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DR ALLISON SIEBECKER

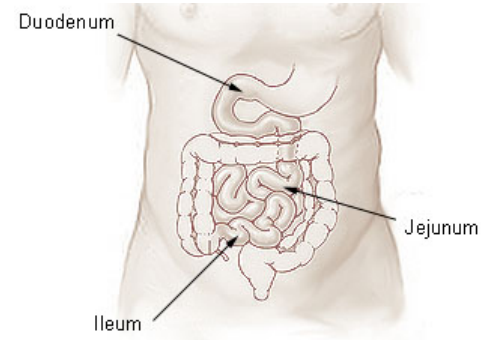
SIBO SUMMIT
2016



SIBO: Causes, Effects and Treatments

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www.siboinfo.com

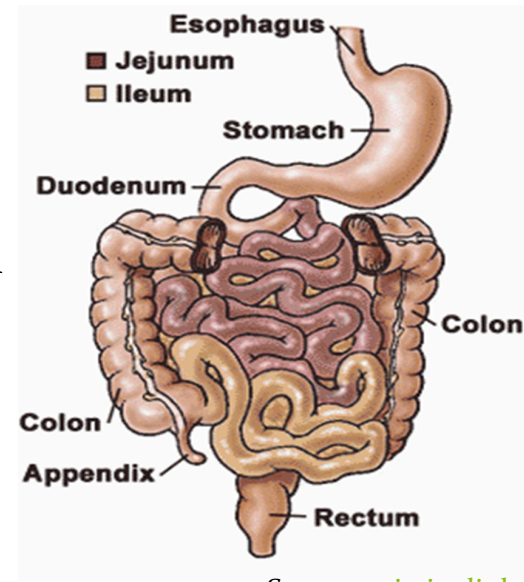
SIBO Summit
October 7 & 9 2016
Australia



Source: boundless.com

SIBO Definition

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



Source: [missinglink](#)



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 sx...
 - Fatigue. Anxiety, Brain Fog.
 - GERD
 - Nausea, Food Sits in Stomach
 - **Signs:** Steatorrhea, Underweight, Anemia (Iron, B12, Ferritin), Assoc Dz
- IBS

SIBO History



(Pimentel, Am J Gastroenterology 2000, 2003)
(Pimentel, 2006)

[Am J Gastroenterol. 2000 Dec;95\(12\):3503-6.](#)

Eradication of small intestinal bacterial overgrowth reduces symptoms of irritable bowel syndrome.

[Pimentel M¹, Chow EJ, Lin HC.](#)

⊕ Author information

Abstract

OBJECTIVES: Irritable bowel syndrome is the most common gastrointestinal diagnosis. The symptoms of irritable bowel syndrome are similar to those of small intestinal bacterial overgrowth. The purpose of this study was to test whether overgrowth is associated with irritable bowel syndrome and whether treatment of overgrowth reduces their intestinal complaints.

- 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

Risk Factors

- Causes of Underlying Cause
 - Diseases, Drugs/Lifestyle, Surgery/Injury, Genetics
 - Large List
 - Prevention



Underlying Cause

- SI has many Protections against bact coloniz
 - 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
- 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



MMC Video

<http://wzw.tum.de/humanbiology/index.php?id=41&L=1>

Then click #13

(# 12, 15 & 17 also show the MMC)

(siboinfo.com; Resources; MMC Video)

