New Diet Therapy of Irritable Bowel Syndrome, Migraine

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Overview

- Case Presentation
- Gut Immunology
- Food Allergy vs. Food Intolerance vs. Food Sensitivity – and testing
- Oral Tolerance
- IBS & Migraine - Standard Treatment
- Mediator Release Testing
- LEAP Dietary Protocols
- Reduction of Global and GI Symptoms Study
- Cytokine Study – If time allows
- Summary
Symptoms Due to Food Intolerances

Symptoms suffered by 122 patients subsequently identifying food intolerances

- Abdominal pain (73%)
- Diarrhea (60%)
- Tiredness (42%)
- Headaches (38%)
- Constipation (23%)
- Bloating (21%)
- Fluid retention (20%)
Gut Immunology

- If you think about it, your intestinal tract is on the outside of your body.
- It is bombarded with countless chemicals, proteins, bacteria and antigens on a daily basis that are trying to cross the gut mucosa and gain access to the body.
- The gut must decide what ‘contents’ are healthy nutrients and allow them to be absorbed and utilized by the body.
Three Major Food Reactions

- Food Allergy – IgE
- Food Intolerance – Non-immunologic
- Food Sensitivity – Non-IgE – But still a gut immune response (GALT)
- Naming is Controversial – Non-IgE immune related responses called ‘non-IgE allergy’ by some
Food Allergy – Type 1

- IgE
- Usually immediate
- Can result in anaphylaxis
- Overall, a relatively small number of patients with IgE mediated allergies - 2-4%
- Peanut, milk, egg, fish, wheat, nuts, soy
Food Allergy Reaction

Antigen is taken up by macrophages

Presented to T-lymphocytes

Rather than becoming tolerant, T-cells react to antigen

T-cells stimulate B-cells to produce IgE antibodies

IgE binds to mast cells

Re-exposed to antigen

Antigen binds to IgE on mast cells

Mast cells degranulate and release mediators including histamine

Histamine causes flushing, shortness of breath, rapid heart rate and various GI symptoms
Allergy - Skin Prick Testing

- Accurate for environmental IgE allergies
- Not accurate for food allergies – Do we really think our skin reacts the same as our gut immune system?
- Positive result is only 30-50% predictive
- If intradermal, ‘may’ increase sensitivity by ‘injecting’ antigen into the body
IgE Allergy – Rast/Elisa Testing

- **RAST** - Radio Allergo Sorbent Test
- **ELISA** - Enzyme Linked Immuno Sorbent Assay

- If negative, does NOT mean “The food will be safe for you”
- If HIGH reaction- stay away from that food
- About 60% accuracy. May not show ‘safe’ foods
Allergy testing-More

- Jejunal perfusion - (research – invasive)
- Colonoscopic allergen provocation test - (research-invasive)
- Histamine - only measures one mediator, not widely studied, accepted or used yet.
Causes of Food Intolerance

- Food aversion – “I hate liver”
- Food poisoning (infectious-bacterial, viral or parasitic)
- Food intolerance
  - Irritant
  - Malabsorption issues – Hydrogen Breath Test
  - Enzymatic
Non-Immunologic Food Intolerance

- Lactose intolerance
- Fructose intolerance – 60 lbs/year average
- SIBO
  [External Link](http://www.uihc.uiowa.edu/FRUCTOSE/index.htm)
- Artificial sweeteners (sugar alcohols)
  - Sorbitol, Xylitol
- Caffeine and other dietary chemicals
- Celiac Disease – [www.celiachealth.org](http://www.celiachealth.org)
Non-Immunologic Food Intolerance

Histamine Reactions
- Aged beef, smoked meats
- Older leftovers, esp. fish
- Immediate reaction

Lectin Reactions
- Carbohydrate binding proteins
- Seeds, tubers, grains, beans, potato
- May get past the gut wall, attach to mast cells
- Immediate or delayed reaction
Food Sensitivity - Type IV

