



Lincoln College of Postprofessional, Graduate and Continuing Education

SIBO and Rheumatology: Does Bacterial Overgrowth Impact Autoimmunity?

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SIBO in the Setting of Rheumatology

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Overview

- Research linking microbiome to autoimmune disease
- Stress and SIBO: How prolonged emotional stress can impact motility, hypochlorhydria and SIBO
- Histamine intolerance: How histamine is often linked to SIBO, and its impact on joint pain and other inflammatory symptoms
- Two case studies: Rheumatoid Arthritis and UCTD
- Unusual cases/presentations
- The importance of modifying diet to the individual
- Other clinical observations

Autoimmunity and the Microbiome

- Increasing research implicating the oral/GI microbiome in the onset and perpetuation of autoimmunity
- Dysbiosis combined with genetic host susceptibility → immune response

References 1-8

Autoimmunity and the Microbiome

- Mechanisms Dysbiosis leading to intestinal permeability; loss of immune tolerance and triggering of cascade immune response; trafficking of activated immune cells to joints, increase in pro-inflammatory cytokines → pain/inflammation
- Contributors Diet, antibiotics and genetics
- Types Prevotella copri; SFB (segmented filamentous bacteria), lactobacillus bifidus have been shown to trigger immune response

References 1-8

SIBO and Autoimmunity

- Scant evidence on connection between SIBO and musculoskeletal autoimmune conditions
- Arthritis triggered by bacterial overgrowth resulting from jejunoileal bypass has been documented ⁽⁹⁾
- Type 1 DM, IBD
- Cross reactivity of anti-CdtB antibodies with vinculin in the ICC leading to dysmotility ⁽¹⁰⁻¹¹⁾

Literature

Few published studies/case studies linking SIBO to inflammatory conditions:

- Rosacea (12)
- PMR (13)
- Hepatic encephalopathy and NAFLD* (14)
- Parkinson's Disease (15)
- Type 1 Diabetes* (16)
- Fibromyalgia (17)
- IBD (18)
- Pancreatitis (19)
- Prostatitis (20)

Most common observed SIBO causes in Rheum.

- **Hypochlorhydria and dysmotility brought on by **stress**
- **PI-IBS r/t food poisoning
- **Adhesions or structural issues
- Hypochlorhydria r/t PPI use
- Dysmotility r/t opioids, other pain/sleep meds
- Dysbiosis r/t extensive antibiotics
- Scleroderma
- Ehlers-Danlos Syndrome
- Hashimoto's Thyroiditis

Stress as SIBO trigger

- Studies have shown emotional stress leads to alteration of gut motility, increase in mast cell activation and changes in the microbiome in the gut ⁽²¹⁻²²⁾
- Reduced HCl → reduced enzyme production ⁽²³⁾
- Dysmotility + hypochlorhydria = increase bacterial concentration in SI. ⁽²³⁾
- Increase in food sensitivity, intestinal inflammation, permeability ^(24, 25)

Stress as SIBO trigger

- SIBO leads to intestinal inflammation, may lead to intestinal permeability ⁽²⁴⁾
- Translocation of certain types of bacteria and endotoxin ⁽²⁵⁾ has been shown to trigger TLR's and cytokine involvement
- Does SIBO initiate autoimmune response as dysbiotic state can?

Stress and Mast Cells

- Stress encourages mast cell stimulation via binding of CRH to mast cell CRH receptor sites
- CRH binding → increase in VEGF production (associated with arthritis and psoriasis)
- Mast cells line the GI tract and strategically located throughout body
- Mast cells secrete histamine and other cytokines
- Increase in histamines/VEGF can lead to both digestive and systemic inflammation

Reference 34-35

Histamine Intolerance and SIBO

- Histamine intolerance in Rheumatology patients with SIBO very common
- Increase intestinal inflammation leads to deficit in DAO enzymes → increase in circulating histamine ^(28,29)
- Excessive histamine production can lead to multiple symptoms including diarrhea, swelling in joints, nerve pain and other symptoms ^(28, 29)
- Impact GI *and* systemic inflammation
- Not everyone who has SIBO has histamine intolerance. Those who do may have prevalence of histamine producing bacteria as their overgrowth

The histamine connection

- Some species of bacteria have been shown to increase histamine production: (*L. casei* and *L. bulgaricus*) ²⁶
- Others have shown to decrease histamines: *L. rhamnosus*, *B. infantis*, *L. plantarum* ²⁷

Assessing for Histamines

Common Symptoms

- Year round allergy symptoms (rhinitis, itchy eyes)
- Worsening of symptoms with stress
- Urticaria
- Anxiety
- Insomnia
- Diarrhea/gas/bloat
- Episodes of tachycardia
- Perimenopause: Increase in hot flashes, insomnia, painful menses
- Worsening of pain with seasonal change
- Hypotension
- Headache/migraine
- Numbness/tingling
- Joint pain/swelling

