Introduction & Overview to:

FUNCTIONAL MEDICINE

What is Functional Medicine and Why Should We Consider it?

Functional Medicine 3 Hour Overview

- Today’s Goal: To delve into the prevalence, trends, and underlying factors contributing to the growing illnes crisis, while exploring innovative approaches, to support our patients' overall health and resilience.

Functional Approach

Focuses on *why* illness occurs and how to help *the body* correct it, rather than just how to temporarily alleviate imbalance or symptoms.

While some providers may not fully adopt a functional medicine approach, incorporating elements of this approach in an integrative way can be beneficial in managing mental health challenges.

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Functional Medicine University
Functional Integrative Medical Practitioner
American Holistic Nurses Association
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Three Formal Degrees:
University of Oklahoma
Oklahoma City University
Certified Business Coach
Published Author: Living Between the Lines
Featured on several media different platforms.

Author of The Upcoming Functional Text:

FUNCTIONAL MEDICINE UNLOCKED

Protocols and Business Success for Purpose-Driven Practitioners

AS SEEN ON

WOZ MARKETING
FOX 43
YOUTUBE LEAD MACHINE
THE CW
AONP Association of Oklahoma Nurse Practitioners

TV

So..Why

Functional & Integrative

Medicine?

People no longer want to just Silence the fire alarms

It's well known
that Chronic
disease is on the
Rise
& people don't
want to stay on
pills.

They want their

Health

back & are losing faith in current systems.

Did you know....

Functional Med is a 28.6 Billion Dollar Industry

But... Expected to Grow

to $229.12 Billion by 2033

Complementary And Alternative Medicine Market Size, Share & Trends Analysis Report By Intervention (Botanicals, Mind Healing, Body Healing, External Energy, Sensory Healing), By Distribution Method, By Region, And Segment Forecasts, 2024 - 2030

What's "Trending" in America

- **26% of adults suffer from a mental disorder**

  An estimated 1 in 4 Americans ages 18 and older -- about 1 in 4 adults -- suffer from a diagnosable mental disorder in a given year. [2]

- The lifetime risk for **Alzheimer's** at age 45 is **1 in 5 for women and 1 in 10 for men**. [2]

- **Depression affects 9.8% of the population [3]**

  The WHO ranked depression at 3rd cause of burden of disease and projected it to be 1st by 2030 [2]

- **Anxiety disorders affect 18% of adults [2]**

  There has been a 77% rise in the number of children needing mental health care in the last decade

  25% increase in incidence in the year preceding 2020 alone [2}

- **America spends 5x our military budget on chronic disease**

  Robert F. Kenedy Jr. Aug. 24, 2024

5-10% of children now have fatty liver disease.

- Approximately 352,000 children and adolescents under the age of 20 have been diagnosed with diabetes, which is about 35 per 10,000 US youths. Of those, 304,000 have type 1 diabetes.

Rising Trends

"To improve is to change; to be perfect is to change often." — Winston Churchill

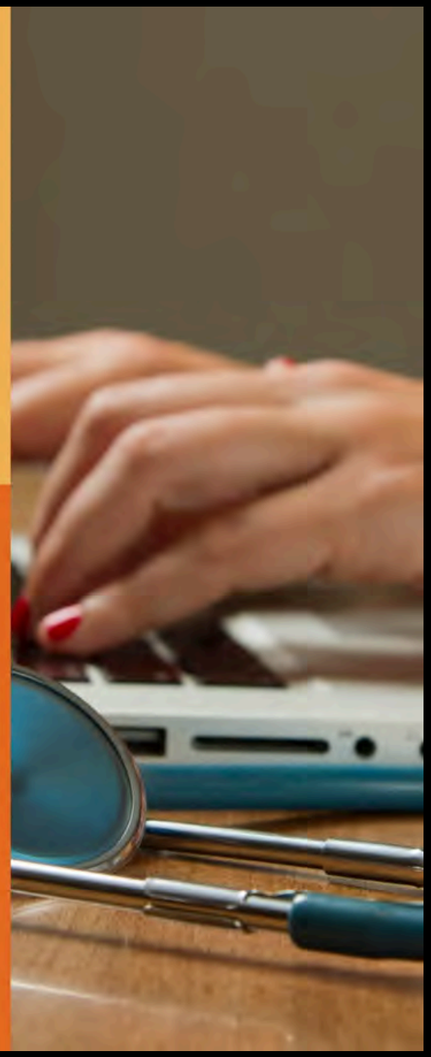
Chronic diseases are increasing in prevalence throughout the US and put a major strain on the health care system."

-CDC.gov Aug. 2024

90% of $4.1 trillion/year health spending is on chronic diseases and mental health

5 of the top 10 leading causes of death in the US are preventable and treatable chronic diseases

An increasing proportion of people in America are dealing with multiple chronic conditions; 42% have 2 or more, and 12% have at least 5 [3]



Health Statistics In School Aged Children

- A few decades ago Autism was 1/2000
- As of May 2024, the CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network estimated that 1 in 36 children in the United States have been identified with autism spectrum disorder (ASD). This is a 312% increase since 2000.

> 40% of school-aged American children have at least 1 chronic health condition.

1980s and 1990s, when obesity prevalence among children and teens tripled, from nearly 5% to approximately **15%. Increased to 20% in 2020; 22% 2024.**

40% of school aged children report persistent feelings of saddness/hopelessness. 57% of females and 27% with serious contemplation of suicide. (down a couple of parents since 2021).

