SIBO Overview:
Causes, Effects, Diagnosis, and Treatment

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Small Intestine Bacterial Overgrowth (SIBO) Overview

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Prevalence & Relevance

- SIBO is common
- Main cause of IBS (Irritable Bowel Syndrome)
  - IBS= up to 20% US pop. Most common GI disorder in the US.
  - IBS Sx: bloating, pain, constipation, diarrhea or both
- Up to 84% of IBS is due to SIBO, on average 60%

What is SIBO?

- Bacterial accumulation in the small intestine with normal flora
  - not pathogenic (not salmonella, c jejuni, cholera...)
- SI should have low bacterial counts (<10^3)
  - otherwise bacteria would compete for host food & interfere with digestion & absorption
    - which is what they do in SIBO
- Issue is Location of bacteria, not Type of bacteria

SIBO Symptoms

- Bloating
  - Belching, Flatulence
- Pain
- Diarrhea, Constipation or Both
- Food Reactions - GI or Systemic Sx
  - Systemic = Leaky Gut: h/a, joint/body pain, skin sx/rash, respiratory sx, brain/mood sx...
- GERD
- Nausea, Food Sits in Stomach
- Signs: Steatorrhea, Underweight, Anemia (Iron, B12, Ferritin), Assoc Dz

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(see siboinfo.com)
SIBO History

- 2000- Pimentel, Chow, Lin
  Eradication of small intestinal bacterial overgrowth reduces symptoms of irritable bowel syndrome
  - Up to 84% of IBS patients had SIBO
  - SIBO eradication = symptom improvement
- 60% average of SIBO in IBS
- SIBO is common - underlying cause of the majority of IBS

Etiology

Underlying Cause

- What is actually wrong in the body
  - Structural, Functional
  - Small list
  - Treatment
- Causes of Underlying Cause
  - Diseases, Drugs/Lifestyle, Surgery/Injury, Genetics
  - Large List
  - Prevention

Risk Factors

- Causes of Underlying Cause
- HCl - kill incoming (bact continually entering via mouth/nose)
- Bile, Enzymes - kill/arrest growth
- Immune System - kill
- Ileocecal Valve - prevents LI backflow
- Normal SI Anatomy - allows bact to move out
- Migrating Motor Complex - moves bact out, prevents LI backflow

- One or more of the protections needs to fail for SIBO to occur
Underlying Causes

- Agreed upon
  - Deficient MMC, Structural Alterations, Frank Immune Def Dz
    - MMC most common
- Debated (but certain Risk Factors)
  - Deficient HCl, Absent/Inefficient Ileocecal Valve
    - An intact MMC can compensate (clear the stomach or LI bacteria)
- Unknown
  - Bile, Enzymes

Agreed

- MMC
  - #1 prevention against SIBO (bact not moved out)
  - Occurs during fasting- between meals & at night, every 90 min. **Eating turns it off
    - In Small intestine, not Large intestine (not related to BMs)
  - Function- clear bacteria, indigestible food, cellular debris into LI
    - “Housekeeper Wave”
- Structural Alterations
  - Partial Obstruction (adhesion, stricture, tumor, compression, twist/kink) (clearance blocked)
  - Non-draining pocket (SI diverticula, blind loop syndrome) (get trapped)
- Frank Immunodeficiency Dz. (not killed or not moved out)
  - However deficient MMC & HCl usually co-exist

Risk Factors

Diseases, Drugs/Lifestyle, Surgery/Injury, Genetics

- Motility/MMC
  - Dz: Food Poisoning, Scleroderma, Diabetes, Ehlers Danlos, Hypothyroid, Parkinson’s
  - Rx: Opiates, Antibiotics (theoretical via C diff & Cdt B)
  - Lifestyle: Stress
- Obstruction
  - Dz: Appendicitis, Endometriosis, Cancer, IBD, Volvulus, Sup Mesenteric Art Syndrome
  - Surgery/Injury: Adhesions
- Frank Immunodeficiency (Def MMC & HCl) (not low SIgA on Stool)
  - Dz: HIV, CLL, T Cell Deficiency
- Hypochlorhydria- Rx: PPI’s  Lifestyle: Stress
- ICV- Dz: low pressure  Surgery: removal

MMC Video

http://wzw.tum.de/humanbiology/index.php?id=41&L=1
Then click #13
(# 12, 15 & 17 also show the MMC)

(available at siboinfo.com; Resources; MMC Video)
Interstitial Cells of Cajal Control MMC (Pokkunuri 2012)

