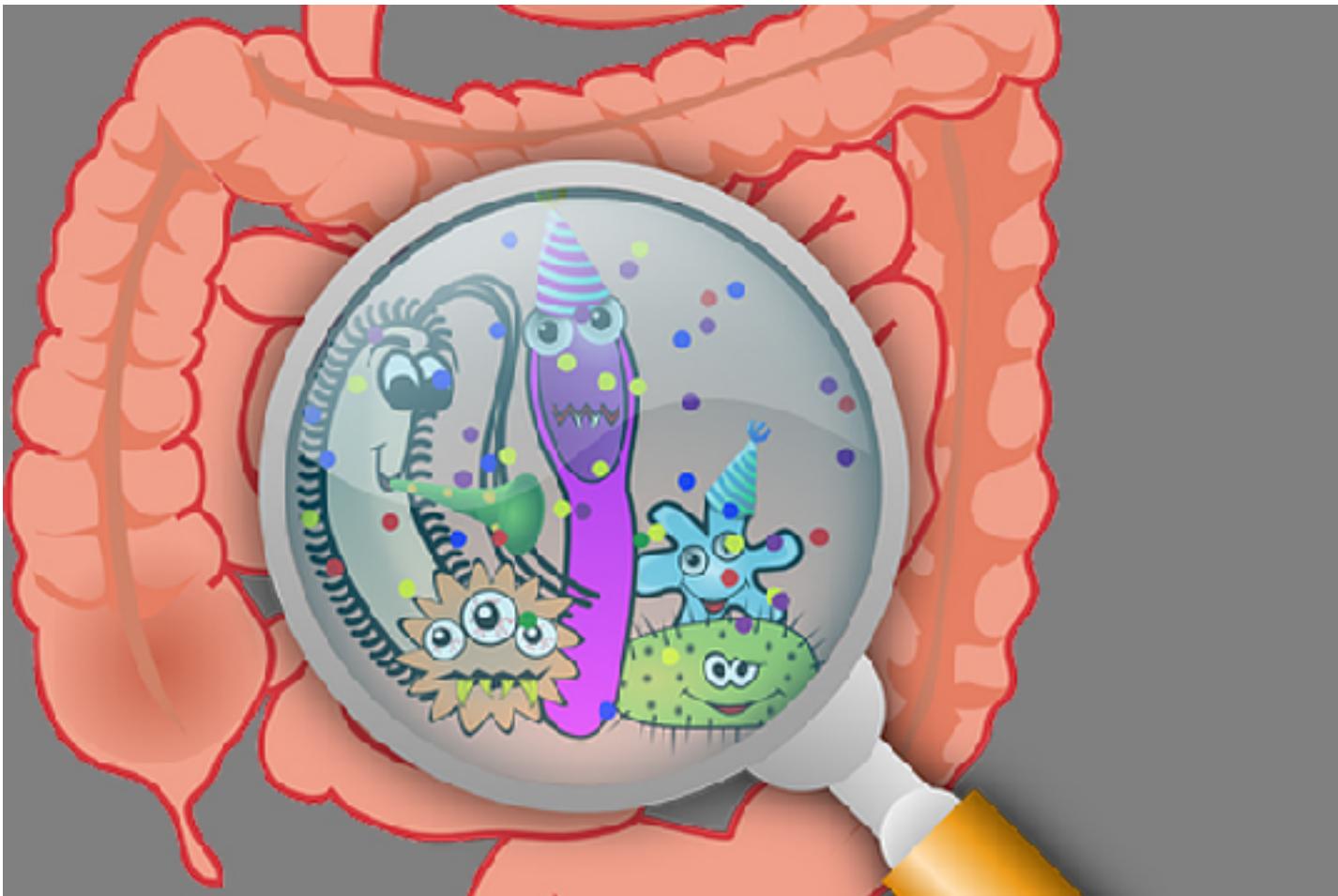


# Treating SIBO: The Missing Link

Eric Balcavage DC, CNS, CFMP, BCIM



# What is SIBO?



CHRONIC CONDITION  
RECOVERY CENTER

Bob's a special kind of friend.  
The kind that drives you crazy.

# What about Bob?



TOUCHSTONE PICTURES Produced by TOUCHWOOD PACIFIC PARTNERS | Written by LAURA ZISKIN Directed by FRANK Oz Starring BILL MURRAY, RICHARD DREYFUS,  
"WHAT ABOUT BOB?" JULIE HAGETTY, CHARLIE KASSEL, RAY MILES GOODMAN, STANLEY BERNARD WILLIAMS, JEFF HONEYMAN, CHATIS, E.G., Music by LES DILEY Cinematography by MICHAEL BILLHAUS

**PG** PARENTAL GUIDANCE SUGGESTED MPAA Rating  
SOME MATERIAL MAY NOT BE APPROPRIATE FOR CHILDREN

DOLBY STEREO™  
A SELECTED THROES

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## Small intestinal bacterial overgrowth recurrence after antibiotic therapy.

Lauritano EC<sup>1</sup>, Gabrielli M, Scarpellin E, Lupascu A, Novi M, Sottile S, Vitale G, Cesario V, Serricchio M, Cammarota G, Gastbarrini G, Gasbarrini A.

### Author information

#### Abstract

**OBJECTIVES:** Current treatment for small intestinal bacterial overgrowth (SIBO) is based on courses of broad-spectrum antibiotics. No data concerning SIBO recurrence are available. The aims of the present study were to investigate SIBO recurrence as assessed by glucose breath test (GBT) after antibiotic treatment and conditions associated to SIBO recurrence.

**METHODS:** Eighty consecutive patients affected by SIBO and decontaminated by rifaximin (1,200 mg per day for 1 wk) were enrolled. Diagnosis of SIBO was based on GBT. GBT was reassessed at 3, 6, and 9 months after evidence of GBT normalization. GBT positivity, recurrence, predisposing conditions, and gastrointestinal symptoms were evaluated.

**RESULTS:** Ten (10/80, 12.6%), 22 (22/80, 27.5%), and 35 (35/80, 43.7%) patients showed positivity to GBT at 3, 6, and 9 months after successful antibiotic treatment, respectively. At multivariate analysis, older age (OR 1.09, 95% CI 1.02-1.16), history of appendectomy (OR 5.9, 95% CI 1.45-24.19), and chronic use of proton pump inhibitors (PPIs) (OR 3.52, 95% CI 1.07-11.64) were significantly associated to GBT positivity recurrence. All gastrointestinal symptoms significantly increased at 3, 6, and 9 months in patients with evidence of GBT positivity recurrence.

**CONCLUSIONS:** GBT positivity recurrence rate was high after antibiotic treatment. Older age, history of appendectomy, and chronic use of PPIs were associated with GBT positivity recurrence. Patients with evidence of GBT positivity recurrence showed gastrointestinal symptoms relapse thus suggesting SIBO recurrence.

PMID: 18802996

[PubMed - indexed for MEDLINE]



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# SIBO Symptoms, Causes & Risk Factors, and Associated Complications

SYMPTOMS	CAUSES & RISK FACTORS	ASSOCIATED COMPLICATIONS
Nausea	Diabetes	Malnutrition
Bloating	Diverticulosis	Vitamin B12 deficiency
Vomiting	Structural defect in small intestine	Anemia
Diarrhea	Injury	Poor absorption of fat
Malnutrition	Fistula	Osteoporosis
Weight Loss	Intestinal lymphoma	Kidney stones
Joint Pain	Scleroderma	Damage to intestinal lining
Fatigue	Celiac disease	
Rashes	Certain Rx medications	
Acne	Rosacea	
Eczema	Aging	
Asthma		
Depression		
Rosacea		

# Current Assessment For SIBO

- Hydrogen / Methane Breath Test
- Endoscopic Aspiration
- OAT Test – Dysbiosis Markers
- Comprehensive Stool Panels
- History and Symptoms

# Current Treatment

## Medical Model

- Rifaximin
- Erythromycin
- Tegaserod

## Functional Model

- Diet changes:
  - AI Diet
  - SCD Diet
  - Low FODMAPS
- Antimicrobials
- GI Repair formulas
- Pre/Probiotics

## Small Intestinal Bacterial Overgrowth

Prevalence, Clinical Features, Current and Developing Diagnostic Tests, and Treatment

