolerances
Management of Patients with Food Sensitivities

Compliance with an elimination diet can be difficult. An experienced dietitian is essential to help patients:

- Where to shop
- What foodstuffs to buy
- How to recognize ‘hidden’ ingredients in processed foods
- Development of new recipes / meal plan
- Search for wider variety of ‘safe’ new foods
- Optimization of patient compliance
- Maintenance of adequate nutrition including dietary supplements
Questions