- If # ICCs decrease below 0.12/villus, SIBO develops

How Food Poisoning Causes SIBO (Pimentel)


Pathophysiology

SIBO Symptoms Are Due To

1. Bacterial Gas made in SI (from Bact eating/fermenting CHO)
   - Hydrogen, Methane, Hydrogen Sulfide
2. Bacterial Damage to SI
   - To digestive and absorptive ability, which furthers fermentation
3. Underlying Cause (or continued risk factors)
   - Poor motility, structural alterations. Low HCl...
1° Sx are due to Bacterial Gas from CHO Malabsorption

- **Bloating** = physical swelling
- **Pain** = intestines sensitive to pressure, Visceral Hypersensitivity feature of IBS, muscles contract against gas
- **Altered BM’s** = Hydrogen> Diarrhea/Mixed, Methane> Constipation
- Belching, Flatulence = gas exiting
- GERD/Nausea = gas back pressure, reverse motility due to methane
- **HS** ~ body pain, constipation, bladder irritation, extremity tingling/numbness, sulfur smelling gas

Small Intestine Damage

SI Bacterial Overgrowth

GI Sx < GAS (Hydrogen, Methane)

Fermentation of Unabsorbed Carbohydrate

- **Bacterial Growth**
  - Increased Inflammatory Cytokines
  - Digest Brush Border
  - Bile Conjugation → fat malabsorption

- **Bacterial Actions**
  - Decrease Disaccharidases
  - Inhibit Carb Transporters
  - Blunted Villi if Severe
  - Intestinal Hyperpermeability → systemic sx

Diagnosis

3 Diagnostics Tests:

1. **Endoscopy: Culture**
   - 38% reproducibility (Quigley 2006, PMID: 16473077)

2. **Breath: Lactulose or Glucose** *
   - 92% reproducibility (Quigley 2006, PMID: 16473077)

3. **Blood: Cdt B & Vinculin Antibodies (IBSChek)**
   - Dx PI-IBS (SIBO from food poisoning); diarrhea/mixed type
   - 91% specificity, 95% dx accuracy (Pimentel 2015, PMID: 25970356)

SIBO Testing

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IBS/SIBO Differential Diagnosis

Sx: bloating, pain, constipation, diarrhea

- Yeast Overgrowth
- Parasitic Infection
- LI Bacterial overgrowth/ infxn
- H pylori infection
- Celiac Disease/NC Glut Intol
- IBD: Crohn’s/ Ulcerative Colitis
- Carbohydrate Malabsorption
  - Lactose, Fructose, Polyol...
- Food Reaction: protein, histamine, salicylates...
- Hypochlorhydria
- Pancreatic Enzyme Insufficiency
- Hypo/Hyper Thyroid
- Bile Acid Malabsorption
- VIPoma
- Zollinger Ellison Syndrome
- Adenomophysicocecal dyssynergia
- Chronic Abdominal Wall Pain
- Endometriosis
- Cancer- Panc/St/SI/LI, Ovarian...
- SI Obstruction
- Immune Deficiency (CVID)
- Stress
- Insufficient Chewing

IBS Symptom Testing- Where to Start?

- The large list of conditions that can cause IBS sx makes testing & properly diagnosing SIBO very important
- SIBO Breath Test is a reasonable place to start since on average 60% IBS is SIBO
  - Breath Test (hydrogen, methane 3 hour)
    - Most helpful for treatment

SIBO Breath Testing: How it works

- Patients drink sugar solution of glucose or lactulose, meant to feed bacteria, after a 1-2 day preparatory diet. Breath samples taken every 15-20 min for 2-3 hours.
- Measures hydrogen & methane (not hydrogen sulfide) produced by bacteria in the intestines that has diffused into the blood, then lungs, for expiration. Hydrogen & methane indicate bacteria since humans don’t make it.
- Timing reflects location: 1st 2 hrs = small intestine, 3rd hr = large intestine (avg)

Breath Testing Important Points

- Glucose & Lactulose (most practitioners use Lactulose)
  - Glucose can be ordered by anyone : Lactulose requires prescriptive rights
  - Glucose only dx proximal SIBO (top 2-3 feet of SI, it absorbs w/in 2-3 feet)
    - It doesn’t test the rest of the 15-20 feet of SI where SIBO is more common
  - A negative glucose BT necessitates a follow up with Lactulose, including a retest after Tx SIBO
- Methane must be tested: older machines or inexperienced facilities don’t test for it or report it
- 3 hr Test is best: better dx of methane & dx hydrogen sulfide
LBT Positive Test Criteria: **Numbers**