ACCORDING TO THE CDC

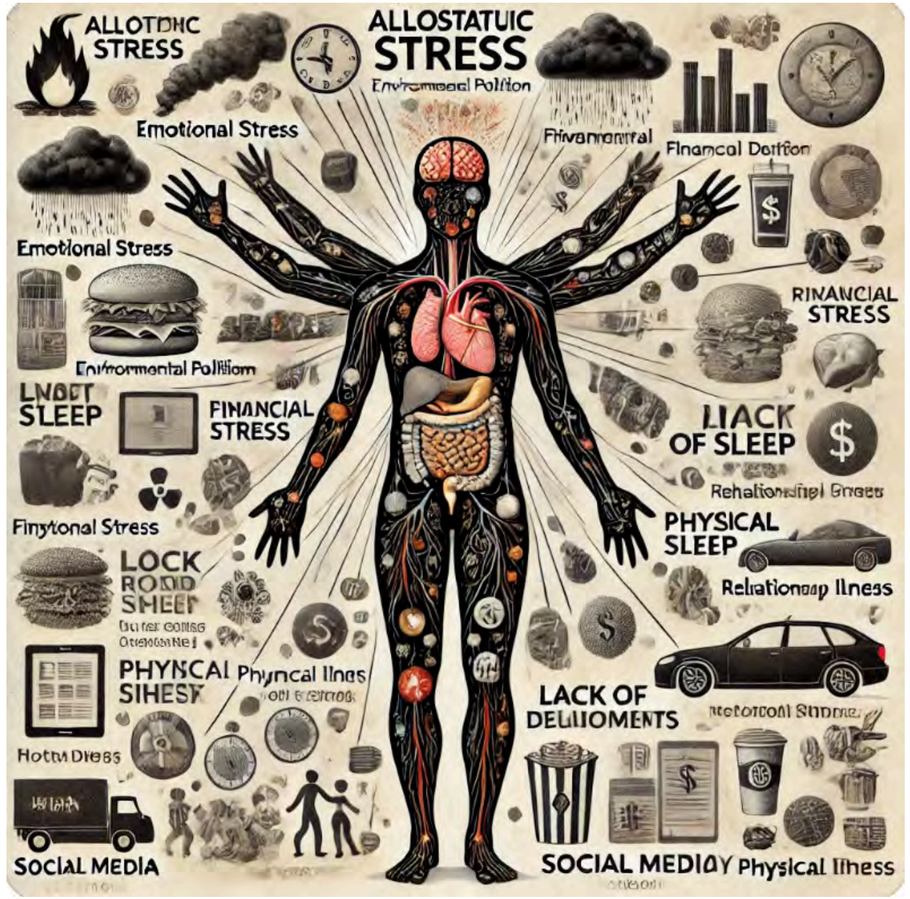
The percentage of individuals using at least one prescription drug in the past 30 days was 48.6% as of 2015-2018.

CURRENTLY

- Adults 65 and older: 54% report taking four or more prescription drugs
- Adults 50–64: 32% report taking four or more prescription drugs
- Adults 30–49: 13% report taking four or more prescription drugs
- Adults 18–29: 7% report taking four or more prescription drugs
- People aged 65 to 69: Take an average of 15 prescriptions a year
- People aged 80 to 84: Take an average of 18 prescriptions a year

“Prevention should not just be early detection. We need to think in terms of Systems not Symptoms.”