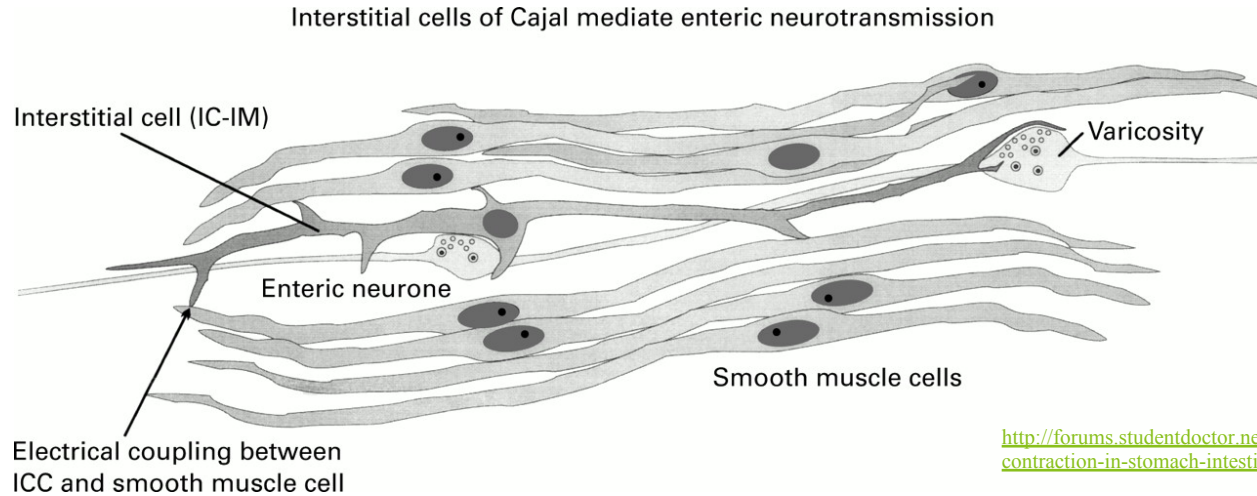


Risk Factors

Diseases, Drugs/Lifestyle, Surgery/Injury, Genetics

- Motility/MMC
 - Dz: **Food Poisoning** & C diff, Scleroderma, Diabetes, Ehlers Danlos, Hypothyroid
 - 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

Interstitial Cells of Cajal Control MMC (Pokkunuri 2012)

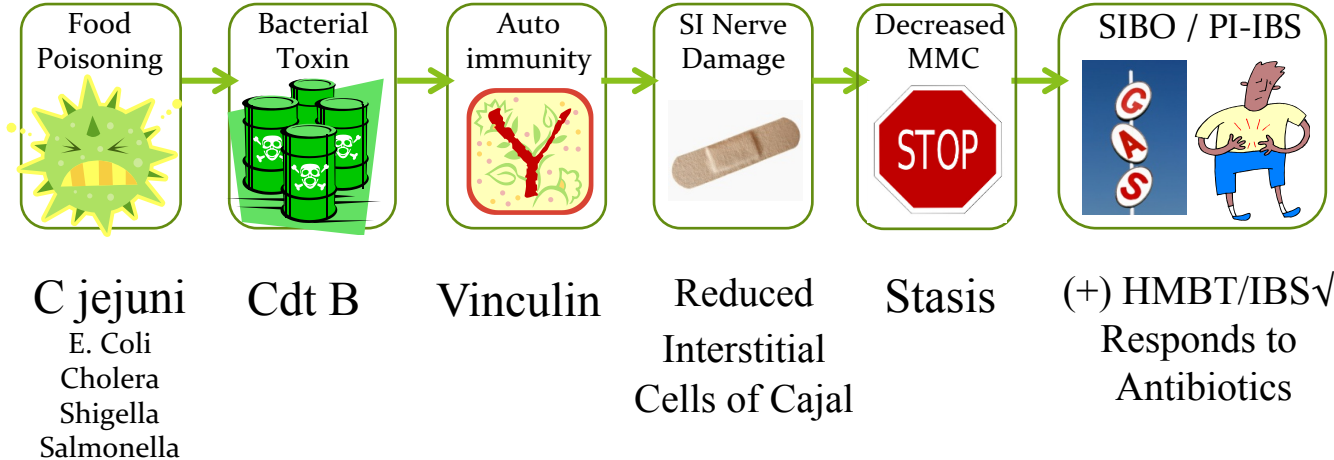


- If # ICCs decrease below 0.12/villus, SIBO develops

How Food Poisoning Causes SIBO (Pimentel)

(Pimentel 2008/2011/2015/ACG13/UEG13, Jee 2010, Morales 2011, Shah 2012, Pokkunuri 2012, Porter 2013, Sung 2013)

Pimentel M, et al. *PLoS One*. 2015;10(5):e0126438.