Impact of histamines in Rheumatoid Arthritis

- Via H1-H4 receptors, histamines impact numerous systems ⁽³⁰⁾
- Research linking histamine (H4 receptors) to RA. ⁽³¹⁾
- Studies have shown increase in H4R in synovial fluid cells. ⁽³²⁾
- H4 antagonist has reduced arthritic pain via reduction IL-17 in vitro. ⁽³³⁾

Histamines in the Diet

- Aged, fermented foods especially high in histamine
- Wine, cider, beer
- Aged meats/cheese/vinegar/pickled foods
- Tomatoes, eggplant, spicy peppers, spinach, pumpkin
- Citrus fruit, banana, raspberries
- Most nuts
- Chocolate, more



Case Study 1: SIBO and Rheumatoid Arthritis

- 36 yo female, highly stressed life, mom/FT job
- RA dx, seroneg. Onset post partum.
- Joint pain in thumb, wrist, shoulder; flares random lasting 3-4 day in duration
- GI: Daily diarrhea (watery, urgent). 11 year history of “sensitive stomach” after travel to Panama. GI workups normal. GI issues intensified post partum.
- HCQ reduced the intensity of pain. Declined Humira.
- Sx worsen with menstruation, stress.
- Chronic allergy sx including itchy eyes, rhinitis

Case Study

4-Week follow-up

- After one day on low histamine diet, significant reduction in joint pain
- Diarrhea reduced in intensity, now soft stools mixed with episodes of diarrhea
- Introduced both histamines and wheat into the diet and found reactivity to both, so has kept out/low
- About 80% improvement in symptoms with joint flares less often, less intense. Still present.

First Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	2	<2				
20 min	3	<2				
40 min	5	<2				
60 min	37	<2				
80 min	94	<2				
100 min	68	<2				
120 min	92	<2				
140 min	113	<2				
160 min	139	<2				
180 min	119	<2				

CS1: Treatment

- Rifaximin: 550 mg tid x 14d
- f/u tx: Erythromycin 250 mg qhs
- Omit fodmaps, starches, limit histamines – yikes!

CS1: 2 wk follow up

- Complete cessation of joint pain, diarrhea during the antibiotics
- 2-3 days post completion, return of diarrhea.
- Rifaximin 550 mg tid x 14 d
- Stools firm, with only occasional diarrhea, joint pain abated
- Ordered follow up HBT

Second Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	2	<2	2	3		
20 min	3	<2	4	3		
40 min	5	<2	4	3		
60 min	37	<2	10	4		
80 min	94	<2	27	7		
100 min	68	<2	27	8		
120 min	92	<2	30	7		
140 min	113	<2	40	9		
160 min	139	<2	58	11		
180 min	119	<2	74	10		

Continued Treatment

- Tried number of herbals and dosages, but patient intolerant to most.
- Settled on 180 mg allicin bid and 60 mg oil of oregano bid x 3 months
- Erythromycin 250 mg ¼ cap qhs ongoing. Takes breaks for efficacy.

Third Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	2	<2	2	3	7	7
20 min	3	<2	4	3	2	3
40 min	5	<2	4	3	3	4
60 min	37	<2	10	4	3	3
80 min	94	<2	27	7	8	8
100 min	68	<2	27	8	31	13
120 min	92	<2	30	7	44	15
140 min	113	<2	40	9	39	16
160 min	139	<2	58	11	56	17
180 min	119	<2	74	10	50	16

Current Status

- Patient continues to do well with no joint pain or diarrhea
- Dc'd HCQ without return of joint pain
- Slight joint flares with menstruation, which she keeps under control with reduced dietary histamines
- Back on gf grains and FODMAP's without issue; uses histamine diet prn
- Self-managed currently

Case Study 2

SIBO and UCTD

- 32 yo mom to two children under 5; FT high level manager at high stress tech company. Self described "Type A."
- Hx: Respiratory infection x 5 weeks, took multiple courses of antibiotics to treat
- Development of hives, asthma, severe seasonal allergies, tingling/itching/rash on arms/neck.
- Musculoskeletal: Severe joint pain in multiple joints; numbness/tingling in extremities
- GI: Slight gas, otherwise stable. Gas increases with pbx. No history of food poisoning, abdominal surgeries, et al
- FMLA from high stress job.
- RF<13; IgE < 20; SED <20

CS #2: Treatment

- Dx: UCTD and AI urticaria
- Rx: Hydroxychloroquine: After 8 weeks, no perceptible benefit.
- Low histamine diet

CS#2: 2 Week Follow Up

- "70 – 80% improvement" in all symptoms, but still wax and wane
- Assessed areas of life that could be stimulating histamine response (hormones, stress, environment, bacteria).
- Assessed gastrointestinal tract *again*. Slight gas? Probiotic intolerance?
- Order HBT to rule out bacterial overgrowth

CS2: First Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	55	3				
20 min	51	2				
40 min	70	3				
60 min	85	4				
80 min	67	2				
100 min	88	4				
120 min	75	4				
140 min	85	3				
160 min	75	3				
180 min	83	3				

CS#2: Treatment

- Treatment Rifaximin 550 mg tid x 14d x 2 rounds with two week break in between
- Erythromycin (1/4 250 mg qhs)
- Diet modification: *Reduce* FODMAPs, small amount of gf grains, limit histamines

Case Study #2: Post antibiotics...