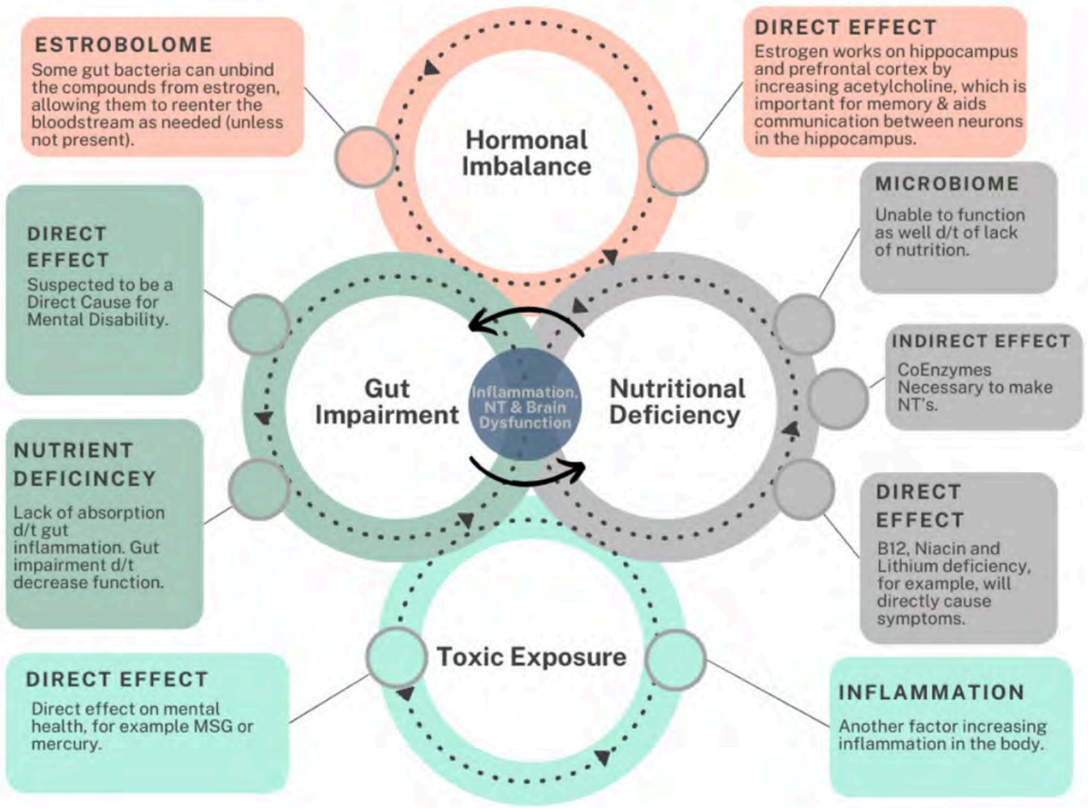
Dr. Mark Hymen, MD

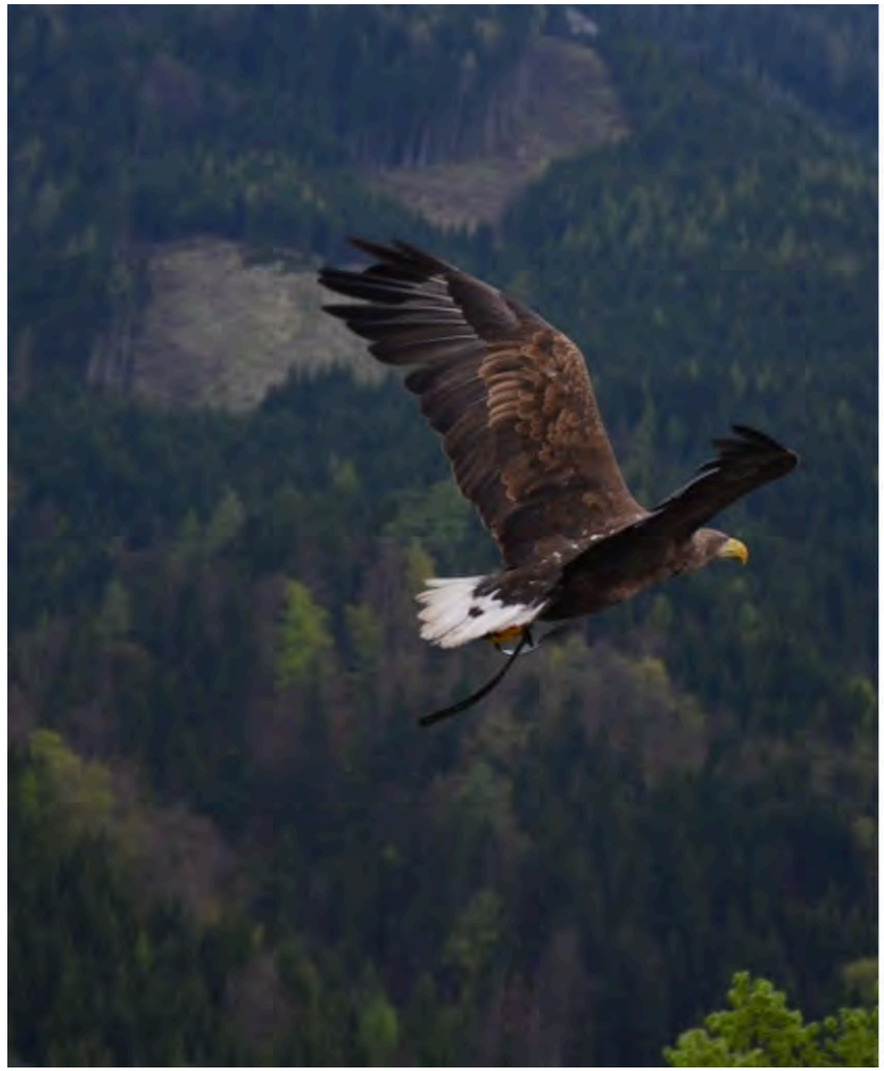


Allostatic Stress

The allostatic load model suggests that stress and its effects take a cumulative toll on the body. Stress leads to the fight or flight response, which triggers the release of hormones, including catecholamines and glucocorticoids, inflammation, and other factors.

McEwen BS, Gianaros PJ. Stress- and allostasis-induced brain plasticity. Annu Rev Med. 2011;62:431-45. doi: 10.1146/annurev-med-052209-100430. PMID: 20707675; PMCID: PMC4251716.


ESTROBOLOME
Some gut bacteria can unbind the compounds from estrogen, allowing them to reenter the bloodstream as needed (unless not present).
Hormonal Imbalance
DIRECT EFFECT
Estrogen works on hippocampus and prefrontal cortex by increasing acetylcholine, which is important for memory & aids communication between neurons in the hippocampus.
DIRECT EFFECT
Suspected to be a Direct Cause for Mental Disability.
MICROBIOME
Unable to function as well d/t of lack of nutrition.
Gut Impairment
Inflammation, NT & Brain Dysfunction
Nutritional Deficiency
INDIRECT EFFECT
CoEnzymes Necessary to make NT's.
NUTRIENT DEFICINCEY
Lack of absorption d/t gut inflammation. Gut impairment d/t decrease function.
DIRECT EFFECT
B12, Niacin and Lithium deficiency, for example, will directly cause symptoms.
Toxic Exposure
DIRECT EFFECT
Direct effect on mental health, for example MSG or mercury.
INFLAMMATION
Another factor increasing inflammation in the body.



Case Study

R.E.S. 37 F

Not Breast Fed as infant

Anxiety and depression was life long.

Several previous providers.

Family Hx of Fibro, Lupus, and Sjogren's in 1st and 2nd-degree relatives

Comorbidities of hypothyroidism, HTN, obesity, fibromyalgia, pre-DM

Life-long pain (part of the reason for starting drug use)

Pt had her first ANA positive at age 5

Gas and bloating was her "norm"

Pain is "unbearable"

Fatigue is draining

Resistant wt loss

"You are a savior. I feel so much better! I've had 4 pounds weight loss (my scale says 8). I feel happy for the first time, pain is bearable & my hair isn't falling out. "

Case Study

52 F of Oklahoma

Anxiety and depression was sever the last 10 years. "I didn't used to be this way."

Several previous providers, psychiatry, counseling, etc.

No significant Family Hx for mental disease.

Comorbidities of hypothyroidism, HTN, pre-DM

"Nervous" diarrhea

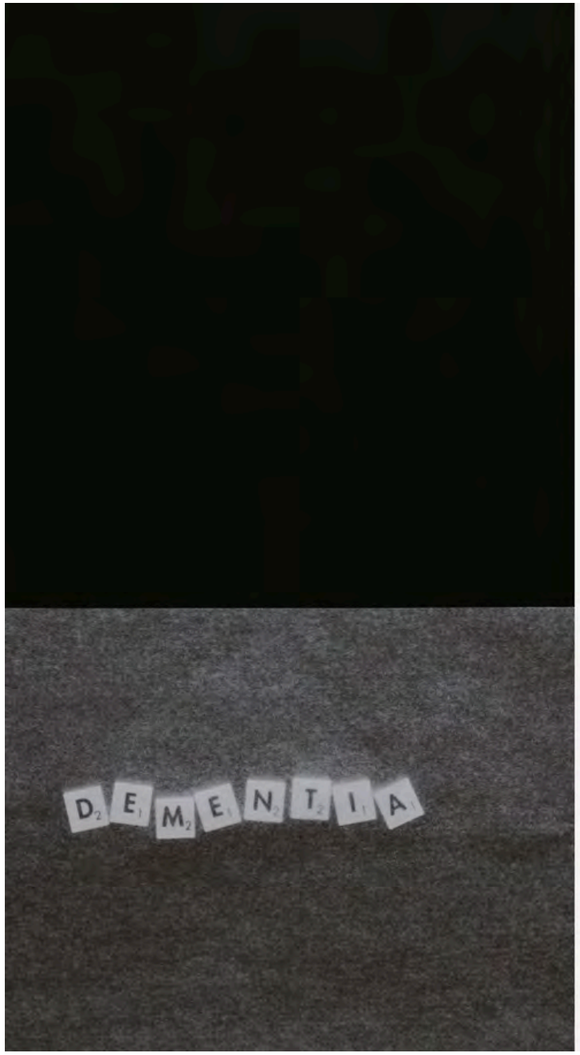
Fatigue was draining.

Fear of leaving house was overwhelming.

"Thank you for what you have done for us. Thank you for not giving up on me."

“Autism: A brain disorder or a disorder that affects the brain?”

Dr. Martha Herbert, MD



Alzheimers' Disease

Increase in significance of 117% in the last 26 years [37]

Projected to nearly double Q 2yr (78 Million year 2030) [37]

Would be the 14th largest economy in the world, if dementia care were a country of its own [37].

