TAKE THREE: GI CONDITIONS
CAUSE, EFFECT, TREATMENT

CONFLICTS OF INTEREST

• No disclosures

GAVE (GASTRIC ANTRAL VASCULAR ECTASIA)

• AKA Watermelon Stomach
• Gastric = “of the stomach”
• Antral = part of the stomach just inside the pylorus
• Vas = “vessel”
• Ectasia = “the resulting lesion from the process whereby a blood vessel becomes dilated or lengthened”

• Can cause acute hemorrhage, chronic occult bleeding or both
CAUSES

- Largely Unknown
- Humoral factors
  - Hypergastrinemia, prostaglandin E2, 5-hydroxytryptamine (serotonin) produced by neuroendocrine cells, vasoactive intestinal polypeptide (VIP)
- Middle aged or older women, often associated with CREST syndrome, atrophic gastritis, chronic renal failure, cardiac and autoimmune diseases, connective tissue disorders, s/p BMT
- Delayed gastric emptying
- Cirrhosis (30%)
  - GAVE vs. PHG (portal hypertensive gastropathy)

PRESENTATION

- IDA often requiring blood transfusion
- Hematemesis
- Melena
- Present with risk factors
**THERAPEUTIC OPTIONS**

- Iron replacement therapy
- Blood transfusion
- Medical
  - Estrogen-Progesterone combo, tranexamic acid (antifibrinolytic agent)
- Endoscopic Treatment
  - APC = treatment of choice
  - Median 4 APC sessions to reduce transfusion requirements
- Surgical
  - Antrectomy, curative, if APC not sufficient. Last Resort

**SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO)**

- A condition in which colonic bacteria are seen in excess in the small intestine.
- Leads to intestinal manifestations and potential for malabsorption
- Intestinal Motility disorders are estimated to account for 90% of cases
  - IBS, chronic pancreatitis
  - Disorders that affect protective mechanisms
ANATOMY 101

Gastric Acidity + Peristalsis = Few Bacteria
Lactobacilli, enterococci, and other gram+ aerobes can be found in the mid to distal jejunum in concentrations of 10^4 organisms/ml
Anaerobes such as Bacteroides, Lactobacillus, Clostridium, and Bifidobacteria in large bowel rarely present in proximal small bowel

TI = transition point from aerobes of the upper meeting with anaerobes of the lower gut

NATURAL PROTECTION
- Gastric acid destroys many microorganisms
- Proteolytic enzymes destroy bacteria in the small bowel
- IC Valve and antegrade motility pattern of the ileum prevent retrograde translocation of bacteria from the colon to small bowel
- IGA secretion originating the GI tract helps prevent bacteria proliferation
CATEGORICAL CAUSES

- Functional and motility disorders
  - Lack of phase III of MMC (Migrating Motor Complex) seen in IBS, narcotic use, intestinal pseudo-obstruction, diabetes, radiation enteritis, scleroderma
- Anatomic disorders
  - Stasis caused by adhesions, strictures, IBD, tumors, small intestinal diverticulosis, blind intestinal loops, gastric bypass surgery
- Metabolic and systemic disorders
  - DM, Pancreatic insufficiency, cdiffs
- Immune disorders
  - IgA deficiency, CVID, acquired immunodeficiency (HIV)

DISORDERS ASSOCIATED WITH BACTERIAL OVERGROWTH

- Small intestinal stasis
- Anatomic abnormalities
- Small intestinal diverticulosis
- Surgically created blind loops (end-to-side anastomosis)
- Strictures (Crohn's disease, radiation, surgery)
- Abnormal small intestinal motility
- Diabetes mellitus
- Scleroderma
- Idiopathic intestinal pseudo-obstruction
- Radiation enteritis
- Crohn's disease
- Abnormal communication between the proximal and distal gastrointestinal tract
- Gastrocolic or jejunocolic fistula
- Resection of the ileocecal valve
- Associations usually with multifactorial causes
- Hypochlorhydria due to atrophic gastritis or medications. These are usually not clinically significant unless they coexist with concomitant motility disturbances of the small bowel.
- Immunodeficiency states (common variable immunodeficiency, AIDS, severe malnutrition)
- Chronic pancreatitis
- Cirrhosis
- Alcoholism
- End-stage renal disease
- Advanced age

EVERY NURSE LOVES A LITTLE PATHOPHYS, RIGHT?!