- Rash cleared, occasional tingling in extremities, joint pain completely abated while on the antibiotics
- Significant improvement in all areas, still having some tingling, rash, but only having occasional episodes
- Tolerance to dietary histamines increasing
- Breath test results returned

CS2: Second Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	55	3	8	3		
20 min	51	2	14	3		
40 min	70	3	19	5		
60 min	85	4	24	4		
80 min	67	2	22	4		
100 min	88	4	16	3		
120 min	75	4	11	3		
140 min	85	3	17	4		
160 min	75	3	17	4		
180 min	83	3	18	4		

CS#2: Continued treatment

- 450 mg allicin tid
- Zinc carnosine/glutamine bid
- Removing either of these led to an increase in joint pain and itching, so maintained both for three months, slowly reducing dosages over time, as tol
- HCl/enzymes q meal (stress)
- Erythromycin x 3 months, then dc'd. IBS Chek negative.
- Plaquenil remained
- Symptoms normalize

CS#2: Current Status

- Low dose garlic maintained @ 180 mg bid
- Added in pbx (good tolerance now)
- Dc'd HCQ without issue
- Able to return histamines, grains and FODMAPs to the diet
- Keeps a gluten and dairy free diet
- Back at work without issue

CS2: Third Hydrogen Breath Test

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	55	3	8	3	4	2
20 min	51	2	14	3	5	2
40 min	70	3	19	5	7	3
60 min	85	4	24	4	8	3
80 min	67	2	22	4	8	3
100 min	88	4	16	3	6	3
120 min	75	4	11	3	6	6
140 min	85	3	17	4	10	5
160 min	75	3	17	4	4	1
180 min	83	3	18	4	6	3

Lupus, elevated ALT/AST
difficulty losing weight
GI stable

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	4	13				
20 min	7	14				
40 min	10	15				
60 min	19	16				
80 min	37	23				
100 min	43	24				
120 min	52	28				
140 min	59	34				
160 min	42	29				
180 min	50	31				

Sx: Glittery eyes, joint pain, fatigue, hair loss
GI: *Past* h/o gastroenteritis, diarrhea; *Stable* currently

Time	#1 H2 ppm	CH4	#2 H2 ppm	CH4 ppm	#3 H2 ppm	CH4 ppm
Baseline	3	2				
20 min	3	1				
40 min	5	3				
60 min	10	5				
80 min	17	7				
100 min	30	10				
120 min	48	11				
140 min	56	13				
160 min	29	10				
180 min	14	7				

Observations

- Treating SIBO in the autoimmune patient doesn't always result in elimination of joint pain
- Chicken/egg?
- If treating the SIBO resolves GI symptoms but doesn't help pain, have to look further
- Ongoing emotional stressors, other food sensitivities, histamines, hormones, etc
- Treat dysbiosis important
- Post tx, baseline diet needs to be reassessed

Dietary Modifications

- Dietary change alone can bring a significant reduction in all symptoms r/t SIBO including GI, joint pain/swelling, migraine, sinus, skin, et al
- Low FODMAP/no grain diet most common rec
- Low histamine can also be beneficial when symptoms not resolving with diet/tx alone

Dietary Modifications

- Difficult to design one diet for an entire population
- The low fodmap/no starch diet will benefit most
- Meat/animal protein based diets can be inflammatory to some
- Low whole grain/high pro diet may cause constipation
- Need to target the diet to the patient depending on their symptoms and needs
- Need to focus them in on plants as much as possible. Easy to fall back on eggs/bacon.

Dietary Modifications

- For low fodmap diets, focus the patient on what plants they can eat and give them ideas that support (smoothies with plant based protein powder, vegetable based soups, fresh veg juices, nut/seed butters, make sure they eat limited high fodmap like broccoli, avocado)
- Encourage grass fed and/or organic meats, if affordable
- Encourage wild caught, omega 3-rich fish
- Cook with anti inflammatory spices such as turmeric, ginger, cilantro, parsley
- Herbal teas with ginger, turmeric, cinnamon

Diet: Support

- Functional RDN or licensed functional nutritionist who specializes in SIBO is important part of treatment plan
- If unavailable or cost prohibitive, have your list of resources to support
- Remember the difficulty of following these kinds of diets (social, psychological, family)
- Assess for h/o food addiction
- Work with the patient to determine what is possible for them to follow. Middle ground may be more sustainable than doctrine.

And so...

- Microbiome is known to be associated with autoimmune disease
- Joint pain, weight gain and other inflammatory symptoms beyond the GI tract may be connected to SIBO
- Consider histamine intolerance/stress connection in your SIBO treatment
- GI symptoms may not always be present
- Diet can be modified to the patient's needs and tolerance. If you don't have time to counsel patient, refer to RDN or functional nutritionist who specializes
- Research is needed in this area!

Thank you!!

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