> “The concept of dementia is obsolete. It combines categorical misclassification with etiologic imprecision.”

JAMA- Hachinski, MD

IDEO

"GOOD" NEWS... YOUR LABS ARE ALL WNL

"GOOD" NEWS... YOUR LABS ARE ALL WNL

But, something is still wrong...

Did You Know, Correcting Gut Health First Can Correct the leading causes of...

MULTIPLE SCLEROSIS

FIBROMYALGIA

SJOGREN'S

CHRONIC PAIN

RA

HASHIMOTOS

TO NAME A FEW

Contrast of Conventional & Functional Interventions

Hypertention:	Lower Blood Pressure w/ Rx	First Replace Nutrient deficiencies
Depression:	Decrease Depressive Symptoms w/ Rx	First Replace Nutrients, Rebalance GI, decreae Inflammation
IBS:	Decrease GI Symptoms w/ Rx	Fix Dysbiosis w/ Natural Pre & Probiotics Correct Inflammation
Eczema:	Topical Steroids	Fix Dysbiosis Eliminate Triggers Correct Inflammation & Immune Support

Socio-Cultural Factors in Functional Medicine

- Prenatal exposure to screen for:
  - Mother experienced high stress, illness or early delivery while pregnant
    - increased risk for neurological impairment in the child
    - extended prenatal Tylenol use can increase the risk for impaired detoxification of child
    - c-section birth decreases child's exposure to natural vaginal flora that colonizes in the child's gut

Source:
AIM (2017). Why pre-natal care is just as important as post-natal care.https://www.aimintegrativemedicine.com/aim-integrative-medicine-blog/2017/2/14/prepping-the-body-for-pregnancy

Socio-cultural Factors in Functional Medicine

Source:
Galland L. (2006). Patient-centered care: antecedents, triggers, and mediators. Alternative therapies in health and medicine, 12(4), 62–70.

- Socio-cultural factors influence health outcomes.
- From a biological perspective, an individual's adverse experiences in the socio-cultural
  - unfavorably influence physiological processes through a variety of means
    - signal transduction
    - chronic stress exposure
    - changes within the brain chemistry and makeup.
- ACEs: "adverse childhood experiences," are one such example but there are many others.
- 3 main factors of socio-cultural factors to focus on:
  - 1) social determinants of health,
  - 2) social needs of health, and
  - 3) implicit bias of the practitioner.
  - These are represented as antecedents, mediators, and triggers, respectively.

Making Sense of Root Cause

- Diseases form through processes that occur in those who are genetically susceptible
  - Just as not all smokers get lung cancer, not all exposed to AI triggers get AI.

- Thousands have reversed even the autoimmune disease process naturally by removing triggers.
- The out-of-control epidemic
  - The American Autoimmune Related Diseases Association estimates over 50 million cases in US alone.

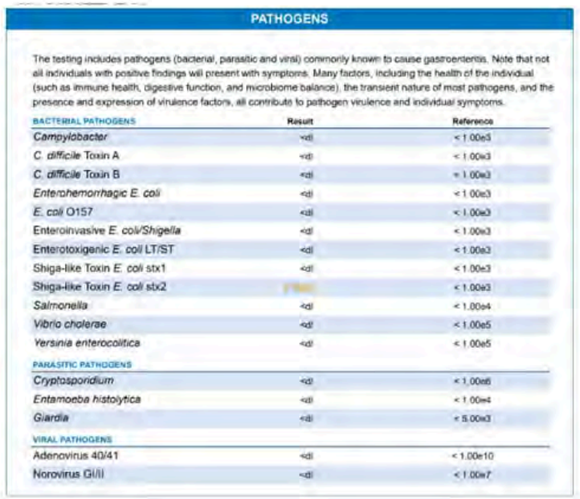
More

Truths About Autoimmunity and Functional Medicine

- Reported to be on the rise around the world, suspected to rival heart disease soon.
- More than 100 different AI diseases identified and at least 40 more suspected to have relations.
- It is considered chronic.
- Can be life-threatening.
- Can affect any system in the body.
- Triggers can include stress, viruses, bacteria, medications, hormones, toxins.
- Is a major cause of Thyroid disease (estimated to be around 90%).
- Conventional medicine treats as incurable.
- Caveat: Damage such as that seen in RA is often irreversible and immunosuppressive drugs do work to decrease that progression (despite sometimes serious SEs).

Lipopolysaccharides (LPS)

- Lipopolysaccharides are an endotoxin from some Gram-negative bacteria such as Salmonella, Enterobacter, Klebsiella, E. coli, Lactic-producing Gram-negatives are protective Lactobacillus, Bifidobacteria, Roseburia, Akkermansie
- LPS-inflamed gut has a loosening of the tight junctions, inducing “Leaky Gut”, oxidative stress, pro-inflammatory cytokines, IL6, TNF-a, IL1B are all increased
- Microglia (brain immune regulators) are activated by LPS administration and are triggered to engulf GABAergic presynapses
- Leading to GABAerginic synapse deficits, neural inflammation [13][14][100][101]
- Memory impairment [16][100][101]
- Depression [100]
- Conventional intervention if pt is acutely ill* Monitor for Hemolytic Uremic Syndrome (decreased urination, hematuria, fatigue).
- Functional treatment: Biofilm Defense, oregano, garlic berberine TID, high dose probiotics; cinnamon or clove also demonstrate effectiveness [148][149]