- Non-IgE/IgG immune response
- Involves different mechanisms, different cells, different mediators
- Much more common than allergy - 15-20%
Oral Tolerance

- The immunologic process of determining that an intestinal antigen is not harmful and subsequently not reacting to it is termed oral tolerance.
- It is the loss of oral tolerance with subsequent food reactivity that causes a large component of the symptoms of D-IBS, migraine and other symptoms.
- Through the Mediator Release Testing it is possible to determine to which foods oral tolerance has been lost and immunoreactivity is occurring.
Type IV Hypersensitivity Reaction

Antigen is taken up by macrophages

Presented to T-lymphocytes

Rather than becoming tolerant, T-cells react to antigen

Cytokines released

Cytokines cause various GI and systemic symptoms
Type IV Hypersensitivity Reaction

- Foods and food additives trigger non-allergic (non-IgE mediated) immune reaction causing mediator release by immunologic cells
  - Histamine
  - Serotonin
  - Prostaglandins
  - Leukotrienes
  - Cytokines
  - Dopamine
  - Others
Type IV Hypersensitivity Reaction

- This in turn leads to physiologic effects of released pro-inflammatory and pro-algesic mediators
  - IBS: Inflammation, smooth muscle contraction, diarrhea, cramping, and visceral hypersensitivity
  - Migraine: Changes in blood flow (vasoconstriction or vasodilatation), inflammation, WBC activation, pain receptor activation
  - Other symptoms: fibromyalgia, muscle and joint aches and pain, fatigue, anxiety, depression, acne, insomnia, mood swings, food cravings. Possibly seizures, autism
Is there any scientific evidence to support the theory of immunologically mediated food sensitivities?
Intestinal Perfusion Studies

- Segment of jejunum is endoscopically isolated by placement of two balloons.
- Segment of jejunum between balloons is perfused with potential food allergen and then jejunal contents are collected.
- Patients with known sensitivity to the allergen had increased production of histamine and prostaglandin E2.
- No response seen in controls.

Knutson et al, J. of Allergy and Clin. Immunology 93; 91(2): 553-9
Increased Mast Cells in IBS

- In 1962 Hiatt and Katz reported increased numbers of mast cells in muscular layer of large bowel in four surgically resected specimens from patients with IBS.
- Cecal and terminal ileal mast cell density was significantly higher in IBS patients as compared to controls.

Above data from various studies.
Increased Mast Cells in IBS

- Mast cells noted in close proximity to unmyelinated nerve cells in the lamina propria at the ileo-cecal region
- In one study of D-IBS patients, rectal mucosal mast cell concentration was positively correlated with increasing anxiety levels

Above data from various studies
**IBS Standard Treatment**
(Diarrhea Predominant IBS)

- **Interest, compassion, and reassurance**

- **Medications:**
  - Anti-cholinergics/anti-spasmodics
    - Bentyl (dicyclomine)
    - Levbid (hyoscyamine)
  - Anti-diarrheals
    - Lomotil (diphenoxylate/atropine)
    - Imodium (loperamide)
IBS Standard Treatment (Diarrhea Predominant IBS)

- Medications (con’t)
  - Anti-depressants
    - Elavil (amitriptyline)
    - (nortriptyline)
    - SSRIs
- “Avoid trigger foods”
- Modify Fiber (Add/avoid)
- Appropriate monitoring and follow up
  - Consider more extensive work up if symptoms don’t improve
However, there is no solid scientific evidence supporting any of these treatments.

Typically, they merely mask the symptoms and do not treat the underlying problem.

Many have unwanted side effects.