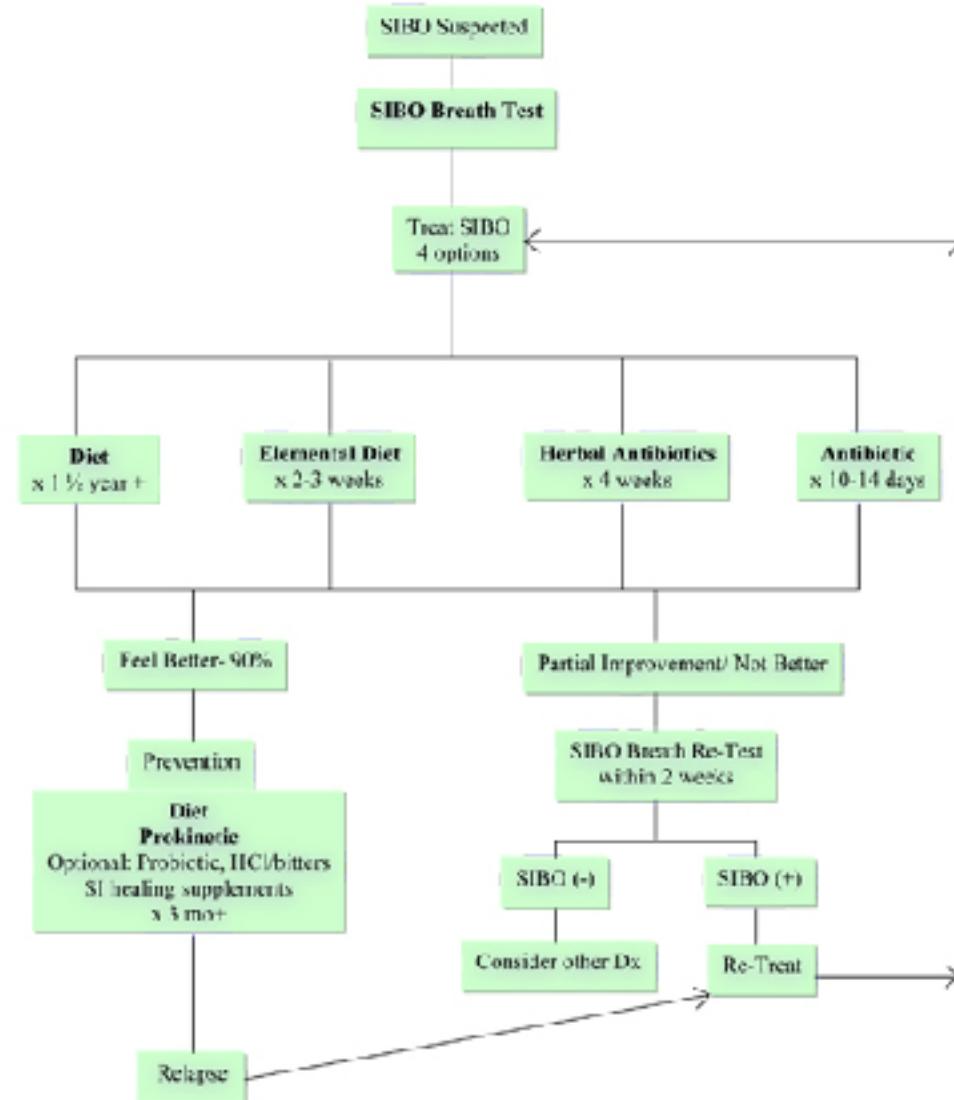
E. Grace; C. Shaw; K. Whelan; H. J. N. Andreyev

Disclosures

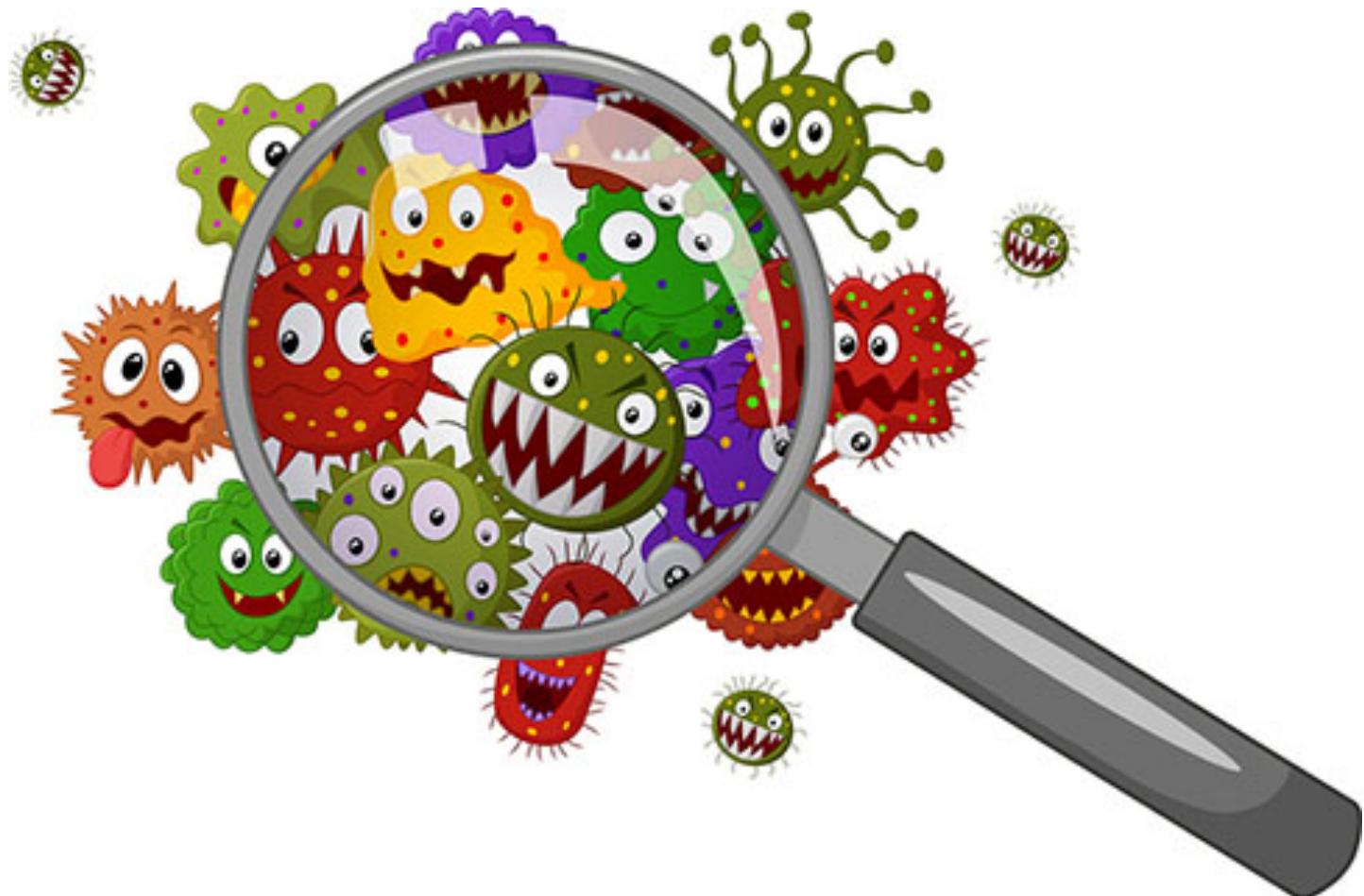
Aliment Pharmacol Ther. 2013;38(7):674-688.

- “Khoshini et al. concluded that no gold standard diagnostic test for SIBO exists. All of the commonly used methods of diagnosing SIBO have inherent limitations”
- “there is no breath test specifically validated for the diagnosis of SIBO.”
- “lack of consensus how to define an abnormal breath test”
- “no standardized approach towards the type, dose or duration of the antibiotics and reported clinical response rates range from 35% to 100%.”
- “As SIBO is often a manifestation of other GI disorders, there is as yet no typical patient.”
- Part of the difficulty in establishing a confident diagnosis of SIBO in patients with common GI symptoms is the lack of a standardized investigative tool.”

**SIBO Treatment Protocol**  
Variation of the Cedars-Sinai Protocol (Pimentel 2005)  
Drs Siebecker & Sandberg-Lewis (2010)



# What Causes SIBO?



# Dysmotility of GI Tract

- Diseases and disorders
- Medications
- Surgery/Obstructions
- Stress
- Disrupted sleep
- Constant grazing
- Hypothyroidism
- Post infection AI to Vinculin

# Loss of Antimicrobial Action

- Antibiotic exposure
- Medications – PPI's, antihistamines
- Hypothyroidism
- Compromised stomach acid
- **Compromised bile physiology**
- Compromised pancreatic enzymes
- Compromised SIgA

# Progression of SIBO

- Reduced antimicrobial capacity &/or motility
- Increased fermentation of sugars
- Bacterial deconjugation / inc secondary BA
- Enterocyte injury / loss of brush borders
- Fermentation of B12 by anaerobes
- Immune activation by bacteria
- Bacterial translocation
- Nutrient malabsorption