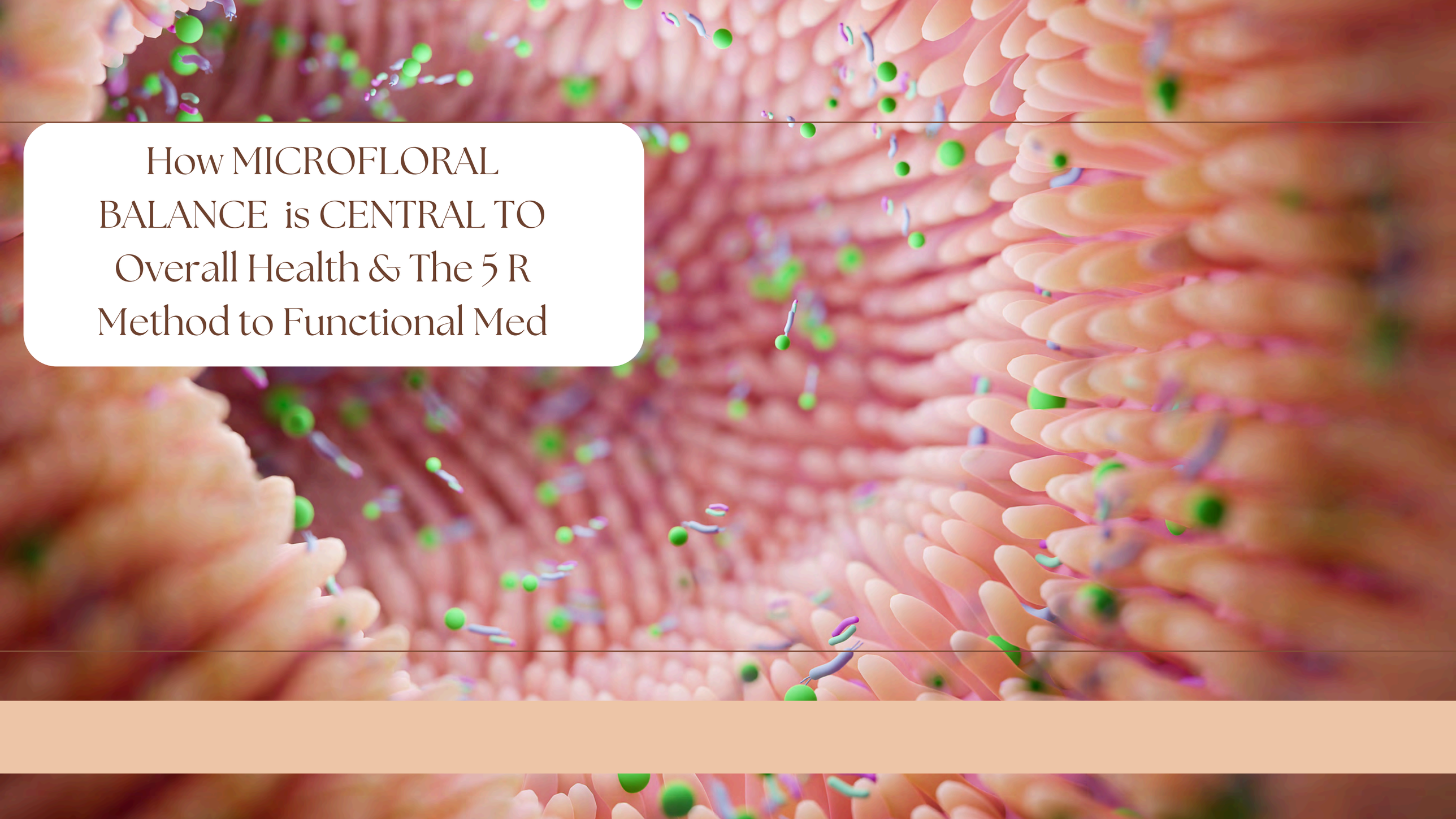
PATHOGENS

The testing includes pathogens (bacterial, parasitic and viral) commonly known to cause gastroenteritis. Note that not all individuals with positive findings will present with symptoms. Many factors, including the health of the individual (such as immune health, digestive function, and microbiome balance), the transient nature of most pathogens, and the presence and expression of virulence factors, all contribute to pathogen virulence and individual symptoms.

BACTERIAL PATHOGENS	Result	Reference
Campylobacter	<dl	< 1.00e3
C. difficile Toxin A	<dl	< 1.00e3
C. difficile Toxin B	<dl	< 1.00e3
Enterohemorrhagic E. coli	<dl	< 1.00e3
E. coli O157	<dl	< 1.00e3
Enteroinvasive *E. coli/Shigella*	<dl	< 1.00e3
Enterotoxigenic *E. coli* LT/ST	<dl	< 1.00e3
Shiga-like Toxin *E. coli* stx1	<dl	< 1.00e3
Shiga-like Toxin *E. coli* stx2	[illegible]	< 1.00e3
Salmonella	<dl	< 1.00e4
Vibrio cholerae	<dl	< 1.00e5
Yersinia enterocolitica	<dl	< 1.00e5
PARASITIC PATHOGENS		
Cryptosporidium	<dl	< 1.00e6
Entamoeba histolytica	<dl	< 1.00e4
Giardia	<dl	< 5.00e3
VIRAL PATHOGENS		
Adenovirus 40/41	<dl	< 1.00e10
Norovirus GI/II	<dl	< 1.00e7

Don't Throw the Baby out with the Bath Water.

- Some people don't respond or want natural treatment.
- Some can't handle harsh medications or also do not see remission.
- I do NOT recommend that as a Functional Provider, encouraging discontinuing prescription medications that you did not prescribe (unless you yourself are a provider).
- I recommend you work with the specialist and PCP.



How MICROFLORAL BALANCE is CENTRAL TO Overall Health & The 5 R Method to Functional Med

Clinical Approach entails the 5 "R" Treatment Protocol:

Remove

Replace

Reinoculate

Repair

Rebalance

Remove

The first step is to remove the offending microorganism (MO). MOs are often a cause of GI symptoms as well as an array of generalized/systemic symptoms such as fatigue, pain, or brain fog. They can even account for thyroid disease and obesity .

Antifungal

Caprylic acid, garlic oil, oil of oregano, olive leaf extract

Antiviral

Olive leaf extract, purified silver, cat's claw, monolaurin, osha root (Ligusticum porteri), vitamin A, Vitamin C, Vitamin D, reishi mushrooms, Echinacea , zinc

Antimicrobial

Broad-Spectrum antimicrobial herbs: berberine, caprylic acid, garlic oil, oil of oregano,, olive leaf extract

Remove (continued)

If Antibiotic is needed, will need prescriptive athority

Antibiotic

Risk for resistance. Compare w/ GI-MAP findings for universal antibiotic resistance genotype

Antiparasitic

Black walnut, garlic oil, oil of oregano, Artemisia (wormwood), berberine, goldenseal, gentian root extract, quassia bark extract, citrus seed extract

Remove (continued)

Chemicals

Medications or chemicals in diet

Diet

Offending foods (dairy, gluten are common examples)

Environmental/toxic exposure

mold, heavy metals

Replace

Digestive Support

Betaine hydrochloride, apple cider vinegar, herbal bitters, ox bile, lactase, pancreatic enzymes (amylase, lipase, protease), Pepsin

Reinoculate

Probiotics

Lactobacillus acidophilus,
Bifidobacterium bifidum,
Bifidobacterium longum,
Lactobacillus rhamnosus,
Bifidobacterium breve,
Lactobacillus casei,
Saccharomyces boulardi