None improve global IBS symptoms.
Frequently, patients state that they think something/s in their diet is causing their symptoms.
Patients Believe That Their IBS Symptoms Are Food Related

- 330 IBS patients and 80 controls completed a food questionnaire
- Asked to subjectively grade their response to 35 different foods
- Food related GI symptoms were significantly higher in the IBS group as compared to controls (p<0.0001)

Simren et al, Digestion 2001;63(2):108-115
Patients Believe That Their IBS Symptoms Are Food Related

- Most frequent offending foods were:
  - Carbohydrates
  - Fats
  - Coffee
  - Alcohol
  - Hot spices
- Females and patients with anxiety had higher frequency of food-related symptoms

Post-Infectious Diarrhea Predominant IBS (D-IBS)

- 25% of patients hospitalized for severe infectious gastroenteritis developed D-IBS
- Colonic biopsies showed increased numbers of gut mucosal lymphocytes as compared to controls
- Abnormal presence of lymphocytes lasted at least a year after the initial infection

Stress and IBS

- Stress has been repeatedly shown to trigger IBS symptoms.
- Both acute and chronic life stresses have been shown to affect intestinal motility and pain sensitivity.
- It is probably a complex neural, hormonal, and immunologic interaction.
Inflammatory Mediators Can Affect the CNS

- Some mediators can open and/or cross the blood brain barrier.
- Systemic cytokines can alter such neurologic functions as food intake and temperature.
- Importantly, cytokines are potent regulators of the neuroendocrine system that regulates the body’s response to stress.
Conditions That May Be Associated with Food Sensitivity

- Celiac disease
- Ulcerative colitis
- Crohn’s disease
- GERD
- Asthma
- Migraines
- Interstitial cystitis
- Tinnitus

- Rhinitis/Sinusitis
- Secretary otitis media
- ADHD
- Urticaria
- Angio-edema
- Rheumatologic disorders
- Atopy
Typical Dietary Recommendations for D-IBS

- “Increase Dietary Fiber Intake” - often brings gas and discomfort requiring much experimentation
- “Eat Small Frequent Meals”
- “Eat Low Fat Content Meals”
- “Drink Lots of Water”
- “Avoid Gas Forming Foods”
- “Avoid Spicy Foods”
- “Avoid FOOD TRIGGERS”
Typical Dietary Recommendations for Migraine

- Limit Pressor Amines (chocolate, red wine, aged cheeses, beer, liver, smoked meats, ripe fruits, etc.)
- Limit dietary histamine (aged/cured meats, liver, leftovers/older fish, sauerkraut, etc.)
- Avoid dehydration-drink plenty of water
- Avoid hypoglycemia
- Eat lower fat meals
- Eliminate caffeine
- Avoid MSG

*Avoid FOOD TRIGGERS*
A Typical Elimination Diet

- Lamb, turkey
- Carrots, spinach, sweet potato
- Rice, cream of rice, rice flour, rice cakes
- Pears, apricots, plums
- Ghee or clarified butter
- Olive Oil
- Water
What Are The Usual Results Of These Wide Ranging Restrictions?

- Poor patient acceptance and compliance
- Poor outcomes and **FRUSTRATION**
- Frequent revisits and guess work
- Poorer quality of life – for everyone
- Increased meds and cost to patient/insurer
- Responsibility placed on RD or physician *in the mind of the patient.*
Lifestyle Eating And Performance
Mediator Release Test (LEAP MRT)

- A patient blood sample is tested for 150 common foods and food-chemicals

The Signet STS 100
MRT Device Circa 2000
Each sample is then analyzed in sequence and compared to the patient's own control samples (patients' immunocytes unchallenged) to check for any mediator release from the cells regardless of cell class or mechanism.

- The cells should not react.
Lifestyle Eating And Performance Mediator Release Test (LEAP MRT)

- The degree of reactivity to the food substance is determined by the degree of actual mediator release from the cells as detected by the instrument.

- The degree of reactivity can be semi-quantified.

A patient specific elimination diet is then developed.

Patients initially eat only the least reactive of the Non-reactive foods.