# The Missing Link - Bile

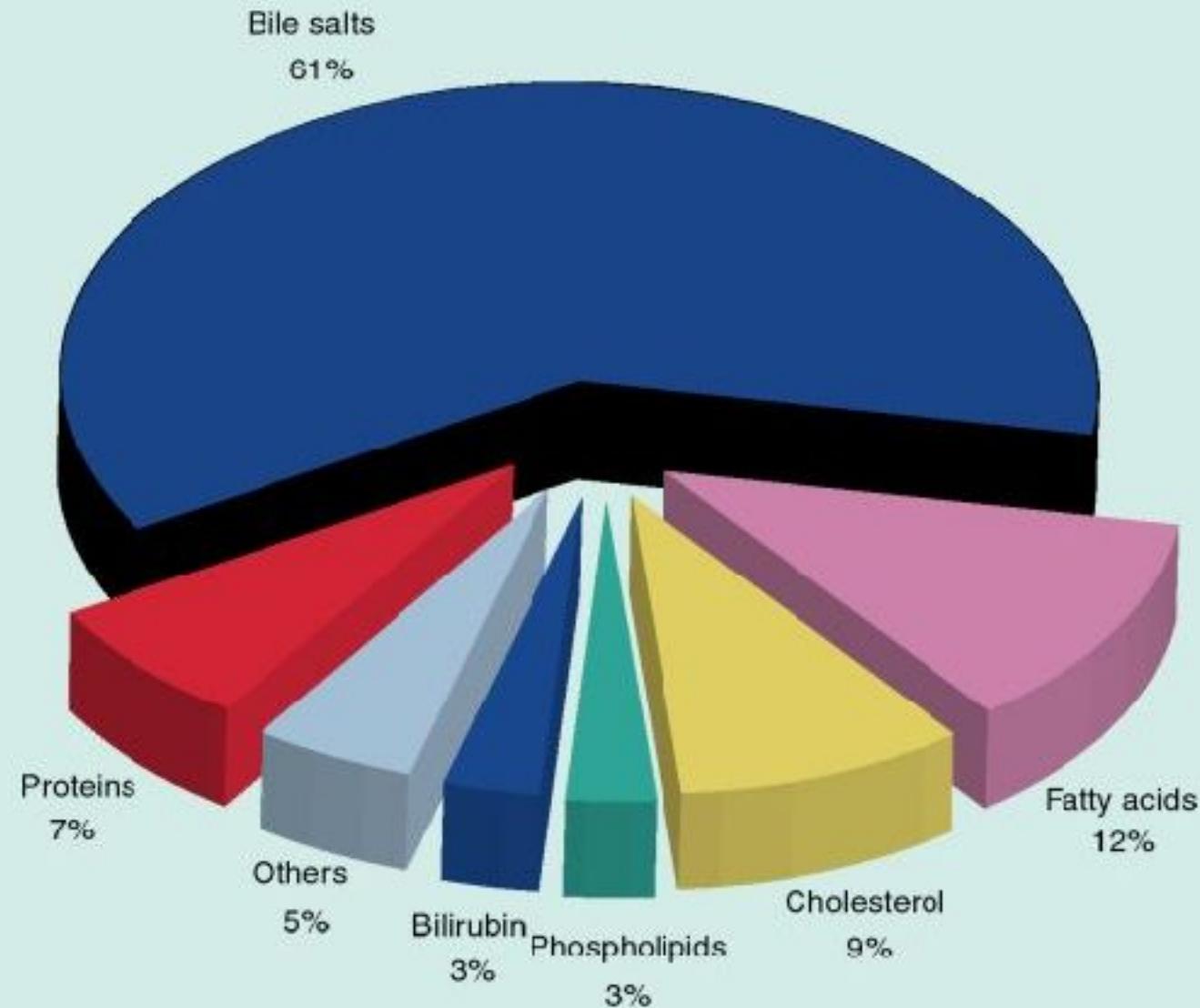
Primary Functions:

- Excretory Function
- Digestive Function
- Endocrine Signaling
- Antimicrobial

# Bile Acids and the Gut Microbiome

The host and microbiome appear to regulate bile acid pool size. The host produces a large, conjugated hydrophilic bile acid pool, maintained through positive-feedback antagonism of FXR in intestine and liver. Members of the microbiome utilize bile acids and their conjugates resulting in agonism of FXR in intestine and liver resulting in a smaller, unconjugated hydrophobic bile acid pool. Hydrophilicity of the bile acid pool is associated with disease states. Reduced bile acid levels in the gut are associated with bacterial overgrowth and inflammation. Diet, antibiotic therapy, and disease states affect the balance of the microbiome-bile acid pool.





# What Disrupts Bile Physiology



# What Disrupts Bile Physiology

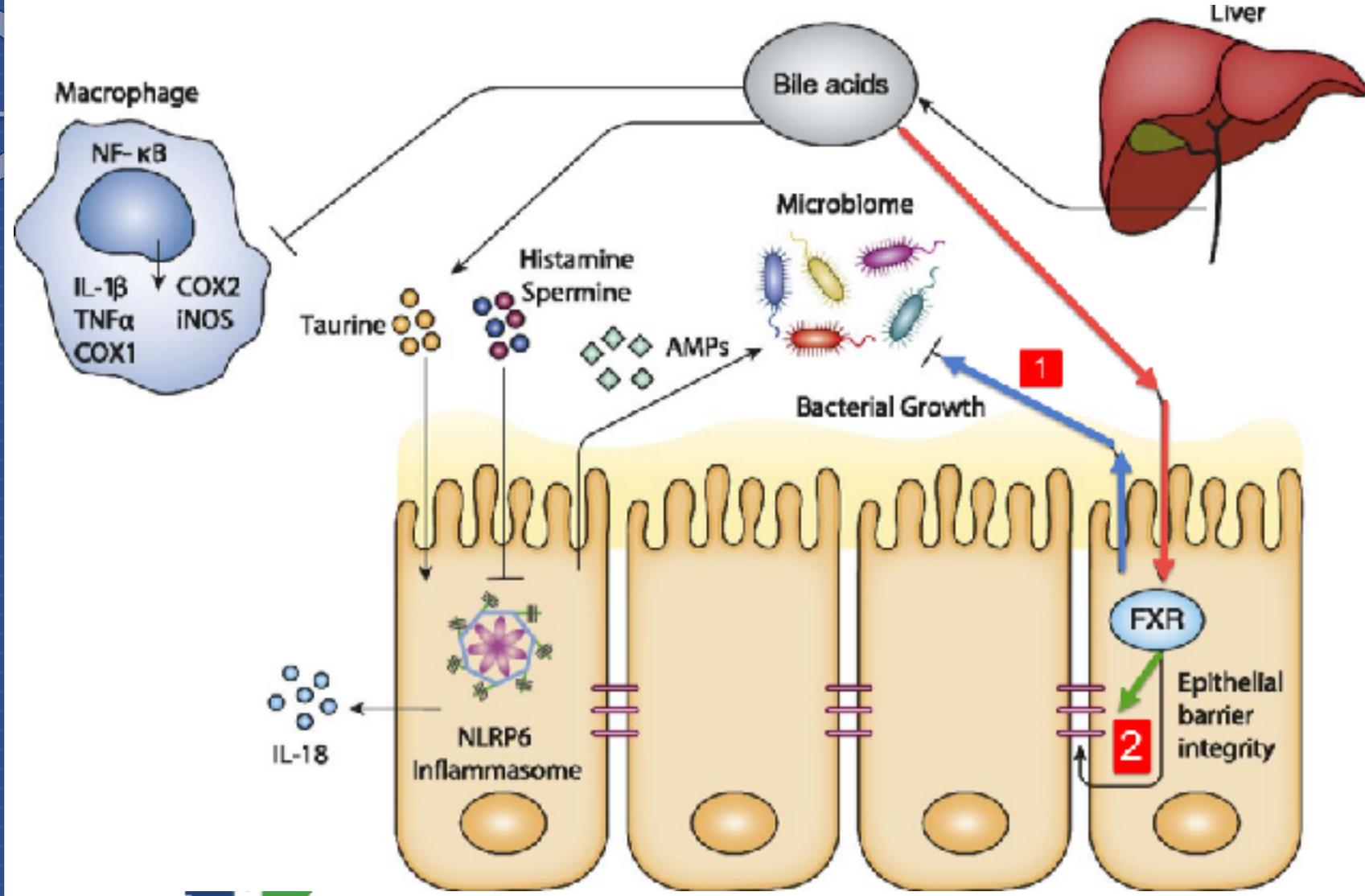
- Low Stomach Acid Production
- Methylation problems
- Sulfation problems
- Estrogen imbalances
- Vitamin A and D deficiencies
- Insulin resistance and diabetes
- Dysbiosis
- Thyroid hormone dysregulation
- Inflammation/cytokines
- Medications

# Direct Antimicrobial Effect



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# Indirect Antimicrobial Effect

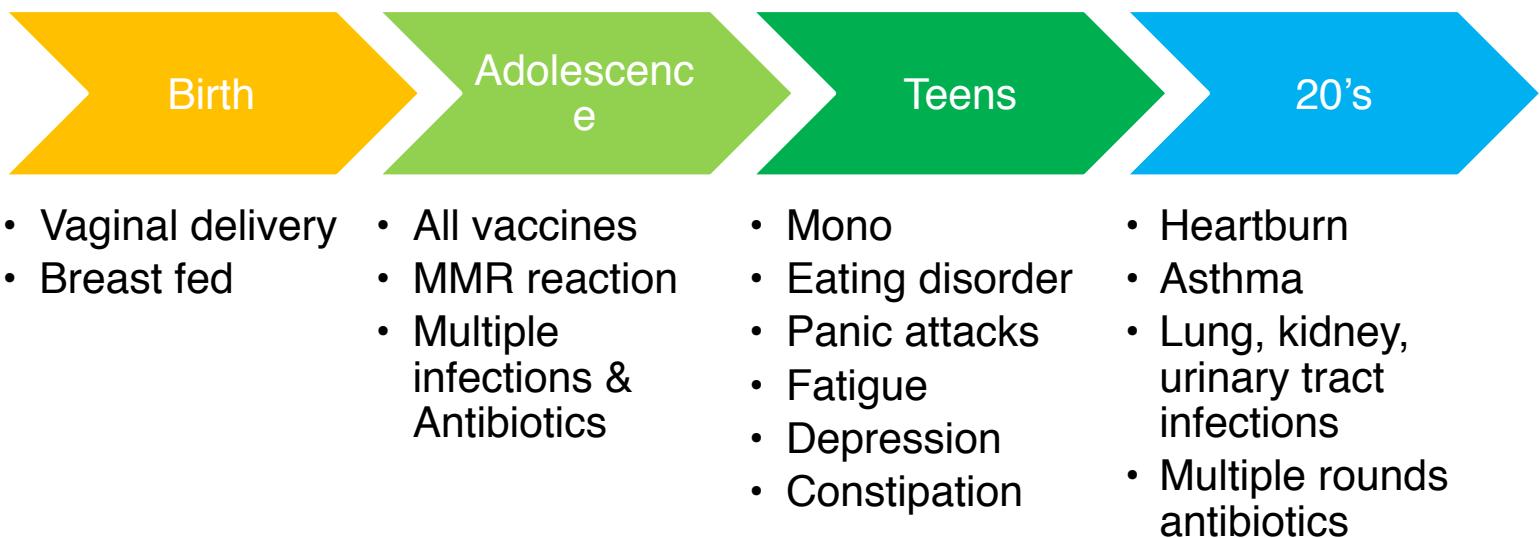


# Case:

- 42 yof
- Presented to office for help with methylation and genetics

SYMPTOMS	Consult
SWOLLEN PAINFUL GLANDS	8
NECK STIFFNESS	8
SWEATS /CHILLS	7
FATIGUE	7
RED EX TOLERANCE	7
IRRITABILITY	7
VIBRATION FEELING	7
MS TWITCHING	6
CONSTIPATION	5
BLOATING	5
BODY ACHES	4
NUMBNESS	3
BRAIN FOG	3
THROAT SWELLING	3