Prebiotics

Beta-glucan, fiber, inulin, pectin, xylooligosaccharides, galactooligosaccharides, larch arabinogalactans

Repair

This is where we restore the integretiy of the gut as the infection or imbalance will inately have residual inflammation that will lead to damage on the intestinal walls

- Treatment to help seal the tight junctions: FODMAP diet helps many [44]
- Glutamine 5G-10G daily x 2 months [43][44]
- Probiotics [44]
- Fiber (in the absence of SIBO) & Prebiotics [44]
- Vitamin supplementation as indicated [16][44][121]
- Medicinal herbs [27][16]
- Prevention: cinnamon (suppresses IL-10), red raspberries (inflammatory factors/NF-kB), blueberries (Inflammatory factors/NF-kB), yogurt [44]
- Yogurt has tight junction proteins; caution if overgrowth of certain strains are present [43]
- Polyphenols (quercetin-also indicated to improve HTN, asthma, and Alzheimer's disease; catechin; epicatechin; berberine; resveratrol; curcumin)[44]
- Movement
  - "The simple act of moving your body will do more for your brain than any riddle, math equation, mystery book, or even thinking itself."
    - -Dr. David Perlmutter

Rebalance

Address whole body wellness and habits in order to prevent future dysbiosis & illness.

Start with Mindset

Sleep

Exercise

Diet

Stress Control

Prevention

Most exposures to pathogenic MOs are via fecal-oral transmission in water, undercooked foods, or improper hand hygiene.
Wash fresh frutis and veggies well

Commensal Bacteria

The good guys.
GI MAP will tell you the different levels over/undergrowth of each.
Yin & Yang.

Sources:
Tian, P., O'Riordan, K. J., Lee, Y. K., Wang, G., Zhao, J., Zhang, H., Cryan, J. F., & Chen, W. (2020). Towards a psychobiotic therapy for depression: Bifidobacterium breve CCFM1025 reverses chronic stress-induced depressive symptoms and gut microbial abnormalities in mice. Neurobiology of stress, 12, 100216. https://doi.org/10.1016/j.ynstr.2020.100216

Akkermansia municiphila

Low levels are associated with **obesity**. High levels have been identified with risk for multiple sclerosis, and low levels of other AI diseases.

Bacteroides fragilis

Constipation can lead to levels dropping too low, which can decrease the anti-inflammatory activity of the GI tract.

Bifidobacterium spp.

Colonizes at birth with exposure to vaginal canal and with breastfeeding. Thrives on many types of prebiotic fibers, meaning that a diet low in whole food fiber will cause deficiency (which is linked to **obesity, diabetes, allergic asthma, celiac disease, inflammation, depression, & dermatitis)**

Commensal Bacteria

Continued

Sources:
GI-MAP Interpretive Guide

Clostridia (class)

Large intestine. Important in production of short-chain fatty acids. Protects against bad GI pathogens. Low levels associated with **autoimmune** disease. High levels associated w/ metabolic disease.

Enterococcus spp.

Low levels can result from constipation or SIBO.

Escherichia spp.

Is a stran of Escherichia coli. Most E. coli are non-pathogenic.
High levels occur as a result of GI inflammation.
Low levels indicate reduced mucosal health and limited protection against the pathogenic strand of E. coli.

Commensal Bacteria

Continued

Butyrate: Is important in protection from inflammation. It maintains our gut barrier by fueling the cells of the GI, suppresses inflammation, boosts the immune system against bad bacteria, r**educes appetite & maintains blood sugar levels.**

Sources:
GI-MAP Interpretive Guide

Faecalibacterium prausnitzii

Major butyrate producer.
Low levels is associated with a wide range of autoimmune and inflammatory diseases.

Lactobacillus spp.

Excessive intake of carbohydrates can cause overgrowth. Low levels can results from **too low of carbohydrate intake** and/or too much salt

Enterobacter spp.

Is closely related to Escherichia coli. Most E. coli are non-pathogenic.
High levels occur as a result of GI inflammation.
Low levels indicate reduced mucosal health.

