Digestive
01/05/15

1. **Food allergy**: immune mediated. The prevalence is on the rise but we are not sure why-perhaps manufacturing changes? Food introduction? Hygiene hypothesis? Overall none are that compelling. It is found in 6 to 8% of children and 3-4% of adults. You can "grow out" of an allergy with age. The diagnosis of a food allergy is a prospective diagnosis. A negative skin test does not necessarily preclude an allergy.
   - Example: Peanut allergy, cow's milk protein allergy
   - MOA: A protein antigen is presented to a T cell by a dendritic cell. There is a TH2 response, which enhances plasma cell production of IgE. Antigen specific IgE binds Fc receptor on mast cells/basophils, which degranulate causing immune response.
   - Presentation: often present *rapidly* (seconds to minutes), hypotension indicates immediate medical care needed, GI disturbances (cramping, bloating), pruritis, etc. Milk and egg allergies often wane with age but peanut/tree nut/shellfish allergies often persist. (Lactose intolerance will have GI disturbance as the main presentation, rhinitis is more consistent with a milk allergy). Symptoms are more prevalent in children.
   - Anaphylaxis: induced rapidly. There can be a biphasic reaction in which the patient may "get better" and then the symptoms recur within 1-4 hours (this is after treatment; mechanism not understood). Anybody with food-induced anaphylaxis should be prescribed an Epi-pen and taught how to use it. The patient should still go to the ER even with administration of an Epi-pen.
   - Diagnostic criteria for anaphylaxis:

Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:
1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
B. Reduced BP* or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence)
2. TWO OR MORE OF THE FOLLOWING that occur rapidly *after exposure to a LIKELY allergen for that patient* (minutes to several hours):
A. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
C. Reduced BP* or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)
D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP* *after exposure to a KNOWN allergen for that patient* (minutes to several hours):
A. Infants and children - Low systolic BP (age specific)* or greater than 30 percent decrease in systolic BP
B. Adults - Systolic BP of less than 90 mmHg or greater than 30 percent decrease from that person's baseline

Food Allergy, IgE testing:

- Skin prick/puncture test: false negatives can occur
- RAST/Immunoassay: may be useful with patients with history of anaphylaxis. Better specificity than sensitivity. This is a blood test. Seems to be better for environmental allergies than food allergies.
- Elimination re-challenge diet: 2 weeks should be sufficient to see a response.

Food Allergy, Non-IgE:

- Example: Celiac disease, Dermatitis herpetiformis, food protein induced enterocolitis syndrome (FPIES).
- MOA: Don't involve IgE antibodies.
- Presentation: The reaction is often delayed taking hours to days. There are non-specific GI symptoms, skin problems (pruritic as well), up to 75% of those that present with urticaria have an undiagnosed non-IgE food allergy. There can also be systemic presentations-dehydration, anemia, anorexia, etc.
- Testing:
    - Atopy patch test: apply antigen to patch, apply to skin
    - Food specific IgG and IgG4 testing: largely unvalidated, often yields multiple positive results.
    - Elimination re-challenge diet: it is flawed and it is hard to do but it is still the gold standard for testing.

IgG4 antibodies:

The presence may be associated with a better chance of growing out of an allergy, may be central to the mechanism of tolerance, may be the way that oral desensitization therapies work (promising), may be marker for presence of trigger foods in IBS, etc.

Dr. Brignall is an opponent of this since it has a strong potential for false negatives and false positives. This is not a test where labs do it the same way everywhere. Different labs come up with different things.

IgG 4 is a sub-fraction of IgG in the gut.

Celiac Disease: found in about 1% of population

- **MOA:**
    1. IgA and IgG antibodies to gliadin, endomysial and tissue transglutaminase.
    2. These immune complexes trigger the immune system
    3. Morphologic changes occur in the small intestine (villous atrophy)
- Diagnostic criteria: truly definitive test is a biopsy though it is often not needed.
- Note: gluten is a culinary term (not a scientific one). These proteins have a high proline content, which allows them to evade complete proteolytic digestion leading to large polypeptide accumulation in the intestine.
- Genetic component: Generally have either HLA-DQ2 or HLA-DQ8
- Diagnostic testing: use if there is a high suspicion due to familial history or symptomatic presentation. Also note that celiac disease may be present in patients that present with elevated liver enzymes, or in patients with T1DM.
    - IgA anti-tissue transglutaminase antibody is the best test-higher sensitivity lower specificity-more likely to get positive but less likely to be correct. It

should be performed during a gluten containing diet for best diagnostic yield. There can be false negative tests so a biopsy can be done even with negative serology.

Food Allergy, Mixed IgE and Non-IgE:

- Examples: Eosinophilic esophagitis/gastroenteritis, atopic dermatitis, cow's milk protein allergy
- Presentation: Minutes to hours after eating food if IgE mediated, days if non-IgE mediated. GI symptoms can be delayed. Eosinophilic gastroenteritis is hard to distinguish from IBS. They often have food impaction history or failed anti-reflux treatments.
- Testing:
    - Eosinophilia in 40-50% of patients
    - Elevated IgE in 50-60% of patients
    - Gold standard: elimination re-challenge diet. Most common foods are cow's milk, egg, soy, corn, wheat, and beef.