# Timeline



# Timeline



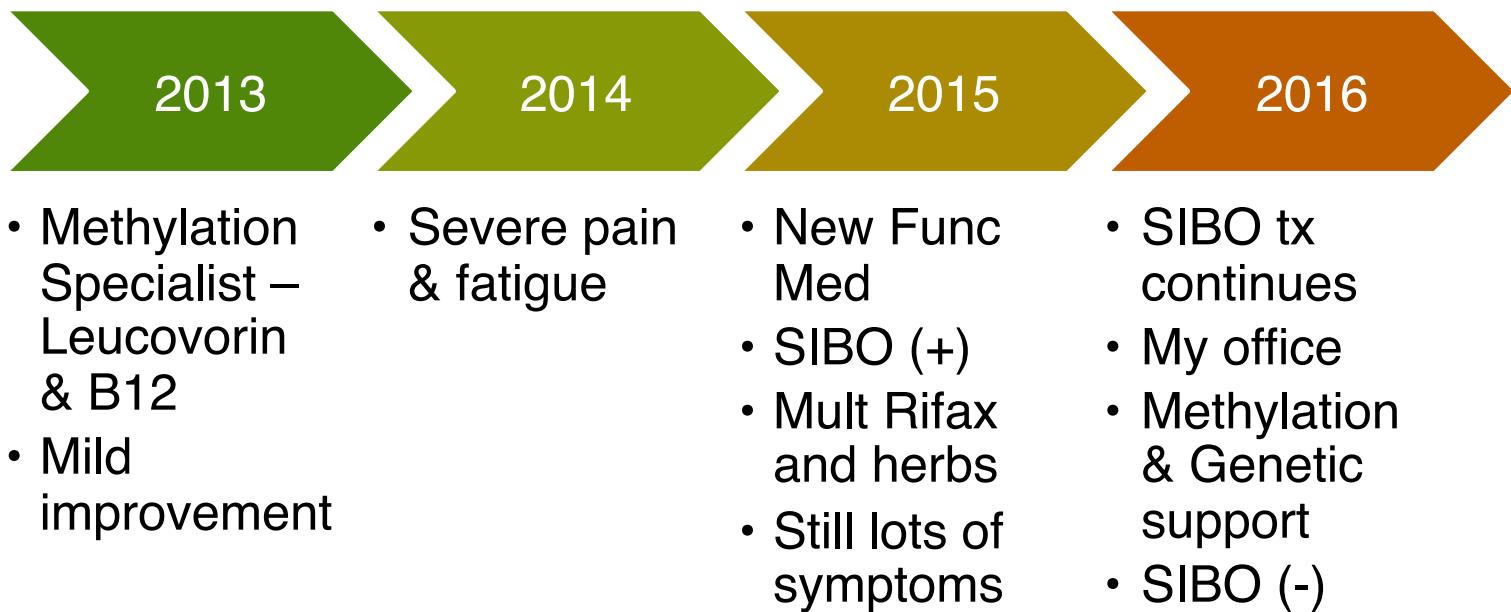
- |   |  |   |   |
|---|--|---|---|
| <ul style="list-style-type: none"><li>• Chronic UTIs &amp; antibiotic use</li><li>• Cont. of other symptoms</li></ul> | <ul style="list-style-type: none"><li>• Mold exposure</li><li>• Asthma</li><li>• Allergies</li><li>• Multiple infections</li><li>• Pneumonia</li><li>• Antibiotics &amp;<br/>Prednison e</li></ul> | <ul style="list-style-type: none"><li>• Severe heartburn</li><li>• Bloating</li><li>• Scopes (-)</li><li>• PPIs</li></ul> | <ul style="list-style-type: none"><li>• Func med</li><li>• Dx; LGS, multiple food sensitivities</li><li>• 4R Protocol</li></ul> |
|---|--|---|---|

# Timeline



- Multiple strep & antibiotics
- Pneumonia & 2 rounds of antibiotics
- Neuro symptoms
- Lyme / Babesia – antibiotics
- Mold exposure
- 6 months antibiotics for recurrent Lyme
- Severe allergies, throat swelling – Benadryl
- Candida – herbals
- MCS

# Timeline



# Case: 46 YOF

1. Nutrient 950 with vit K- 6 pills a day
2. Optimal mag 2 pills 2x a day
3. Vit c 2000mg a day (sodium ascorbate)
4. Liver Nutrients 2pills 2x a day
5. Leucovorin 5mg 2x a day
6. Methylation Complete 1 pill 2x a day
7. PQQ 20 mg a day
8. Adenosylcobalamin 3000mc a day
9. Beyond Balance mc-bfm-p enzymes 4 2x a day
10. Prescript Assist probiotic 2 pills a day
11. Neem Synergy 2 pills 2x a day (biopureuse)
12. Berberine complex 2pills 3x a day  
(intergrative therapeutics)
13. Natural d-hist 2 pills a day (ortho molecular)
14. Zeobind (biopure) 1 scoop a day
15. GI revive- 6 pills 2x a day
16. Rifaximin 550 mg 2x a day
17. Low dose naltrexone 4mg at night

SYMPTOMS	Consult
SWOLLEN PAINFUL GLANDS	8
NECK STIFFNESS	8
SWEATS /CHILLS	7
FATIGUE	7
RED EX TOLERANCE	7
IRRITABILITY	7
VIBRATION FEELING	7
MS TWITCHING	6
CONSTIPATION	5
BLOATING	5
BODY ACHES	4
NUMBNESS	3
BRAIN FOG	3
THROAT SWELLING	3

# Methylation Panel

## DERIVATES

S-Adenosylmethionine (RBC)

**223** µmol/dl

221 - 256

S-Adenosylhomocysteine (RBC)

**54.6** µmol/dl

38.0 - 49.0

## FOLIC ACID DERIVATES

5-CH3-THF

**8.6** nmol/l

8.4 - 72.6

10-Formyl-THF

**5.8** nmol/l

1.5 - 8.2

5-Formyl-THF

**1.90** nmol/l

1.20 - 11.70

THF

**0.58** nmol/l

0.60 - 6.80

Folic Acid

**8.9** nmol/l

8.9 - 24.6

Folinic Acid (WB)

**7.1** nmol/l

9.0 - 35.5

Active folate (RBC)

**332** nmol/l

400 - 1500

## NUCLEOSIDE

Adenosine

**26.0**  $10^{-8}$  M

16.8 - 21.4

## AMINOACIDS IN PLASMA

Glutathione (oxidised)

**0.56** µmol/L

0.16 - 0.50

Glutathione (reduced)