Tips for Decreasing Inflammation

- Treatment to help seal the tight junctions: FODMAP diet helps many [44]
- Glutamine 5G-10G daily x 2 months [43][44]
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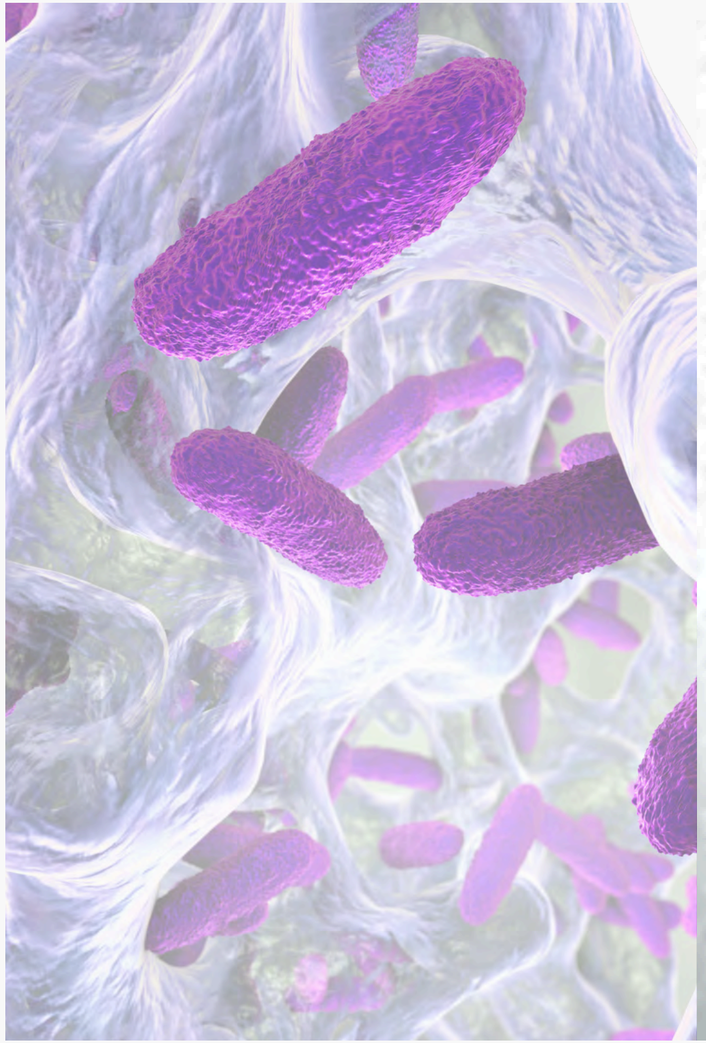
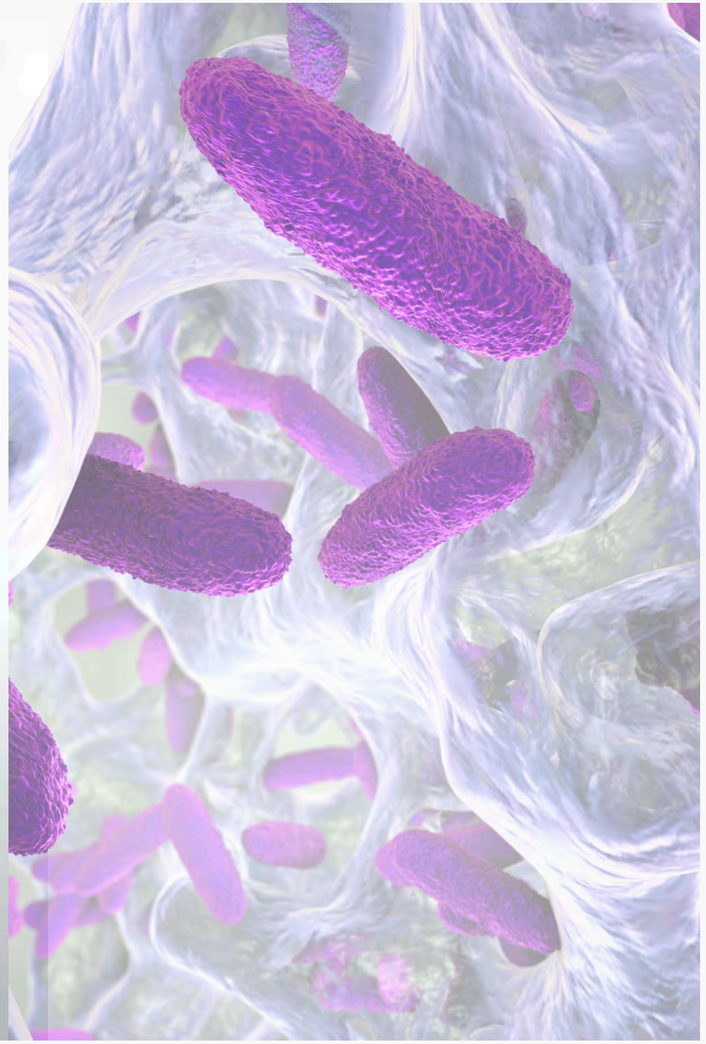
Biofilm disruptor and



Digestive Enzymes (Full spectrum)

Protease (pH 3.0-9.0)
Papain (from papaya)
Bromelain (from pineapple)
Amylase
Amyloglucosidase (glucoamylase)
Cellulase
Beta-Glucanase
Alpha-Galactosidase
Invertase
Peptidase (29 DPPIV)
Pectinase
Lactase
Phytase
Acid Stable Protease (pH 2.0-3.5)
Lipase
Xylanase
Hemicellulase



To keto or not to keto?

Lactobacillus spp. is not readily available in most keto diets:
It is found in Buckwheat, Barley, Walnuts, Artichoke, chicory root, wheat bran, apples, konjac flour, chokeberry

- L. acidophilus
  - Treatment in ulcerative colitis
- L. Plantarum
  - Prevention and management of IBS, IBS, coronary heart disease, cancer, and GI symptoms
- L. reuteri
  - Helps in infantile colic, h. pylori prevention, urogenital disease, dental caries and food hypersensitivities
- L. helveticus
  - Better memory & lower anxiety
- L. casei
  - Also inhibits H. pylori growth and pathological c.Diff; associated with improved mood & memory
- L. paracasei TD062 (Dang, et al., 2018).
  - positive effect on expression levels of genes related to glucose metabolism and prevention of T2DM development

Dang, F., Jiang, Y., Pan, R. , Zhou, Y., Wu., S., Wang, R., Zhuang, K., Zhang, W., Li,. T., Man, C., (2018) Administration of Lactobacillus paracasei ameliorates type 2 diabetes in mice. Food and Function journal. Retrieved from:
DOI
https://doi.org/10.1039/C8FO00081F

Balancing Commensal Bacteria

High Firmicutes and low Bacteroides (high F/B ratio) may lead to increase caloric extraction from food, fat deposition & lipogenesis, poor insulin sensitivity & further inflammation.

Use of probiotics:

For example:
Bifidobacteria & Saccharomyces boulardii
Lactobacillus spp.& Bacillus spp. can also elevate Firmicutes

If Conventional Medicine
puts out smoke alarms,
Functional Medicine
puts out the fire.

Perfectionism:

Kills more dreams than mistakes ever can.

THIS IS THE FUTURE OF HEALING. BUT, IF YOU ARE SITTING THERE THINKING, "YES.. BUT LATER..." I CAN TELL YOU YOU WON'T BE THE ONE WHO LEADS THE PACK. YOU ARE PERFECTLY POSITIONED TO LEAD THIS WAVE!

Constipation

Non Chronic

- Treatment of underlying cause/SIBO/IBS, etc.
- Higher doses of vitamin C have been shown to have a natural laxative effect, which can provide some relief for constipation sufferers.
  - To get a high enough dose of vitamin C, supplements are required “Emergency C”. High dosing vitamin C over a number of hours is what we call a ‘C’ Flush.
  - Vitamin C I said to energize the GI tract until it flushes and you experience waterfall-like bowel motions.
    - Caution Dehydration
- 2-3 Kiwi every morning for 4 weeks
- Psyllium powder
- Magnesium

Gut Dysbiosis, SIBO, IBS/IBD
Exploring Root Cause

- Poor diet
  - Not enough of the good food and too much of bad
- Chronically high cortisol levels
  - Either from stress or diet
- H. Pylori infection
  - Tx: Jarrow BroccoMax 1 cap TID with meals and 500 ml of 100% cranberry juice (unsweetened)
- Parasitic infection:
  - Two classes: Protozoa & Helminths
  - Protozoa have 2 stages the trophozoite stage that is metabolically active, invasive stage and the cyst stage. The cyst stage is a vegetative inactive form and resistant to unfavorable conditions outside the human host.
  - Helminths are multicellular
  - Symptoms can include diarrhea, mucous, blood fever, nausea or abdominal pain