Cow's Milk Protein Allergy (CMPA):

This is common in kids. Usually 2 hours is enough to trigger the reaction, the more immediate the reaction the more likely there will be a positive skin test.

- Workup: it is complex.

Food Protein-Induced Enterocolitis Syndrome:

This tends to be self-limiting condition that kids grow out of. Soy and dairy are the most common etiologic agents.

- Presentation: Projectile vomiting can occur with this condition.

2. Food intolerance: non-immune mediated. This is more common than food allergies.

Metabolic food intolerances:

- Examples: Lactose intolerance, pancreatic insufficiency secondary to CF, or pancreatitis.
- MOA: absence of enzyme, or damage to mucosa leading to less lactase
- Presentation: symptoms after ingestion of lactose/dairy
- Testing: give bolus dose of lactose and check BG. False negatives can occur. It is fairly specific. A positive is a change in blood sugar that is less than 20mg/dl and development of symptoms. It can also be done with a lactose breath hydrogen test but antibiotics/smoking can change the results.

Toxic Intolerances:

A toxin contaminates a food causing symptoms. Some are reportable.

- Examples: Scromboid (histamine) poisoning, Staph aureus enterotoxin B

Pharmacologic/Food Additive Intolerance:

- MOA: mechanism is unknown. A definitive test is therefore problematic

- Testing: elimination re-challenge. Can also do an aspirin challenge test to look for salicylate allergy. This elimination is more stringent.
- Prevalence: .01 to .23% of the general population
- Presentation for Tartrazine: often co-exists with salicylate sensitivity.

Idiopathic food intolerance:
On elimination/re-challenge report reactions don't fall into clear diagnostic categories. This is controversial and more commonly part of a discussion with CAM providers

Psychological Food Intolerance:
- Examples: Food phobia/aversion, anxiety, orthorexia

Self-diagnosis of food intolerances is much higher than true intolerance. If this is suspected take a step back and ask yourself if this self-diagnosis is causing other health concerns.

Pattern of food introduction:
An immature gut will have a higher permeability but introducing foods prior to 6 months makes them less immunogenic. Right now it looks like it is best to introduce the most allergenic foods between 4 and 6 months.

FALCPA: Food Allergen Labeling And Consumer Protection Act of 2004
This required manufacturers to identify major food allergens on food labels. This is not the case with imported foods.

Remember with all of this to First Do no Harm:
At risk populations: children, people with metastatic cancers, people with eating disorders, people with already restrictive diets.

Wrap up:
Remember there are other diagnoses to exclude.
Allergy workup: skin test, RAST test, elimination re-challenge; probably will re-introduce unless anaphylactic response.
Intolerance workup: diagnosis based on presentation.

Dr. Yarnell:
Case 1: 73 year old white male presents constant (for years) weird, vague GI "complaints." Finally it was realized that it was triggered by eating. The pre-dominant symptom is bloating. SIBO (small intestinal bacterial overgrowth) was diagnosed-it is a dysbiosis of place. Keep in mind that it could also be gastric or esophageal overgrowth.

Gut flora:
- Clostridium coccoides is the most common bacteria in the gut-obligate anaerobe.
- Bacterioides thetaiotamicron: eats fiber.

Fiber recall: We can't break down fiber, bacteria have to break it down into short chain fatty acids (ie: butyrate) for us to use. 10% of our energy is from our gut flora doing this for

us. Some people have more of this than others. In the process of making short chain fatty acids a gas is formed-hydrogen and CO2. With this accumulation of hydrogen there is bloating and interruption of motility. Small gaseous molecules act as neurotransmitters causing reflux so the lower esophageal sphincter stops working properly. So what keeps it in check?

> Archaea: 1 strain in our adult gut (methanobrevibacter). This is a methanogen meaning it eats hydrogen and creates methane. This gas inhibits other gases so we can still get energy from our other bacteria. This was identified with DNA testing. (recall that anaerobes can't be cultured with stool samples). Testing is done for hydrogen or methane. The patient's methane levels were off the chart. He had methanobrevibacter overgrowth.

SIBO breath testing: collect baseline results, given 10g of lactulose. Then tested at least 3 times over 3 hours. http://sibocenter.com/sibo-testing/

Treatment: rifaximin 550mg TID for at least 10 days. Lower doses don't work. This is easily $800.00. This alone won't kill the methanobrevibacter, you have to add neomycin (500mg QID for 10 days).

Natural approach: lactoferrin 250mg TID for 30 days, oregano oil 3-5 drops TID or 1-2 capsules, + a "berberine containing something" 250-500mg TID. Do NOT aggravate by adding probiotics, probiotics often worsens symptoms.

How did this happen? Low stomach acid, antibiotic use, motility problem, etc.