**3.3** µmol/L

3.8 - 5.5

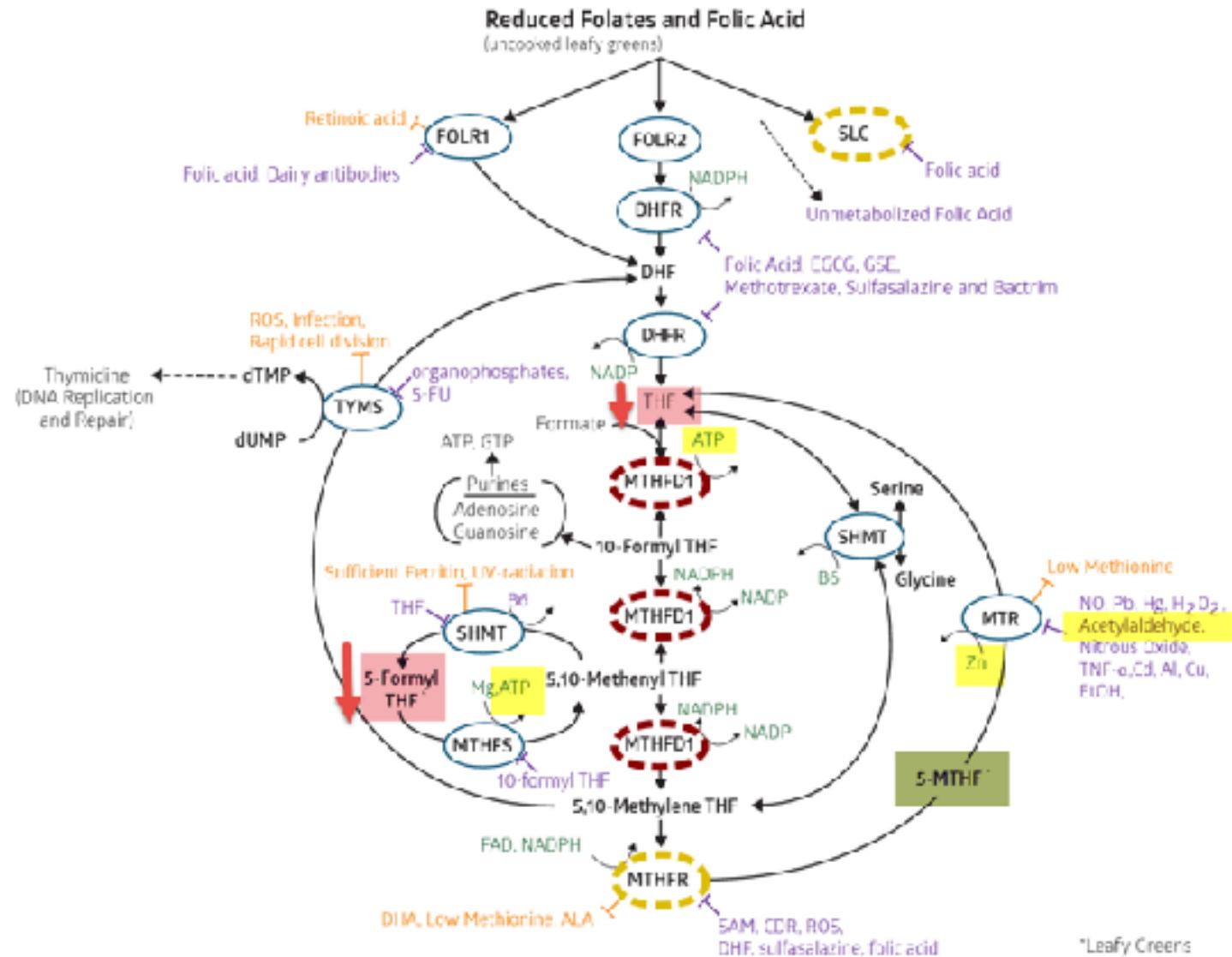


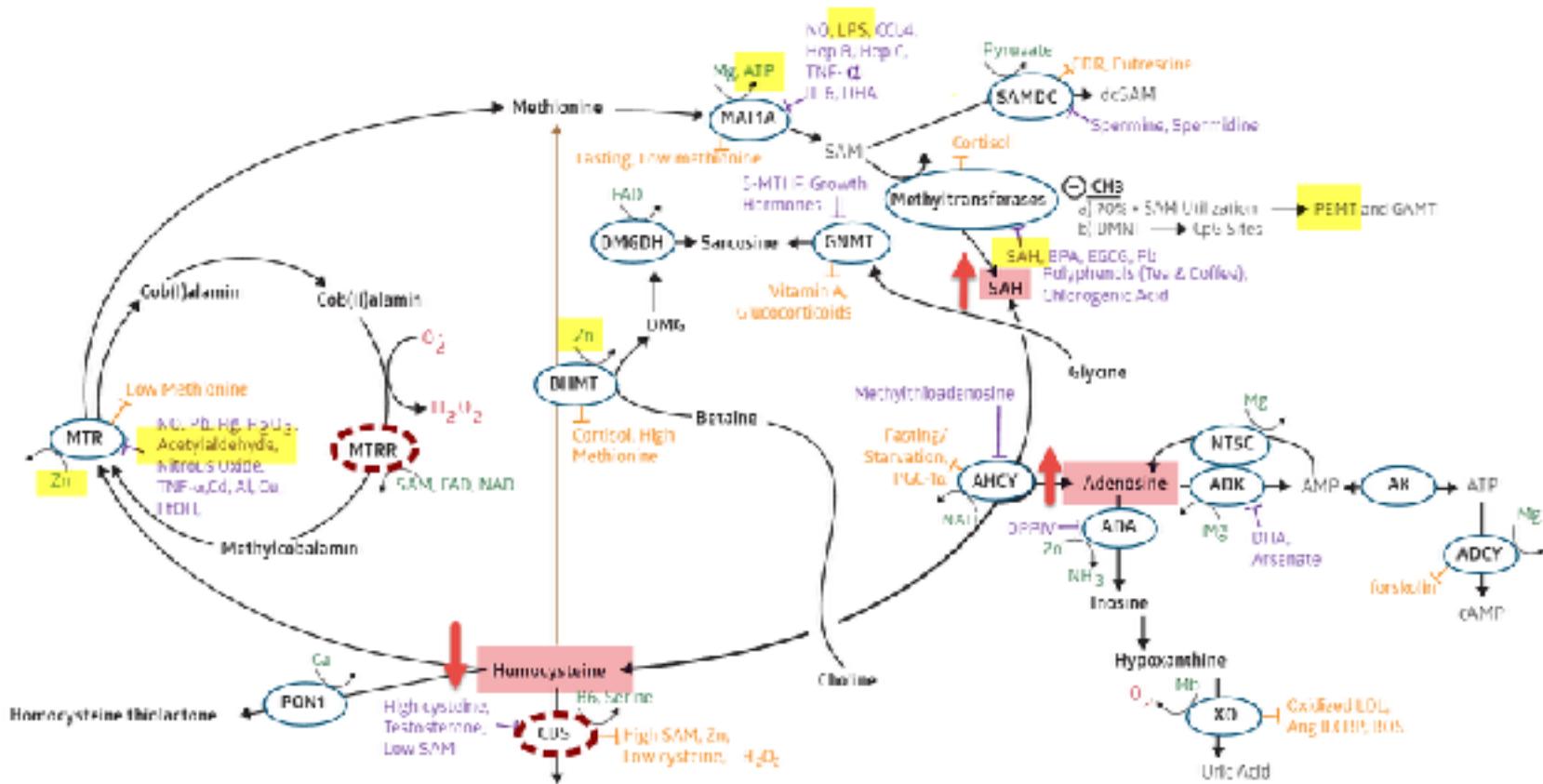
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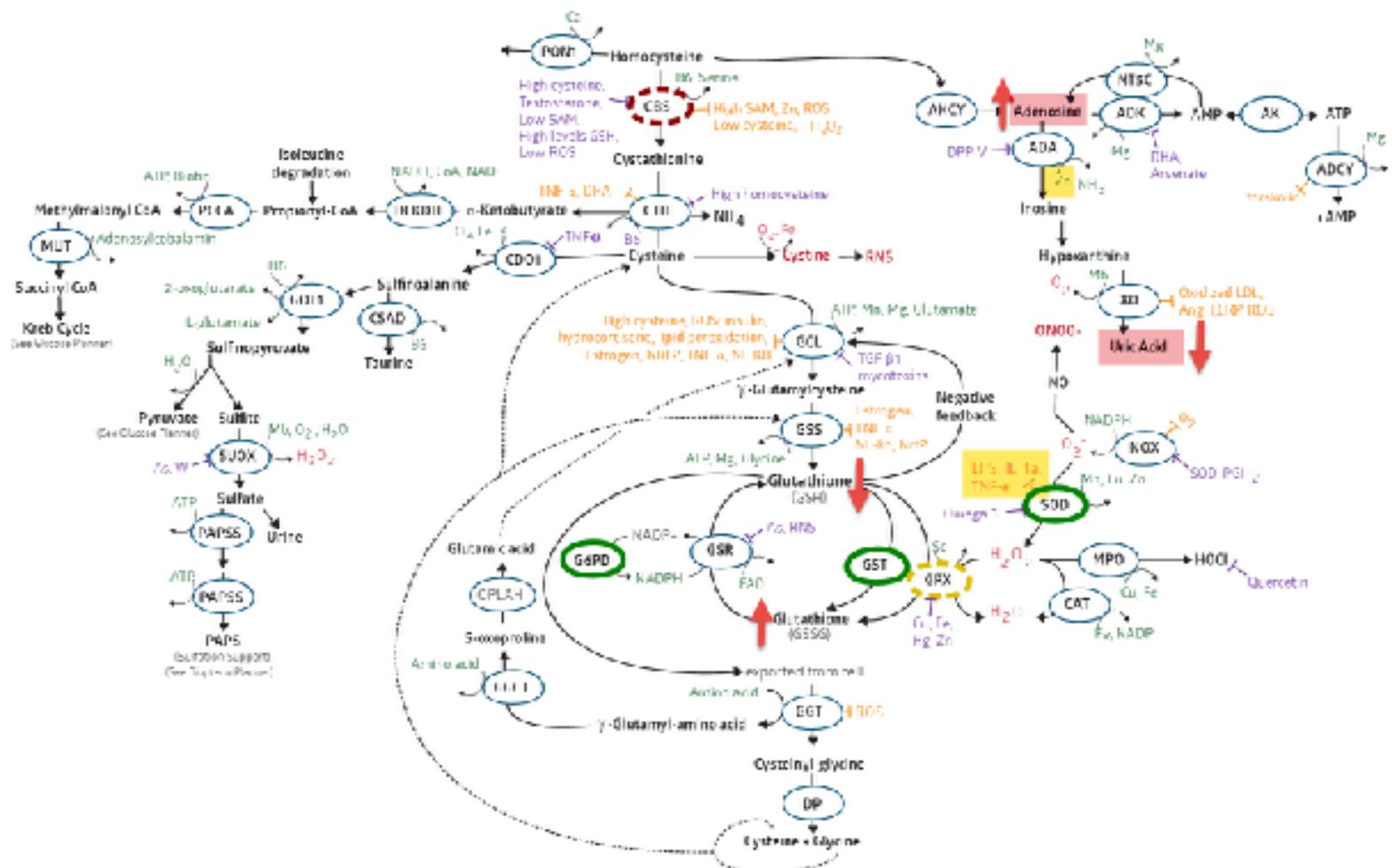
Pathogens			
Bacterial Pathogens	Result	Expected	
Campylobacter	Negative	Neg	
<i>C. difficile</i> Toxin A	Negative	Neg	
<i>C. difficile</i> Toxin B	Negative	Neg	
<i>E. coli</i> O157	Negative	Neg	
Enterotoxigenic <i>E. coli</i> LT	Negative	Neg	
Enterotoxigenic <i>E. coli</i> ST	Negative	Neg	
Shiga-like Toxin <i>E. coli</i> stx1	Negative	Neg	
Shiga-like Toxin <i>E. coli</i> stx2	Negative	Neg	
<i>Salmonella</i>	Negative	Neg	
<i>Shigella</i>	Negative	Neg	
<i>Vibrio cholerae</i>	Negative	Neg	
<i>Versinia enterocytica</i>	Negative	Neg	
Parasitic Pathogens			
<i>Giardia lamblia</i>	Negative	Neg	
<i>Entamoeba histolytica</i>	Negative	Neg	
<i>Schistosoma</i>	Negative	Neg	
Viral Pathogens			
Adenovirus 40	Negative	Neg	
Adenovirus 41	Negative	Neg	
Norovirus GI	Negative	Neg	
Norovirus GII	Negative	Neg	
Rhinovirus A	Negative	Neg	
<i>H. pylori</i>			
Helicobacter pylori	<dl	<7.0 E3	
Virulence Factor, cagA	Negative	Neg	
Virulence Factor, vacA	Negative	Neg	
Fecal Microbial flora			
<i>Bifidobacter</i>	2.1 E30	>8.9 E9	
<i>Enterococcus</i>	6.7 E8	1.2 E4 - 8.1 E9	
<i>E. coli</i>	4.8 E7	1.0 E4 - 8.8 E7	
<i>Lactobacillus</i>	1.6 E7	1.0 E6 - 5.3 E9	
Opportunistic Bacteria			
Potential Autoimmunity Triggers	Result	Range	
<i>Listeria</i> spp.	<dl	<1.0 E4	
<i>Klebsiella pneumoniae</i>	2.3 E2	<7.2 E3	
<i>Proteus</i> spp.	<dl	<6.2 E3	
<i>Proteus mirabilis</i>	5.6 E2	<1.0 E3	
<i>Yersinia enterocolitica</i> (from pg 1)	Negative	Neg	
Additional Dysbiotic/Overgrowth Bacteria			
<i>Morganella morganii</i>	<dl	<1.0 E3	
<i>Pseudomonas</i> spp.	<dl	<2.5 E3	
<i>Pseudomonas aeruginosa</i>	<dl	<1.0 E3	
<i>Stenotrophomonas</i> spp.	<dl	<1.0 E4	
<i>Streptococcus</i> spp.	<dl	<1.0 E3	
Parasites			
<i>Blastocystis hominis</i>	Negative	Neg	
<i>Dientamoeba fragilis</i>	Negative	Neg	
<i>Endolimax nana</i>	Negative	Neg	
<i>Entamoeba coli</i>	Negative	Neg	
<i>Ciliates</i> mesnili	Negative	Neg	
<i>Chilosphaera caveronensis</i>	Negative	Neg	
<i>Pentastichomonas hominis</i>	Negative	Neg	
Fungi/Yeast			
<i>Candida albicans</i>	<dl	<5.0 E3	
<i>Candida</i> spp.	Low	Neg	
<i>Geotrichum</i> spp.	Negative	Neg	
<i>Microsporidia</i> spp.	Negative	Neg	
<i>Trichosporon</i> spp.	Negative	Neg	
Additional Tests			
SgA	573	510-2040 uM/ml	
Anti-d IgG in SgA	2.6	0.0-6.4 ug/ml	
Elastase 1	69	Low	>200 ug/ml
Lactoferrin	0.6		0.0-7.2 ug/ml
Occult blood	Negative	Neg	