After Pimentel 2013
Slice credit: Dr Sandberg-Lewis



Pathophysiology



SIBO Symptoms Are Due To

- Bacterial Gas made in SI
 - Hydrogen, Methane, Hydrogen Sulfide
- Bacterial Damage to SI
 - To digestive and absorptive ability
- Underlying Cause
 - Poor motility, structural alterations, low HCl...

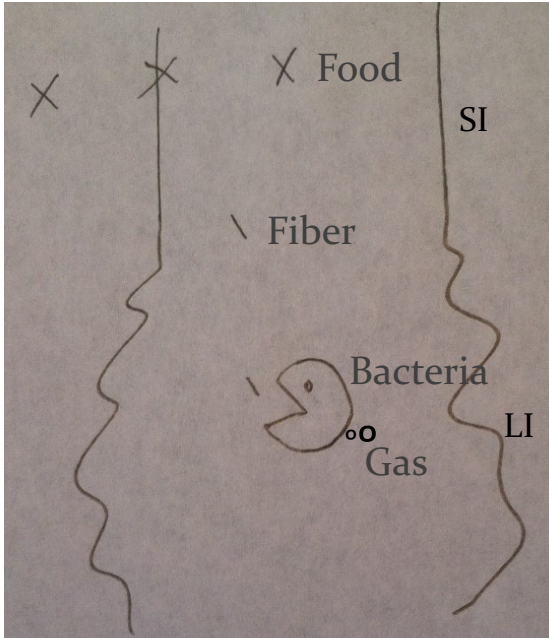


1° Sx are due to Bacterial Gas from CHO Malabsorption

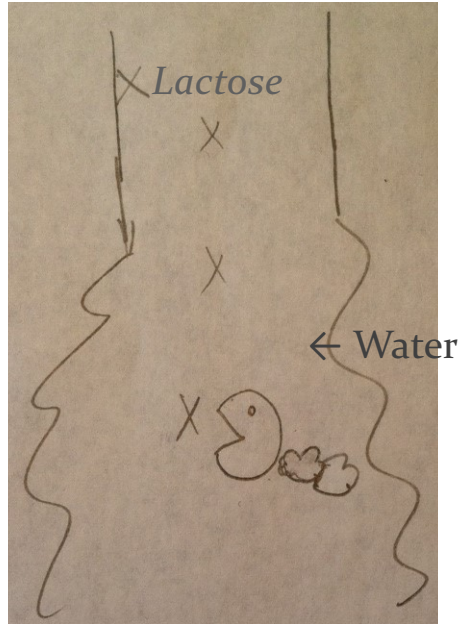
- Bloating= physical swelling
- Pain= intestines sensitive to pressure, Visceral Hypersensitivity feature of IBS, muscles contract against gas
- Altered BM's = Hydrogen> Diarrhea/Mixed, Methane> Constipation
- Belching, Flatulence= gas exiting
- GERD/Nausea= gas back pressure, reverse motility due to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

