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

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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

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
    • 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
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)
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

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Interstititial Cells of Cajal Control MMC (Pokkunuri 2012)

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

http://forums.studentdoctor.net/threads/cells-responsible-for-contraction-in-stomach-intestine.1040323/
How Food Poisoning Causes SIBO (Pimentel)

Food Poisoning → Bacterial Toxin → Autoimmunity → SI Nerve Damage → Decreased MMC → SIBO / PI-IBS

C. jejuni
E. coli
Cholera
Shigella
Salmonella
C. diff
Cdt B
Vinculin
Reduced Interstitial Cells of Cajal
Stasis
(+ HMBT/IBS)√ Responds to Antibiotics

After Pimentel 2013
Slice credit: Dr Sandberg-Lewis

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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

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Small Intestine Damage

SI Bacterial Overgrowth

Bacterial Growth

GI Sx ← GAS (Hydrogen, Methane)

Fermentation of Unabsorbed Carbohydrate

Bacterial Actions

Increased Inflammatory Cytokines
Digest Brush Border
Bile Deconjugation → fat malabsorption

Damage the Brush Border

Decrease Disaccharidases
Inhibit Carb Transporters
Blunted Villi if Severe
Intestinal Hyperpermeability → systemic sx

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?

- 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**

My Opinion

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

“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)

SIBO Suspected

SIBO Breath Test

Treat SIBO 4 options

Diet ongoing

Elemental Diet x 2-3 weeks

Herbal Antibiotics x 4-6 weeks

Antibiotic x 2-3 weeks

Feel Better - 90%

Partial Improvement/ Not Better

Prevention

Diet Prokinetic
Meal Spacing x 3 mo/ongoing

Prokinetic

SIBO Breath Retest within 2 weeks

SIBO (-)

Consider other Dx

SIBO (+)

Re-Treat

Relapse
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...

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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

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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 hs
• MP 3 hs
• Ginger 1000 mg hs

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

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Prokinetic Points

• Natural Pk & LDN are not strong enough for many
  – If you want to be sure = erythromycin, prucaloopride

• 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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