# Metabolic Panel

- Hypochlorhydria
- Low Uric Acid (Molybdenum def)
- Low Alk phos (zinc def)
- Functionally low iron / ferritin
- Func low WBC
- Func low Trig (45), low normal cholesterol
- Func low: T4 (5.5), T3 (90), fT3 (2.7)
- T3/rT3 ratio: 7 (<10 = cellular hypoT)
- Func low Vitamin D
- Low HCY (5)
- ALT, AST, GGT - normal







# Clinical Considerations

1. Does she really need more methylation support?
2. Am I going to provide supplement recommendations based on the genetic report?
3. Does she have dysbiosis and possibly still have SIBO?

# SIBO Recurrence

- GI MAP: Klebsiella, Proteus, Candida, Low pancreatic enzymes
- Metabolic Panel: hypochlorhydria, low trigs, low iron/ferritin, cellular hypoT
- Symptoms: bloating, constipation, joint pain, fatigue, histamine response
- Missing in the previous support was acid and bile support

# 5 Month Support Process

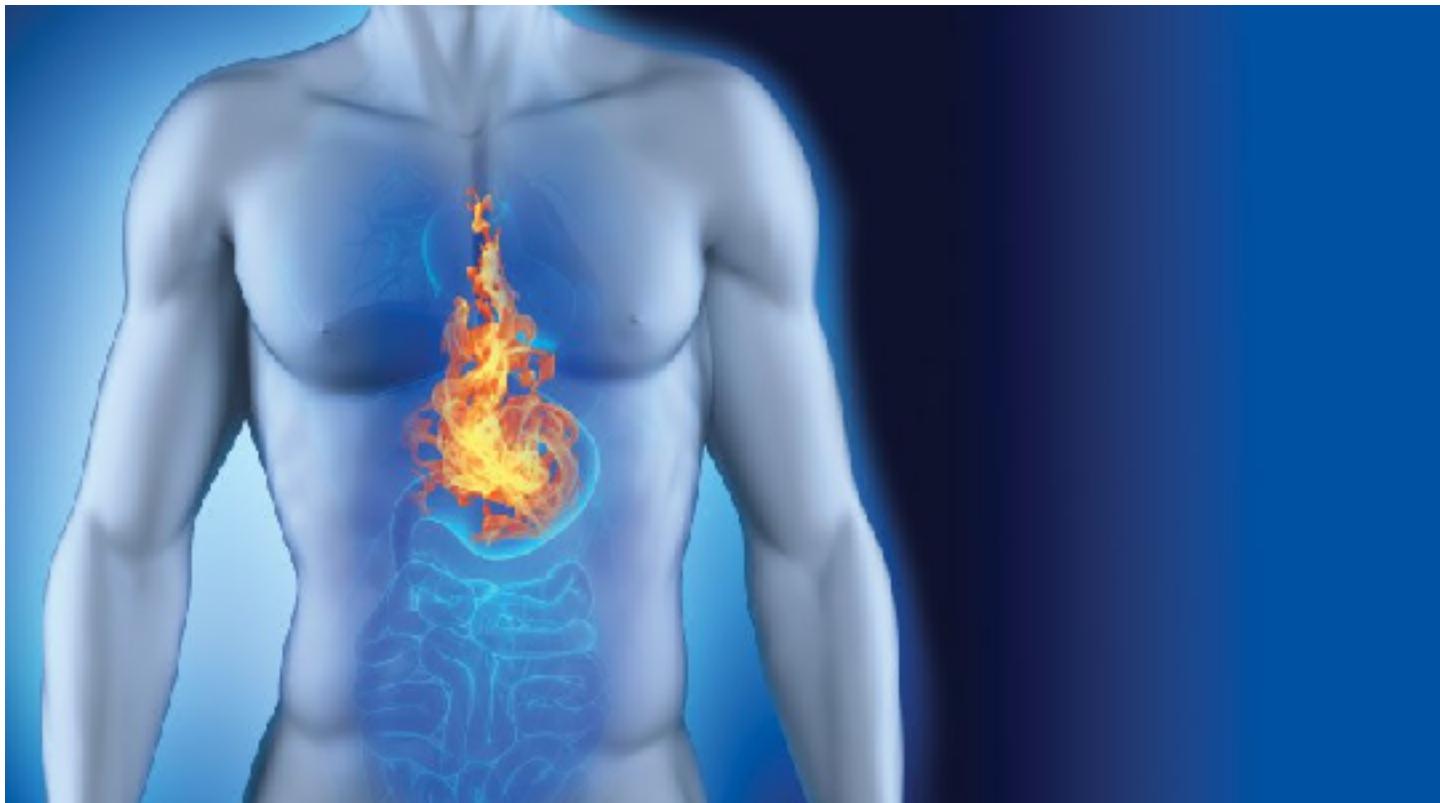
- Reduce current supplement load
- Address dysbiosis with support products:
  - Seaprose – biofilm
  - Glutamine based GI powder
  - Anti-microbial support for bacteria and yeast
  - Probiotics
  - HCL support – Betaine HCl
  - Digestive enzymes
  - Bile support: Ox bile, glycine
  - 5 HTP