- No rise calculation needed
- Hydrogen: $\geq 20$ ppm w/in 120 min, after baseline
  - w/in 140 min with severe constipation
- Methane: $\geq 12$ ppm w/in 180 min, including baseline
  - 3-11 ppm w/in 180 min with constipation
- Combined H & M: $\geq 15$ ppm after baseline
  - H at any time-point + M at any time-point, after baseline
- Hydrogen Sulfide: all zeros or close (0-6 ppm H, 0-3 ppm M w/in 180 min)

**My Opinion**

- Improper Prep = High baseline that plummets in 1st 2 hr
  - (highest # within the 1st 2 hrs is at baseline)
  - may rise in 3rd hr due to LI bact
- Methane = starts high, stays high (often no real rise)
- Hydrogen Sulfide = no rise H/M in the 3rd hour: “flat line”
- Proximal SIBO clearing on Retest= lower #’s earlier (a good sign)
  - Sometimes the ppm’s are still (+) at a later time, but most of the SI has cleared
- Hydrogen Rises when Methane decreases = On Retest
  - Common; 4 H’s make 1 M

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LBT Positive Test Criteria: **Patterns**

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**Layers of SIBO Treatment**

1. **Symptomatic**
2. **Bacterial = SIBO**
3. **Underlying Cause**
**IBS/SIBO Treatment**

- **1st Line:** Diet & Lifestyle
- **2nd Line:** Supplements
  - Pbx, Enz, Fiber, Prebx, bitters/ACV/HCl, herbal tonics
- **3rd Line:** SIBO Tx Algorithm
  - For when 1st & 2nd line therapy has failed

- General: anemia/low ferritin, adrenal, thyroid, hormone & any other conditions present

**Treatment Notes**

- **SIBO is a chronic condition for the majority**
- **Estimate:** 2/3 of cases are Chronic (1/3 not)
  1. Ongoing management is expected
  2. Relapse is expected (unless underlying cause is treated)
     - Common relapse timeframes: 2.5 mo avg (Target 3), 2 wks, 2 days (Siebecker)
  3. 100% symptom resolution is not expected
     - 80-90% is standard. 100% can happen but it’s not standard
     - Underlying cause generates sx & has not been tx in most cases

**Antibiotic Protocols**

- **3 =** Rifaximin 550mg tid, Neomycin 500mg bid, Metronidazole 250mg tid
  - Rifaximin= all SIBO
  - Add Neo or Met to Rif = methane/constip
- **Basic Approach**
  - Hydrogen only: Rifaximin
  - Methane/Constipation alone or with Hydrogen:
    - Rifaximin + Neomycin or Metronidazole
- **Duration = 2 weeks (1 course)**
  - 3 wks for high gas. Minimal added benefit past 3 wks.
**Herbal Antibiotic Protocols**

- 4 = **Berberine** 5g/d, **Oregano** 200-600 mg/d, **Neem** 900 mg/d, **Allicin** 2700 mg/d
  - Berberine, Oregano, Neem = all SIBO cases (like Rifaximin)
  - Add Allicin = methane/constip (like Neo, Met)
    - Purified Allicin pills, not whole garlic or garlic oil pills which are fermentable = aggravates SIBO
- I use 2 herbs: 4 don’t work better vs 2
  - Keep some herbs in reserve for next rounds
  - Most I see need multiple rounds & concerned HAbx resistance
- Duration = 4 wks (=2 wks Abx), takes longer vs Abx
  - 6 wks-2 mo for high gas (=3 wks Abx)
  - Max 2 mo, minimal added benefit (often start to relapse)

**Common HAbx Protocols I Use**

- Berberine = Rifaximin
- Hydrogen only
  - Berberine + Neem or Oregano. Neem + Oregano (occasionally).
- Methane/Constipation, Methane + Hydrogen
  - Allicin + Berberine or Neem. Allicin + Oregano (occasionally).
- I prefer single herbs to big combos dt high sensitivity of SIBO pt’s I see
  - It’s easier to figure out what’s bothering them & remove it
  - Concern of HAbx resistance for next round if everything was already used
  - But I see challenging cases & mb most don’t need to worry @ it...