- Excessively high bacterial population of the small bowel, doesn’t necessarily cause harm
- **Clinically Significant SBO requires bacterial count exceeding $10^3$ org/mL in a patient with typical clinical features (Abdominal pain, bloating, diarrhea etc.)
- Invasive strains are more likely to cause inflammation and cellular changes
  - Facultative anaerobes: Streptococci, Bacteroides, Escherichia, Lactobacillus adhere to intestinal surface and release enterotoxins
  - Aerobes can produce enzymes and metabolic products capable of inducing cellular injury.
PATHOPHYS

- Impaired absorption
  - Malabsorption vs. maldigestion at the level of the intestinal microvillus membrane r/t enterocyte damage
  - Fat, Vitamins ADEK, Carbohydrate, Protein, B12 deficiency
- Diarrhea
- Impaired Small bowel motility
  - Causes Nausea, anorexia, bloating

SYMPTOM BREAKDOWN BY CAUSE

1. Mucosal Injury by bacteria and/or toxins
   Injury to epithelium, inflammation, Carb. Maldigestion, protein-losing enteropathy, liver injury, systemic inflammatory response

2. Luminal Competition with host for nutrients
   Consumption of dietary protein, Vitamin B12, Thiamine, Hyponatremia, edema, nutrient deficiencies

3. Bacterial Metabolism
   Fermentation of unabsorbed carbs, conjugation of bile acids, synthesis of Vitamin K, folate, alcohol, acetaldehyde bloating, distension, flatulence, diarrhea, interference with Coumadin dosing, High folate levels, Liver injury etc.

TOO MUCH PATHOPHYS?

- To Sum it up...
  - Excessive bacterial in the small bowel when present in clinically significant numbers can cause a host of issues and symptoms such as bloating, flatulence, abdominal discomfort, and diarrhea.
  - Rarely, patients have weight loss secondary to severe diarrhea, malabsorption or poor oral intake.
  - May present with signs and symptoms secondary to nutritional deficiencies.
DIAGNOSIS

- **Jejunal or Duodenal Aspiration and Culture**
  - Bacterial count exceeding $10^3$ org/mL in a patient with typical clinical features
  - Limitations in sensitivity and specificity
    - Poorly reproducible
    - Invasive testing required

DIAGNOSTICS

- **Breath Tests**
  - Capitalizing on Bacteria's need to eat and excrete!
  - Lower sensitivity and specificity than aspirate cultures
  - Non-invasive, widely used
  - Lactulose and glucose most common
  - Should be done with concurrent methane testing
  - Should be done with Scintigraphy for those with hx of abdominal surgeries, short gut etc.
  - Prep Required
    - Bread, pasta, fiber to be avoided 12 hours prior to test
    - Abstinence from smoking or physical exercise 2 hours prior
    - Pre-test mouth washing to prevent false +

PATIENT INSTRUCTIONS

Preparing for the Breath Test must be followed in order the test will be successful and valid:

Do not eat, drink or smoke 12 hours before the start of the test.

The ENTIRE day prior to study you may ONLY eat these seven (7) food items.

1. Meat - fowl or fish (any type) unbreaded and unsauced; baked, broiled or fried
2. Sugar free Jell-O
3. Eggs, any style
4. Cheese including cottage cheese
5. Nuts
6. Avocado
7. Iceburg lettuce, 1 Tbsp. oil & vinegar (only type of dressing allowed)

Salt, Pepper, water, diet soda, tea and black coffee and artificial sweeteners are OK to have.

No ketchup, mustard, mayonnaise, bread, soy sauce or steak sauce.

No Sugar, creamer, honey, syrup.

No cream, milk, juice or sports drinks.

No beans, peas, bran cereal, Metamucil, Citrucel, Benefiber, probiotics or laxatives for 48 hours before the start of the test.

You must be off antibiotics for at least 6 weeks prior to the test.

You must brush your teeth and use mouthwash the morning of the test (Do not swallow any toothpaste)

You may take your regularly scheduled morning medication with small sips of water.

After the test you can resume your normal diet and activities.
DIAGNOSIS

- **Empiric Treatment**
  - Reasonable for those with known or suspected underlying cause
  - Lacks standardization with respect to treatment choices, dose and duration of therapy, and appropriate outcome measures

TREATMENT

1. Treat Underlying Disease/Cause
   - If not medically or surgically reversible, should avoid medications known to cause intestinal stasis or decrease gastric secretion and motility

2. Eradicate bacterial Overgrowth
   - Must Cover aerobic and anaerobic microbes
   - 7-10 day course of abx
     - Improves symptoms for up to several months in 46-90% of patients. Render breath test negative in 20-70% of cases. (Sleisenger and Fordtran’s, 2016)

3. Address associated nutritional deficiencies
   - Replacement of fat soluble vitamins, Calcium, Magnesium, B12. Lactose free diet.