# SIDEWAYS

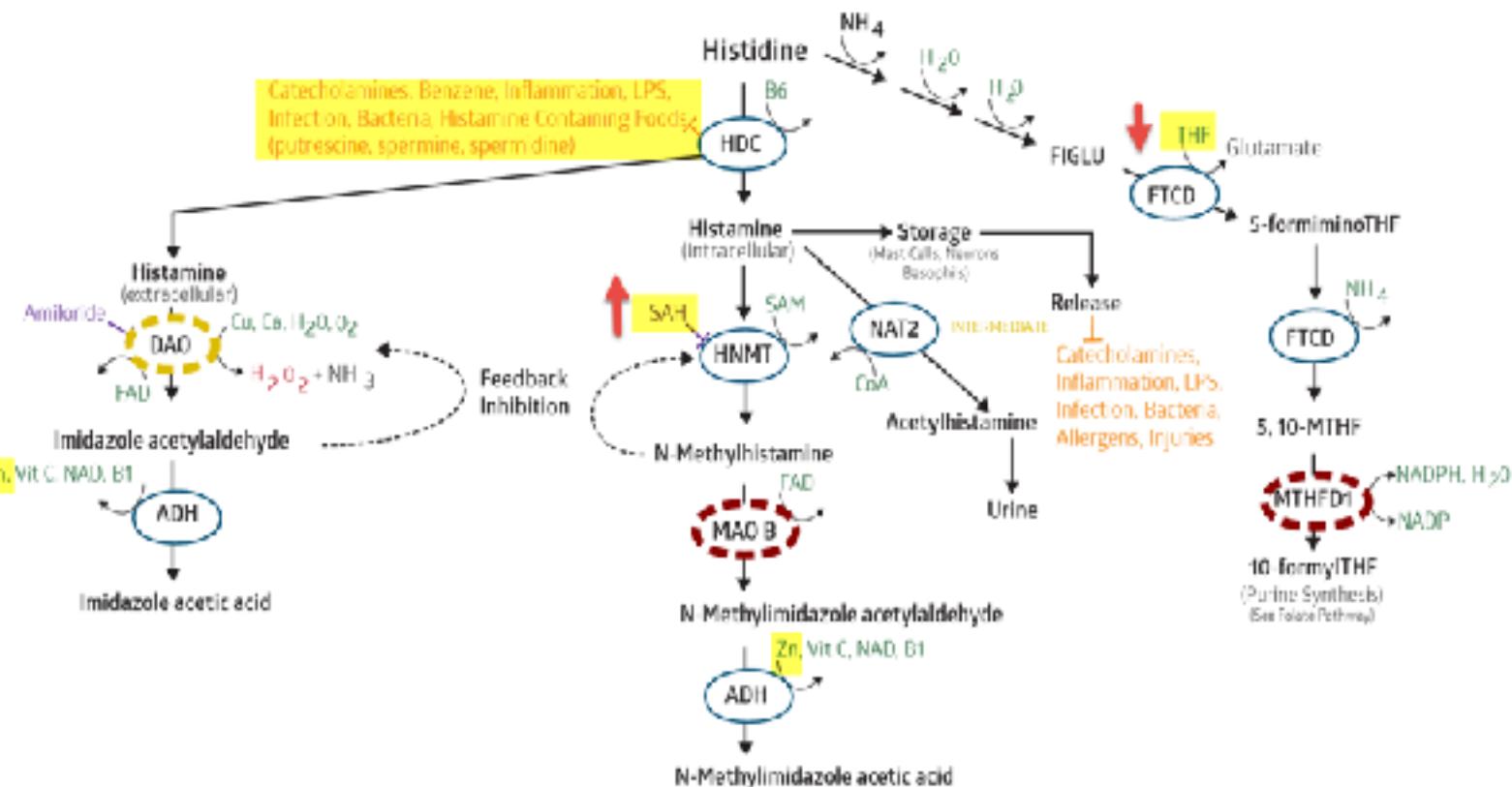


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# Aggravation of Reflux Symptoms



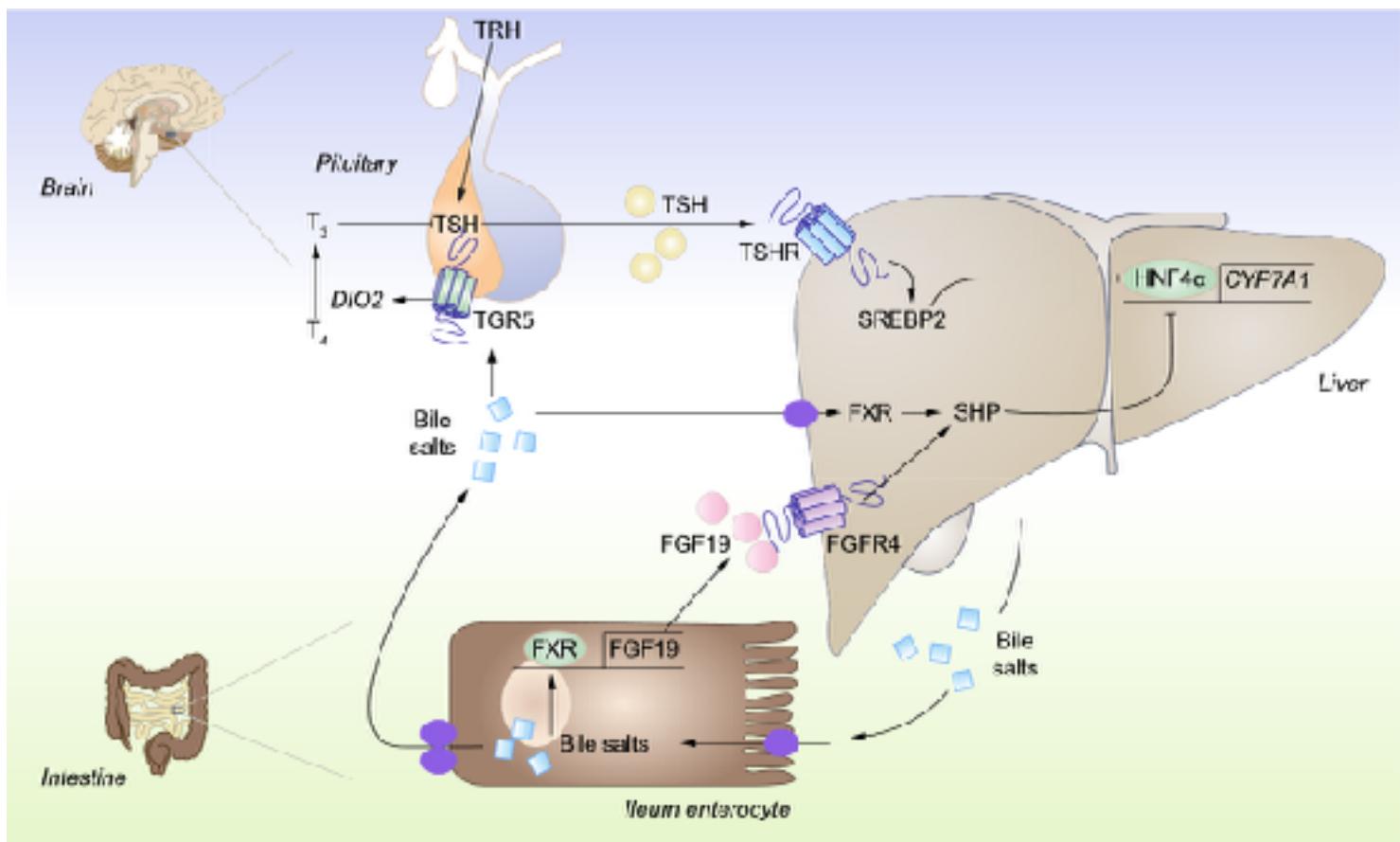
# Aggravation of Asthma Symptoms



# Hypothyroid Symptoms



# Bile Blues and Hypothyroid Symptoms

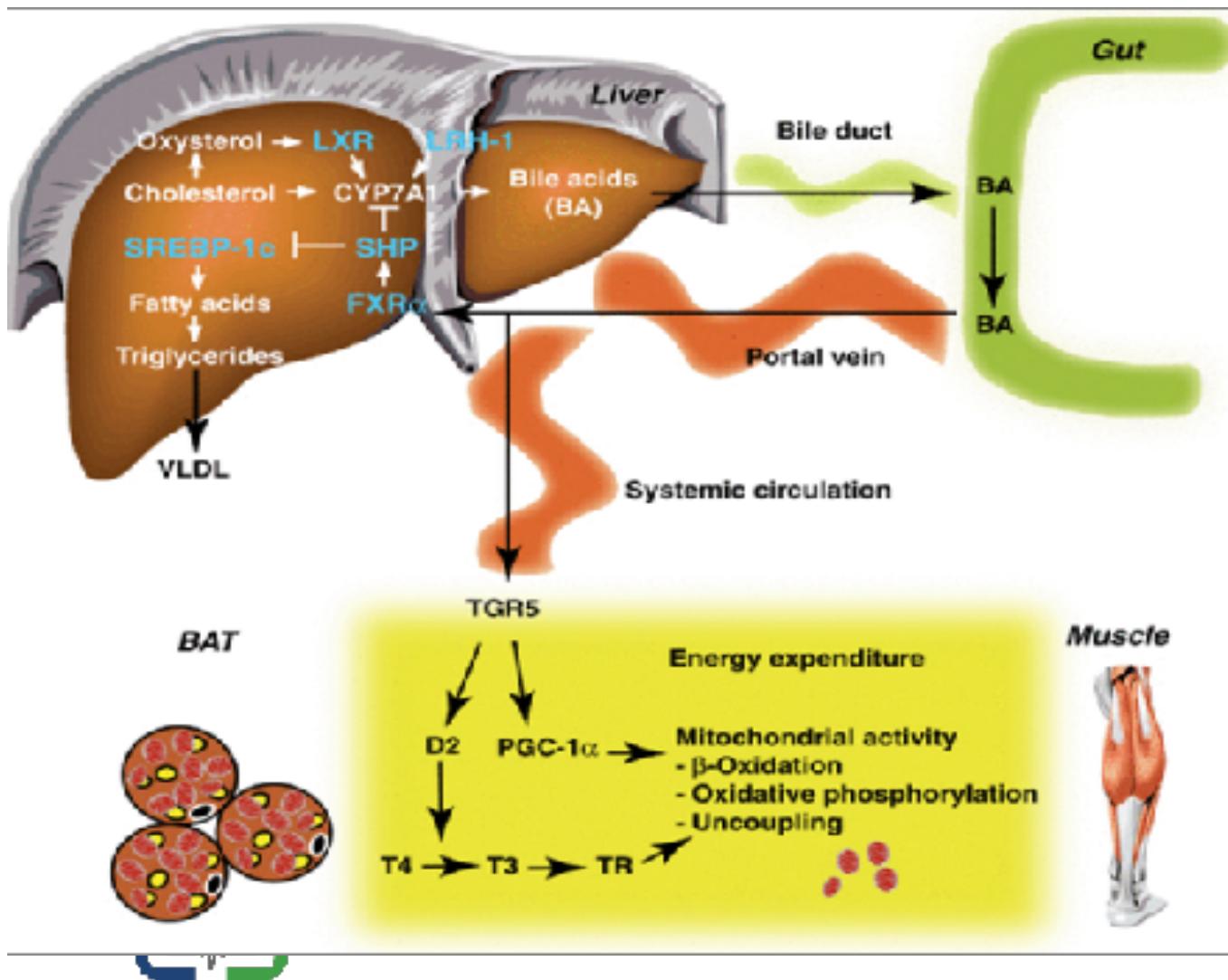


[https://www.researchgate.net/publication/272185376\\_Pituitary\\_TSH\\_controls\\_bile\\_salt\\_synthesis](https://www.researchgate.net/publication/272185376_Pituitary_TSH_controls_bile_salt_synthesis)