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<th>Fruits</th>
<th>Reaction Level</th>
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<tbody>
<tr>
<td>apple</td>
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<td>apricot</td>
<td>Moderately Reactive</td>
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<td>Watermelon</td>
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Lifestyle Eating And Performance Mediator Release Test (LEAP MRT)

- Slowly, they are allowed to reintroduce new Non-reactive foods
- They are advised to avoid all Moderately Reactive and Reactive foods
In time, they are advised to rotate all foods.

They continue to add ‘untested’ foods and monitor tolerance.

In time, reactive foods are added.
RD’s Role

- Possibly ordering or requesting testing
- Providing general instruction
- Providing recipe/menu ideas—creativity
- Support client in lifestyle change
- Monitor for compliance—hidden ingredients
- Document outcomes!
Cytokine Profile in D-IBS

- 40 year old male with lifelong IBS
- Had been on LEAP MRT elimination diet for greater than one year and symptom free
- A baseline plasma cytokine profile was obtained
- Patient then purposefully violated his diet and consume foods to which he was known to be intolerant
- His typical GI and systemic symptoms quickly recurred
Cytokine Profile of Individual D-IBS Patient

See Specific Cytokine Key

- Patient on LEAP diet
- Patient off LEAP diet

1 IL-2
2 IL-4
3 IL-6
4 IL-8
5 IL-10
6 GM-CSF
7 IFN-g
8 TNF-a
9 IL-1b
10 IL-5
11 IL-7
12 IL-12
13 IL-13
14 IL-17
15 G-CSF
16 MCP-1(MCAF)
Cytokine Profile in D-IBS Patients Versus Normal Controls

- Normal people without D-IBS symptoms were tested by the LEAP MRT and found to have no reactivity to the 150 food antigens consistent with a generally intact oral tolerance system.
- Their plasma cytokine levels were also measured.
Cytokine Profile in D-IBS Patients Versus Normal Controls

- A group of D-IBS patients whose blood was submitted by referring physicians for the LEAP MRT also had plasma cytokine profile performed.

- The LEAP MRT showed that these patients had a number of reactive foods consistent with a loss of oral tolerance.
Mean Human Plasma Cytokine Levels Healthy Controls (upper bars) vs. IBS-D Subjects (lower bars)

Plasma Cytokines: IBS-D vs Normals
Evidence Based Medicine Per JADA March 2005

Evidence-based practice uses:

- The best available evidence
- The results of peer-reviewed scientific studies
- And, when science is lacking, expert opinion and experience

Per ADA President, Susan H Laramee
Functional Medicine - A science-based field of healthcare that is grounded in the following principles:

- Biochemical individuality
- Patient-centered care
- Dynamic balance of internal and external factors
- Web-like interconnections of physiological factors
- Health as a positive vitality
Summary

- Food Allergy, Food Intolerance and Food Sensitivity (as discussed) are three different processes.
- Food Sensitivity causes significant problems for millions of people and can dramatically reduce quality of life, reduce productivity and costs billions of dollars in health care, diagnosis and medication.
Summary

- Standard therapy with various medications is frequently ineffective and often causes significant side effects.
- These medications do not treat the underlying cause of the problem, but merely mask the symptoms.
- MRT/LEAP - Part of the puzzle – but not the entire puzzle.
Summary

- LEAP is a revolutionary approach to the treatment of D-IBS, migraine and Fibromyalgia.
- The diet gets right to the “guts” of the matter which is namely a loss of oral tolerance to common foods with subsequent non-IgE cell mediated reactivity to foods.
- The mediators released by these activated immunologic cells are responsible for evoking the GI and systemic symptoms.
Summary

- By selectively removing the reactive foods, immunoreactivity does not occur and hence, no cytokines are released.
- Patients often have a dramatic improvement in their systemic symptoms.
- Unlike medications, it is safe and has no side effects.
- By having LEAP MRT available, it is changing how food sensitivities are treated.
- Quality of Life is significantly improved.