ANTIBIOTIC REGIMENS

- Cipro 250 mg BID
- Norfloxacin 800 daily
- Flagyl 250 mg TID
- Bactrim 160/180 mg BID
- Doxy 200 mg BID
- Augmentin 500 mg TID
- Tetracycline 250 mg QID
- Rifaximin 800-1200 mg once daily.
  - Poorly absorbable, better tolerated, availability has lead to more studies.
  - Pricey $$$
TREATMENT

- Recurrence in up to 44% of patients after 9 months
  - More common in elderly, S/P appy and chronic PPI use
  - Use Cyclical or continuous courses
  - Alternate abx regimen to prevent resistance

** No repeat testing needed. Monitor symptom response

EOSINOPHILIC ESOPHAGITIS

- AKA “EOE”
- Not to be confused with “EE”

EOSINOPHIL BASICS

- Variety of white blood cells produced in the bone marrow.
- Contain specialized secondary granules potentially toxic to a variety of tissues including intestinal epithelium
- Protein matrix can be deposited and measured in those with suspected eosinophilic gastroenteritis.
- Present in low levels in numerous healthy tissues
- Esophagus normally eosinophil-free
**EOE**

- “A chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.”
- Esophageal Eosinophilia vs Eosinophilic Esophagitis

---

**EPIDEMIOLOGY**

- First cases reported in late 1960’s early 1970’s
- Reported in North and South America, Asia, Europe, and Australia. No case reports from Africa
- Prevalence increasing
  - Increased recognition unlikely to fully account for increase
- Regional variation
  - Higher prevalence in Northeastern states, lower in west
  - More common in urban vs rural settings
  - Higher prevalence in colder and arid climates vs tropical zones

---

**CLINICAL MANIFESTATIONS**

- Dysphagia
- Food impaction
- Chest pain not responsive to antacids
- GERD-like symptoms, refractory heartburn
- Upper abdominal pain
- Symptoms can be non-specific, delaying diagnosis
  - Median 6 years
  - Increase prevalence of fibrosis and esophageal strictures
ASSOCIATIONS

- Allergic conditions present in 28-86% of adults with EoE (Uptodate, 2016).
- Celiac disease
- GERD

DIAGNOSIS

- Based on symptoms, endoscopic appearance and histology.
- EGD with esophageal biopsies from distal and mid or proximal esophagus
- Must Meet Criteria
  - Symptoms of esophageal dysfunction
  - Eosinophil-predominant inflammation noted on biopsy with at least 15 eosinophils/HPF
  - Mucosal eosinophils of the esophagus persisting after 2 month trial of PPI therapy
  - Secondary causes ruled out
  - Response to treatment (elimination diet, topical steroids) are supportive but not required.

ENDOSCOPIC APPEARANCE

- Stacked, Circular Rings
- Proximal strictures
- Attenuation of sub epithelial vascular pattern
- Linear Furrows
DIFFERENTIALS

- GERD
  - Obtain biopsies two months after PPI therapy trial. Consider pH/impedance testing to rule out reflux
  - Histologic features suggestive of EoE vs GERD
    - Large numbers of intraepithelial eosinophils, proximal esophageal involvement, subepithelial and lamina propria fibrosis, eosinophilic abscesses, basal cell hyperplasia, mucosal mast cells, degranulating eosinophils
- Prediction Model
  - Younger age, male sex, presence of dysphagia and food allergies, esophageal rings, furrows, plaques, lack of hiatal hernia

PPI-RESPONSIVE EOSINOPHILIA

- Clinical and histologic features consistent with EoE, but respond histologically to PPI
- Distinct Disease from EoE?
  - Acid Suppression Critical
    - Some with large numbers of eosinophils can achieve complete histologic resolution after PPI therapy

FURTHER WORKUP

- Barium Studies
- Labs
- Allergy Evaluation
- Therapeutic Trial
TREATMENT

- Goal: Clinical and/or histologic remission?
- Commonly used
  - Elimination or elemental diets decrease allergen exposure
  - Acid suppressive therapy to rule out PPI-REE
  - Topical glucocorticoids decrease esophageal inflammation
  - Esophageal dilation to treat strictures
  - Antihistamines, systemic glucocorticoids, immunomodulators

ELIMINATION DIET

- Based on observation that EoE pts have high rates of food allergies which may contribute to EoE
- Moderate evidence to support, often conditional
- Should always be done under supervision of dietician
- Consultation with allergist
- Elemental, Empiric, or Targeted Elimination diet (6 Food Elimination diet)
  - Endoscopy with esophageal biopsy to assess response to dietary treatment when food antigens are withdrawn from and reintroduced to the patient

SIX FOOD ELIMINATION DIET (SFED)

- Removes milk, egg, soy, wheat, peanuts/tree nuts, and fish/shellfish
- Collaboration with allergy/immunology, gastroenterology, dietician for best outcomes.