Absorption & Malabsorption

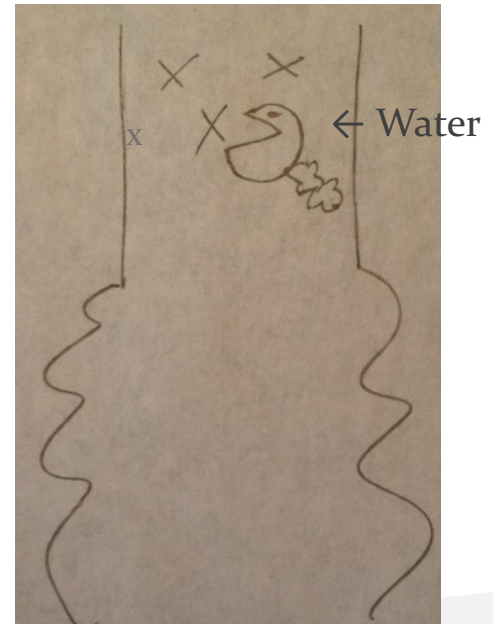
Normal Absorption



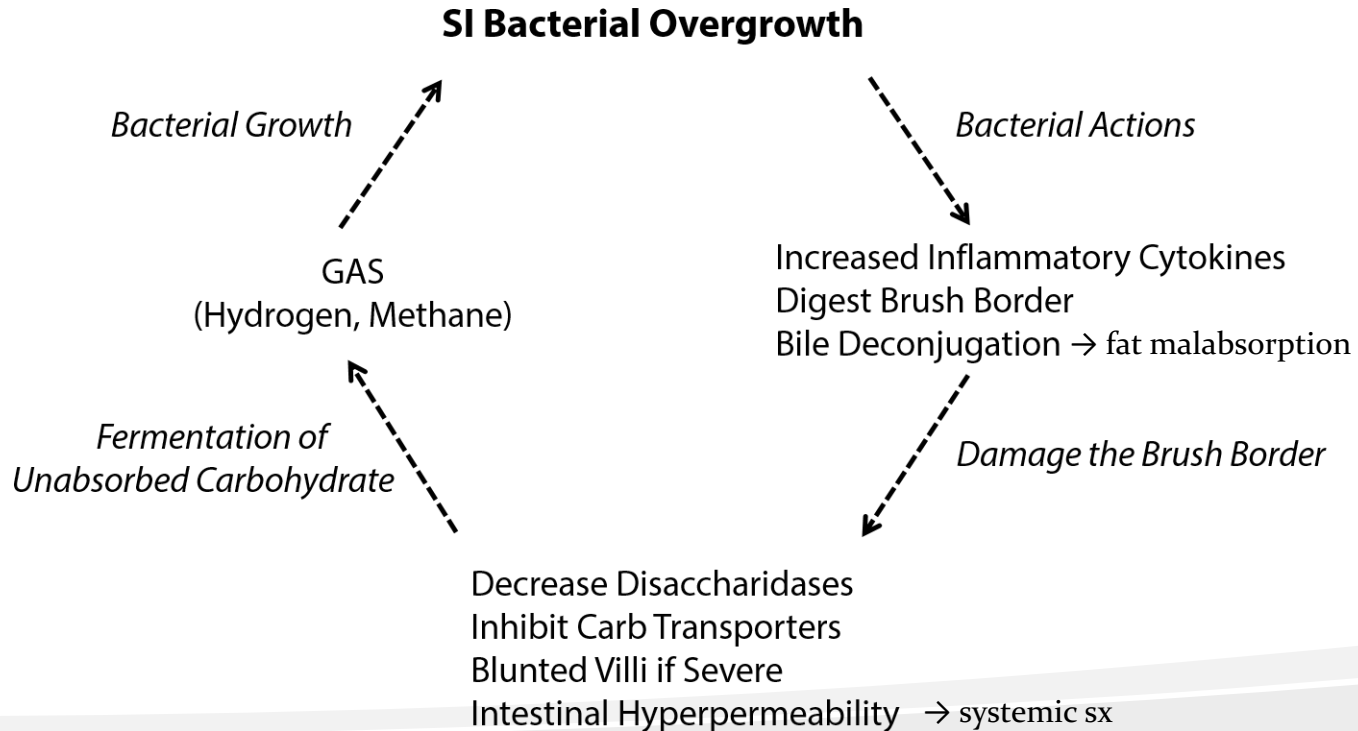
Standard
CHO Malabsorption



SIBO
Malabsorption



Small Intestine Damage





Diagnosis



SIBO Testing

- 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: 25970536)



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
- Abdomino-phrenic 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?

- SIBO Breath Test is a reasonable place to start since on average 60% IBS is SIBO
- ❖ The large list of conditions that can cause IBS sx makes testing & properly diagnosing SIBO very important
- 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 in 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. Exclusive bacterial gases hydrogen & methane indicate bacterial presence.
- Timing reflects location: 1st 2 hrs = small intestine, 3rd hr = large intestine (avg)
- Note: if glucose is neg, f/u w/lactulose (gluc only test 1st 3 ft of SI)



LBT Positive Test Criteria: Numbers

My Opinion

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



LBT Positive Test Criteria: Patterns

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



Treatment



Layers of SIBO Treatment

1. Symptomatic
2. Bacterial = SIBO
3. Underlying Cause



Order of IBS/SIBO Treatment

- Before testing (depending on severity)
 - 1st Line: Diet & Lifestyle
 - 2nd Line: Supplements
 - Pbx, Enz, Fiber, Prebx, bitters/ACV/HCl, herbal tonics
 - SIBO (+) via test
 - 3rd Line: SIBO Tx Algorithm
 - For when 1st & 2nd line therapy has failed
- ☐ General: anemia/low ferritin, adrenal, thyroid, hormone