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# Muscle Twitching



# Sweats & Chills

## Plasma Bile Acids Are Associated with Energy Expenditure and Thyroid Function in Humans

### Conclusions:

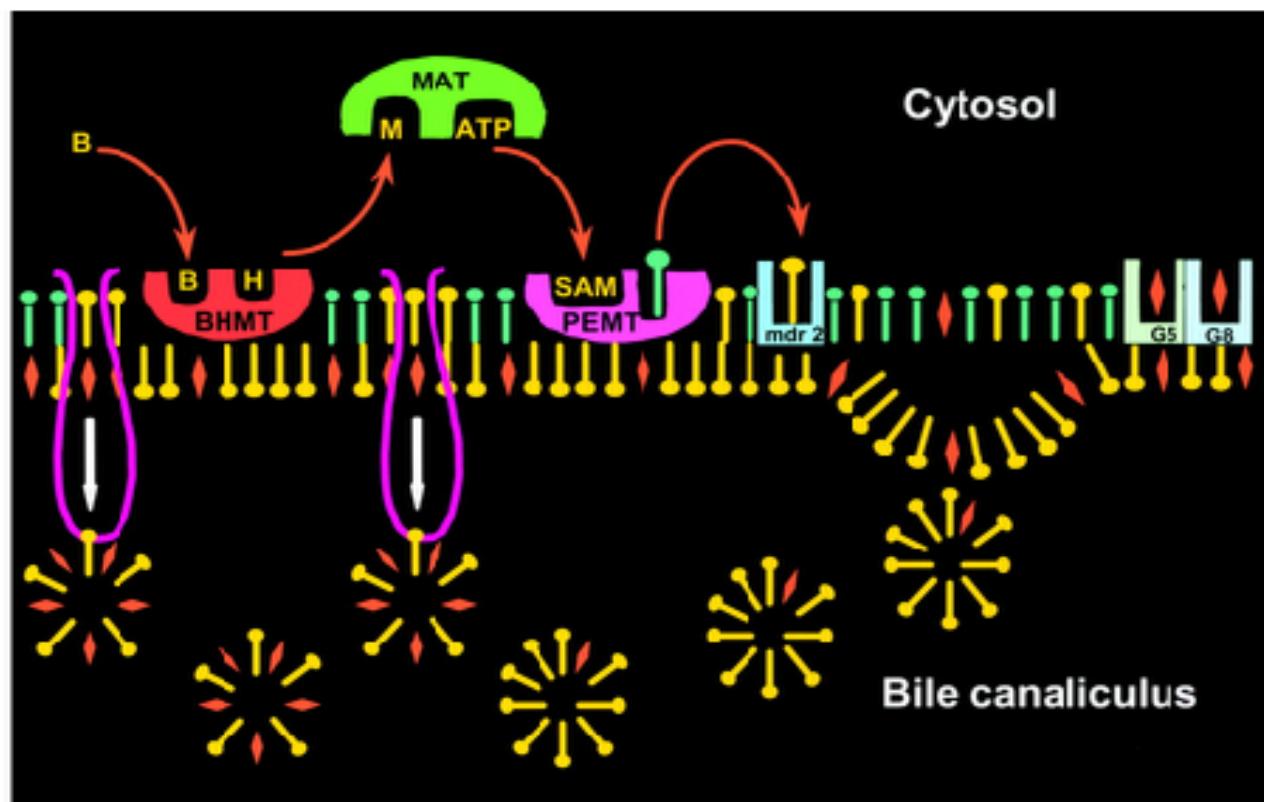
Our data support a role of BA in human energy metabolism and in thyroid hormone control. Even though no convincing response to BA was demonstrated in TSHoma and TaT1 cells, the TSH decrease after a nutritional challenge suggests an interaction of BA on the set point of the thyroid axis.

A growing body of evidence suggests that bile acids (BA) are not only key components of cholesterol homeostasis and lipid absorption but are also involved in the regulation of energy expenditure (EE) (1–3). In a breakthrough study in mice, Watanabe et al. (4) demonstrated increased EE by oral ingestion of cholic acid (CA) based on BA binding to and activation of TGR-5, a G protein-coupled receptor. In the brown fat of mice, but also in human skeletal myocyte cultures, TGR-5 activation stimulated intracellular cAMP formation and activated type 2 iodothyronine deiodinase (D2), which in turn converted T<sub>4</sub> to T<sub>3</sub> and mediated the thermogenic effects of BA (4). Because both brown adipose tissue and skeletal muscle are the main sites of adaptive thermogenesis, the authors hypothesized that BA specifically impact on thermogenesis and not on ATP production. Brown adipose tissue and its activation after cold exposure have subsequently been demonstrated also in adult humans (5–7).



# Methylation & Bile

Proposed model of how canalicular membrane phosphatidylcholine synthesis, mdr2, and SR-BI coordinately promote biliary cholesterol excretion.



Ephraim Sehayek et al. J. Lipid Res. 2003;44:1605-1613

# Effect of Bile on Vitamin B12 Absorption

The standard double-isotope Schilling test was used to study vitamin B12 absorption in seven patients with obstructive jaundice and 10 with T-tube bile duct drainage after cholecystectomy and bile duct exploration. In three and five of these patients respectively absorption was impaired. In the second group six patients were restudied after removal of the T tube, and in each case absorption was improved. Similar results were obtained after bile duct ligation in rats. Bile exclusion produced a 50-60% reduction in renal and hepatic uptake of vitamin B12 from the intestinal lumen. The malabsorption was corrected by replacing bile. These studies suggest that bile plays a part in the normal absorption of vitamin B12.

# Irritability



# 5 Month Support Process

- Detoxification and methylation support
  - Sauna
  - B1-6
  - Glutathione Recycling support
  - Phase 1 and 2 support products
  - Bile support:
    - Vitamin C, Dandelion Extract, Milk Thistle Extract, Phospholipid/Phosphatidylcholine, Taurine, Ginger, Beet, Cellulase, Peptidase, Lipase
- We worked on lifestyle factors: sleeping, breathing, proper cardio and strength training

# 5 Months:

SYMPTOMS	Initial Consult	5 Months	% Improv
SWOLLEN PAINFUL GLANDS	8	2	75%
NECK STIFFNESS	8	4	50%
SWEATS /CHILLS	7	2	71%
FATIGUE	7	2	71%
RED EX TOLERANCE	7	3	57%
IRRITABILITY	7	6	14%
VIBRATION FEELING	7	3	57%
MS TWITCHING	6	4	67%
CONSTIPATION	5	1	80%
BLOATING	5	3	40%
BODY ACHES	4	1	75%
NUMBNESS	3	2	30%
BRAIN FOG	3	1	60%
THROAT SWELLING	3	2	30%



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**WHERE  
ARE  
WE NOW?**

# Key Factors in SIBO

- Stressors and lifestyle
- Starve SIBO – appropriate diet
- Restore / Support Motility
  - Vagal exercises, visceral manipulation, Prokinetics
- Replenish / restore innate antimicrobial capacity
  - HCL, Bile, Pancreatic Enzymes
- Suppress infections
- Crowd out
- Multi-system restoration
- Optimize diet and lifestyle

# Products

- Biofilm disruptors: Seaprose, NAC, Nato, Lumbro, and Serratopeptidase
- Innate antimicrobial: Betaine HCL, Bile, Pancreatic enz Support
- GI healing: Glutamine, Sunfiber, Aloe
- Antimicrobials: Garlic, Berberine, Neem, Oregano, Olive leaf
- Prokinetics: Bitter Herbs, 5HTP, Triphala, Melatonin
- Diet: AI, FODMaps, Bi-phasic, SCD, Histamine, Oxalates, Salicylates

# Enteric Serengeti



# References

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- <http://www.caltech.edu/news/microbes-help-produce-serotonin-gut-46495>
- <http://themedicalbiochemistrypage.org/bileacids.php>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1111842/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4091928/>
- PubMed: 24731596 DOI: 10.1016/j.tem.2014.03.007
- [https://www.researchgate.net/publication/272185376\\_Pituitary\\_TSH\\_controls\\_bile\\_salt\\_synthesis](https://www.researchgate.net/publication/272185376_Pituitary_TSH_controls_bile_salt_synthesis)
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- <http://www.nature.com/nrendo/journal/v10/n2/full/nrendo.2013.226.html>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4215539/>