THE PROCESS

- EGD #1 (Initial diagnosis)
- Start Diet
- EGD #2 in 6-8 weeks after starting diet
- If clinical and histologic improvement, reintroduce food one at a time x 8-12 weeks. If improvement repeat EGD. Repeat process for each food.
- If no improvement noted on EGD #2, start pharmacologic therapy or more stringent diet
- If symptoms return during reintroduction, avoid that food, proceed with reintroduction once symptoms subside

ELIMINATION DIET

Pros:
- Non-pharmacologic intervention

Cons:
- Risk of nutritional deprivation
- Difficult to follow
- Unnecessary food aversion
- Relapse upon continuation of diet common
- Serial Repeat EGD’s required
- High rate of non-compliance

ACID SUPPRESSION

- May reduce acid in patients with co-existent GERD or by other yet undefined inflammatory process
- Protect inflamed esophagus already predisposed to injury
TOPICAL GLUCOCORTICOIDS

- Good response, reoccurrence common upon d/c
- Fluticasone, Budesonide, Ciclesonide
- Fluticasone 220 mg 2 sprays BID
  - Metered dose inhaler without spacer. Sprayed into mouth then swallowed. Nothing to eat or drink for 30 min after.
- 8 weeks, if relapse consider Budesonide or dietary changes
- Budesonide
  - Oral, viscous slurry using nebulizer solution
  - Order as compound: 1.0-2.0 mg/2 ml Pulmicort Respules with 10-1 gram Splenda packets per 1 mg Budesonide for total of 8 cc

GOOD TO KNOW

- Compounding pharmacies in the area
  - Walgreens on the corner of Mayfair and North Ave in Milwaukee at 2275 N Mayfair Road. 414-774-4821.
  - Children’s Hospital Skywalk Pharmacy
  - MDCustom Rx at 19035 W. Capitol Drive Suite 102 in Brookfield. 262-373-1050
  - CHW Pharmacy uses lower dose steroid but more viscous solution, possibly more effective.
  - Less cost per volume vs Walgreens
  - No refrigeration
  - Place the order in Epic as “compound” and free text in the information.
  - Exp: Budesonide oral viscous suspension for Eosinophilic Esophagitis 0.125 mg/mL.
  - Swallow 8 mL (1mg) twice daily. Do not ingest any solid or liquid for 30 minutes after taking medication. Dispense 480 mL.

ESOPHAGEAL DILATION

- Limited Role
- Those with severe disease and structural changes refractory to medical management
- Risks - mucosal tears, esophageal perforation
EXPERIMENTAL

- Montelukast (Singulair) – leukotriene inhibitor showed promising data, although most recent data is mixed.
- Provider preference and clinical experience

NURSING INTERVENTIONS

- Coping mechanisms
  - Avoid highly textured foods (meats, bagels etc.), cut foods into small pieces, drink plenty of liquids/lubricate foods, extensive chewing, prolonged mealtimes
  - If food impaction occurs, drink liquid, raise hands above head, jump up and down, wait for food to dissolve or pass
- Education, Advocacy, Research and Support
  - American Academy of Allergy, Asthma, and Immunology: www.aaaai.org
  - American Partnership for Eosinophilic Disorders: www.apfed.org
  - Campaign Urging Research for Eosinophilic Disorders: www.curedfoundation.org

MAINTENANCE THERAPY

- High relapse rates when therapy discontinued
- Recommend some degree of maintenance therapy (medical or nutritional)
- Consider PRN basis
- Generally well tolerated
  - Risk for candidal esophagitis
- Surveillance Endoscopy?
  - No reports of malignant potential. Repeat when symptoms change or if dilation required
QUESTIONS?

• We Covered A Ton and briefly touched on topics with enough information to discuss for days. Please contact me if there are questions. If I don’t know the answer, I will happily find out!
  • Semelroy@mcw.edu

REFERENCES

• http://www.gastrotraining.com/educational/learning-modules/gastrointestinal/watermelon-stomach
• http://www.uptodate.com/contents/image?imageKey=GAST%2F81285&topicKey=GAST%2F4776&rank=1%7E135&source=see_link&search=SIBO+diagnosis&utdPopup=true
• Eosinophilic Disorders of the Gastrointestinal Tract (Book) Rothenberg, Marc E., Haberman, Yael. Sleisenger and Fordtran’s Gastrointestinal and Liver Disease, Chapter 29, Pages 454-463.
• Small Intestinal Bacterial Overgrowth (Book) Gajdecki, Eamonn. Sleisenger and Fordtran’s Gastrointestinal and Liver Disease, Chapter 29, Pages 1824-1832 via ClinicalKey.com.
• Vascular Disorders of the Gastrointestinal Tract (Book) Brandt, Lawrence. Sleisenger and Fordtran’s Gastrointestinal and Liver Disease, Chapter 37, Pages 617-635 via ClinicalKey.com.
• Sleisenger and Fordtran’s Gastrointestinal and Liver Disease, Chapter 105, Pages 1824-1831 via ClinicalKey.com.