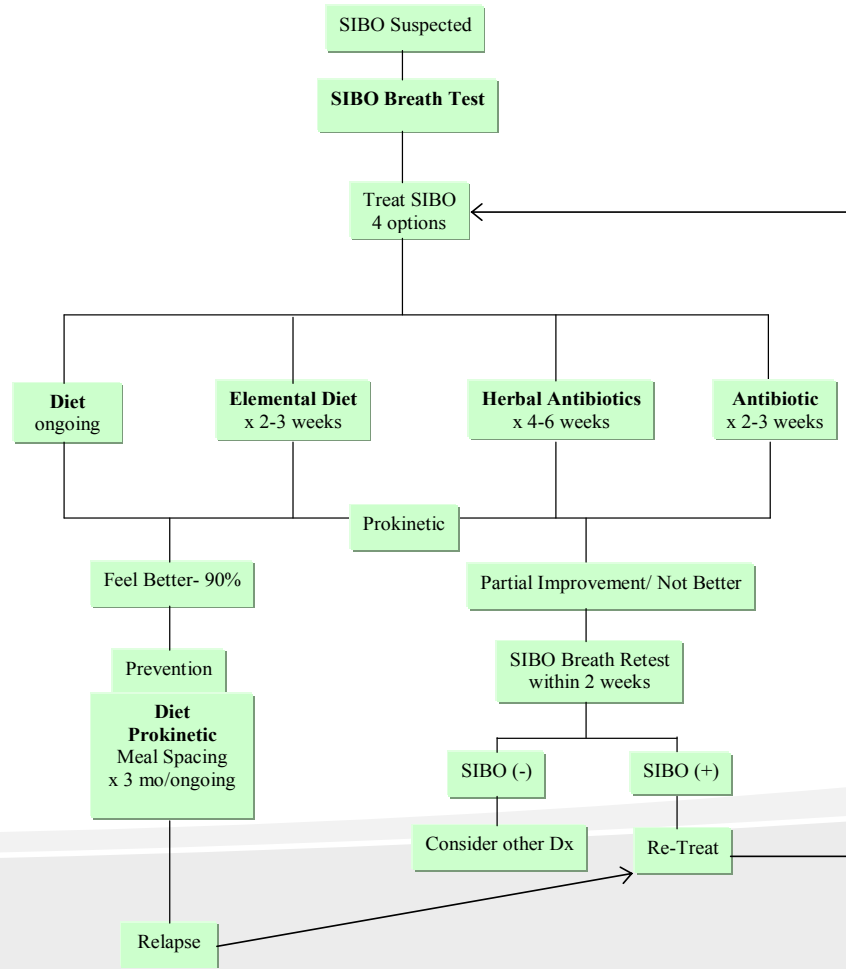


Treatment Notes

- SIBO is a chronic condition for the majority
- Estimate: 2/3 Chronic (1/3 not)
 1. Ongoing management is expected
 2. Relapse is expected (unless underlying cause is treated)
 - Common relapse timeframes: 2 mo, 2 wks, 2 days
 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

“SIBO is often a secondary disease, and unless the underlying problem is addressed and well controlled, the chance of recurrence remains high. However, in the majority of cases, elimination of the underlying cause is not possible.” *Pimentel, Rao, Rezaie '16*

SIBO Treatment Protocol
Variation of the Cedars-Sinai Protocol (Pimentel 2006)
Drs Siebecker & Sandberg-Lewis (2010)





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:
 - 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, not whole garlic which is highly 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
 - Berberine + Neem or Oregano. Neem + Oregano (occasionally).
- Methane/Constipation
 - 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: Protocol

Multi Center Study

- 2 Combination Formulas, used together
 - ‘HAbx Equivalent to Abx for SIBO’ ([Chedid '14](#))
 - 2 Protocols Used- of 2 Combo products used together
 - Oregano, Thyme, Lemongrass, Sage AND Oregon Grape, Coptis, Phellodendron, Skullcap, Ginger, Licorice, Rhubarb
 - 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)

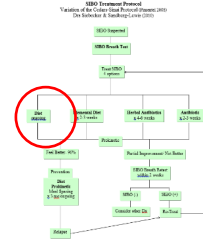


Elemental Diet Key Points

- 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




- 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 (Robillaird)

❖ All target & reduce Carbohydrates (CHO= bact 1° food)



Why Use Diet?