**Herbal Antibiotic Study (Multi Center)**

- ‘HAbx Equivalent to Abx for SIBO’ (Chedid ’14)
- 2 Protocols - of 2 Combo products used together
  1. Oregano, Thyme, Lemongrass, Sage **AND** Oregon Grape, Coptis, Phellodendron, Skullcap, Ginger, Licorice, Rhubarb
  2. Tarragon, Tinospora, Horsetail, Thyme, Pau D’Arco, Nettle, Olive **AND** Dill, Stemona, Wormwood, Java Brucea, Pulsatilla, Picrasma, Cutch tree, Hedyotis, Yarrow
- Missing Allicin= add it in to combos for CH4/constipation

**Elemental Diet**

- Powder of predigested nutrients drunk in place of all meals x 2–3 wks (no solid food eaten). Or a mixture of below ingredients if homemaking.
  - Protein= amino acids, Fats= oils, CHO= glucose or maltodextrin, Vitamins, Minerals, Salt
- Used as an alternative to Abx/HAbx
  - As effective as Abx= 80-85% success (Pimentel ’04)
- Starves bacteria but feeds patient (absorb w/in 1st 2 ft SI)
Elemental Diet Key Points

- Elemental Diet can decrease severe gas levels in one 2 week course (up to 150ppm). Abx/HAbx= 30ppm avg/course.
- Protocol -Test on day 15
  - Need results asap. Ask for overnight results with kits.
  - If still (+) = continue 1 more wk (3 wks total), at 3 wks retest & stop
  - If (-) = stop ED & begin prevention
- No Abx/HAbx concurrently- bact are hibernating
- Caution- Diabetes & Dialysis (Pimentel)

SIBO Diets

- All target & reduce Carbohydrates (CHO= bact 1° food)
  - Specific Carbohydrate Diet (SCD) (Haas/Gottschall)
  - Gut and Psychology Syndrome Diet (GAPS) (Campbell-McBride)
  - Low FODMAP Diet (LFD) (Shepherd/Gibson)
  - Cedars-Sinai Low Fermentation Diet (C-SD) (Pimentel)
  - SIBO Specific Food Guide (SSFG) (Siebecker)
    - SIBO Bi-Phasic Diet (Jacobi)
    - Fast Track Digestion (Robillard)

Prokinetics (Pk)

- (+) MMC to help prolong remission/prevent relapse
  - Not (+) Large Intestine/BMs: OK to use with diarrhea
- Essential part of Tx, esp for 2/3 chronic cases
- Started the day after finishing Tx or soon after
- OK to re-test while on them & take during next round
- Esp important to be on Pk between tx courses- to keep gains made & prevent backslide

Prokinetics

**Pharmaceutical**
- Low Dose Erythromycin 25-62.5 mg hs
- Low Dose Prucalopride 0.5 mg hs
- Low Dose Naltrexone 2.5-4.5 mg hs

**Herbal**
- STW 5 60 gtt’s hs
- MP 3 hs
- Ginger 1000mg hs

  - STW 5= Iberis amara, angelica, chamomile, caraway, milk thistle, melissa, peppermint, celandine, licorice
- MP= 5Htp, Acetyl L Carnitine, Ginger, Vit C, B6
Prokinetic Points

- Natural Pk & LDN are not strong enough for many
  - If you want to be sure = erythromycin, prucalopride
- Many need Pk ongoing, esp w/SIBO > 5 yrs
- Ok to do a trial removal at any time- the only risk is relapse
  - Titrate down slowly to catch a relapse quickly (every other night x 2 wks, then every 3rd night...)
    - If Relapse & it’s caught quickly= Restart Pk at full dose to see if that corrects it. If not then a short course of treatment may be needed.

Prevention: Other

- Low Carb/Fiber Diet (Classic= Cedars-Sinai Diet)
- Meal spacing= 4-5 hrs apart/12 hr overnight fast
  - To allow MMC
- Decrease Stress (rushing, worrying). Increase gratitude, rest.
- Visceral Manipulation/body work
- Difficult cases= ongoing Tx
  - Cyclic or ongoing Abx/HAbx, ED (Low dose or Full dose)

Summary

- Average 60% of IBS is caused by SIBO (Ghoshal '14 + Pimentel '03)
- Main Sx are bloating, pain, constipation/diarrhea/both + food sens
- Food Poisoning = most common risk factor of SIBO (IBSChek tests for this)
- Deficient Migrating Motor Complex= most cmn underlying cause
- Bacterial fermentation of CHO = 1° pathophysiology/cause of Sx
- Diagnosis is by the Lactulose Breath Test (+ history)
- It is a chronic, relapsing condition in 2/3 = ongoing management
- Main Tx: Diet + Abx, Herbal Abx, Elemental Diet; Prokinetics

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