1. Prevention (along with prokinetic): essential
 2. Manage symptoms while treatment is in progress
 - Abx/HAbx tx can take time to achieve sx relief if gas is high
 - May not apply to ED: 1 course can give sx relief (not eating during tx)
 3. Decrease extra-intestinal sx & improve overall health
 - Esp with low carbohydrate diets: SCD, GAPS, SSFG
 - Exception: low carb causing unwelcome weight loss or hypothyroid
- My experience: Diet alone is not enough to eradicate SIBO



Choosing a SIBO Diet

- **SCD**= 1. Moderate SIBO 2. IBD/Celiac/diarrheal disease
- **GAPS**= GI issues that coexist with mood/brain disorders
 - Autism, ADD, depression, anxiety, bipolar, dyslexia, narcolepsy
- **SIBO Specific Food Guide**= 1. Severe SIBO (less foods tolerated)
2. Inadequate relief from other diets
- **LFD**= 1. Prevention once tolerances have expanded 2. Underweight patients 3. Mild SIBO (those that tolerate grains/starch/fiber/sucrose) 4. Vegetarians/Vegans
- **C-SD**= same as LFD + 5. those that can't/won't do other diets (it's the easiest to follow)



SIBO Diet Tips

- Avoid raw food/salad
- Choose low fodmap fruit and veg
- Avoid whole grains & beans. Careful with nuts/seeds.
- Starch may be tolerated: white rice, white potato, white wheat (if gluten is tolerated). Often one of these is tolerated but not another.
- Lactose Free dairy is often well tolerated
- Sugar & clover honey are often well tolerated (unless there's yeast)
- Amount matters- small amounts of individual foods may be tolerated when larger amounts aren't



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 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 gtts 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 MOA

Adapted from Scarpignato '98 with Manabe '10, Simmen '06

Table II. Prokinetic compounds: drug-receptor interaction.

Compound	D ₂ receptor antagonism	5-HT ₃ receptor antagonism	5-HT ₄ receptor agonism	Motilin receptor agonism	CCK-A receptor antagonism	M ₃ receptor agonism	Opioid receptor antagonism
Metoclopramide	yes	yes	no	no	no		
Domperidone	yes	no	no	no	no		
Cisapride	no	yes	yes	no	no		
Erythromycin	no	no	no	yes	no		
Prucalopride	no	no	yes	no	no	no	no
STW ₅	no	yes	yes	no	no	yes	yes
<i>Low Dose Naltrexone</i>	no	no	no	no	no	no	yes



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/occ at Full dose)

Key SIBO Tx Points for Success

1. Test (3 hour Lactulose Breath Test: hydrogen methane)
2. Successive Treatment Rounds needed (Abx/HAbx)
3. Methane &/or constipation cases are harder to tx
4. Different Tx needed for Methane &/or constipation
5. Die Off is common
6. Vary Tx method as needed (Abx, HAbx, ED: often 1-2 don't work)
7. Re-Test to assess results
8. Both Prokinetic & Diet for prevention
9. Customize Diet to the individual





Summary

- Average 60% of IBS is caused by SIBO
- Food Poisoning = most common cause/risk factor of SIBO
 - *IBSChek* tests for this
- Deficient Migrating Motor Complex= most cmn underlying cause
- Carb malabsorption via bacterial fermentation= 1° pathophysiology
- SIBO Diagnosis= LBT (+ history)
- Chronic/relapsing in 2/3= ongoing management
- Tx: Diet + Abx, Herbal Abx, Elemental Diet; Prokinetics



- SIBO News = Join My Newsletter

SIBOINFO.COM

Welcome page

Sent Quarterly

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