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

- Comprehensive stool analysis:
  - Lysozyme: enzyme secreted at site of inflammation in IBD patients
  - Lactoferrin: quantitative GI marker that helps to diagnosis IBD and differnciate it from IBS
    - Also helps to monitor progress through treatment
  - Secretory IgA* secreted by mucosal tissue. It is the 1st line of defense of GI tract. Elevated sIgA leves are associated with upregulated immune responses.
  - Will also include screening for yeast
    - yeast is normally found in small quantities in the skin mouth intestines and mucocutaneous Junctions
    - Can cause abdominal pain, cramping, irritation, cravings for sugar or ETOH, fatigue, hair loss, generalized feeling of illness/nausea
    - Undetectable low levels of yeast may still be harmful to the individual While others may not be affected

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

- Food Sensitivity Testing:
- 1) Gluten, wheat and food sensitivities test from Cyrex Laboratories
- 2) Meridian Lab FoodSafe Combo Lab
- 3) IgE Reactions
  - a) These reactions cause hives, as well as throat swelling with potential anaphylactic reactions
  - b) May also induce wheezing, coughing, a runny nose, vomiting, swelling of the lips or tongue, tearing or erythematous eyes, hypertension, and loss of consciousness.
  - c) Common foods that trigger IgE reactions include foods such as peanuts, shellfish, egg, dairy products, soy, tree nuts, wheat and fish.

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

IgA Reactions

- IgA immunoglobulins resign in the mucus membranes
- Important in fighting against bacteria and viruses.
- IgA increases in response to foods when the foods cause inflammation. Also triggered in response to stress, disease, or alcohol.
- An IgG reaction to food proteins suggests tolerance related to immune cell

- reaction.
- b) However, repeated exposure leads to inflammation, and immune reactivity
- contribute to sensitivity and high IgG in response to these proteins.
- 6) Gliadin is associated with gluten reaction

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

- Calprotectin is a protein released by neutrophils, a type of white blood cell, during inflammation.
    - Non Specific but if positive be considering working with gastro as a diagnosis to rule out Chrones and monitor may become necessary

Delaying or not starting immunologic treatments for Crohn's disease can be a big deal because it can lead to more severe complications, reduced quality of life, and potentially long-term damage to the digestive tract.

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

The GI-MAP: Gut Flora:

- Akkermansia muciniphila: Normal Range: 10-50K Units
  - Good bacterium represents 3-5% of microbial composition in healthy balance
  - Reduces gut barrier disruption & insulin resistance
  - Mucin-degrading
    - Mucins:
      - Coat the surfaces of cells linging the digestive, urogenital, & respiratory systems
      - Increased production occurs as a results of cancer in the pancreas, lung, breast, ovary, colon and other
      - Over production of mucins, which are proteins produced in epithelial tissues, also seen in in lung disease such as ashtma, bronchitis, COPD and cystic fibrosis
- Those with obesity, metabolic disorders, and TIIDM tend to have insufficient amounts.
- Being studied to help in the treatment of Obesity b/d of its inverse relationship

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

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Gut Dysbiosis, SIBO, IBS/IBD
Stool Analysis

PATHOGENS

The testing includes pathogens (bacterial, parasitic and viral) commonly known to cause gastroenteritis. Note that not all individuals with positive findings will present with symptoms. Many factors, including the health of the individual (such as immune health, digestive function, and microbiome balance), the transient nature of most pathogens, and the presence and expression of virulence factors, all contribute to pathogen virulence and individual symptoms.

BACTERIAL PATHOGENS	Result	Reference
Campylobacter	<dl	< 1.00e3
C. difficile Toxin A	<dl	< 1.00e3
C. difficile Toxin B	<dl	< 1.00e3
Enterohemorrhagic E. coli	<dl	< 1.00e3
E. coli O157	<dl	< 1.00e3
Enteroinvasive *E. coli/Shigella*	<dl	< 1.00e3
Enterotoxigenic *E. coli* LT/ST	<dl	< 1.00e3
Shiga-like Toxin *E. coli* stx1	<dl	< 1.00e3
Shiga-like Toxin *E. coli* stx2	<dl	< 1.00e3
Salmonella	<dl	< 1.00e4
Vibrio cholerae	<dl	< 1.00e5
Yersinia enterocolitica	<dl	< 1.00e5
PARASITIC PATHOGENS		
Cryptosporidium	<dl	< 1.00e6
Entamoeba histolytica	<dl	< 1.00e4
Giardia	<dl	< 5.00e3
VIRAL PATHOGENS		
Adenovirus 40/41	<dl	< 1.00e10
Norovirus GI/II	<dl	< 1.00e7

Gut Dysbiosis, SIBO, IBS/IBD

Stool Analysis

HELICOBACTER PYLORI

H. PYLORI & VIRULENCE FACTORS	Result		Reference
Helicobacter pylori	2.79e3	High ↑	< 1.00e3
Virulence Factor, babA	Negative		Negative
Virulence Factor, cagA	Negative		Negative
Virulence Factor, dupA	Negative		Negative
Virulence Factor, iceA	Negative		Negative
Virulence Factor, oipA	Negative		Negative
Virulence Factor, vacA	Negative		Negative
Virulence Factor, virB	Negative		Negative
Virulence Factor, virD	Negative		Negative

COMMENSAL/KEYSTONE BACTERIA

COMMENSAL BACTERIA	Result	Reference
Bacteroides fragilis	3.35e11 H	1.6e9 - 2.5e11
Bifidobacterium spp.	5.67e10	> 6.7e7
Enterococcus spp.	2.32e6	1.9e5 - 2.0e8
Escherichia spp.	2.33e8	3.7e6 - 3.8e9
Lactobacillus spp.	1.68e7	8.6e5 - 6.2e8
Enterobacter spp.	1.72e6	1.0e6 - 5.0e7
Akkermansia muciniphila	<dl L	1.0e1 - 8.2e6
Faecalibacterium prausnitzii	9.03e2 L	1.0e3 - 5.0e8
Roseburia spp.	3.90e9	5.0e7 - 2.0e10
BACTERIAL PHYLA		
Bacteroidetes	4.17e12 H	8.6e11 - 3.3e12
Firmicutes	1.27e11	5.7e10 - 3.0e11
Firmicutes:Bacteroidetes Ratio	0.03	< 1.0

Gut Dysbiosis, SIBO, IBS/IBD

Stool Analysis

An overgrowth of opportunistic bacteria may result from not enough of the healthy bacteria as a result of parasitic infection, poor diet, weakened immune system and/or history of antibiotic use.

OPPORTUNISTIC/OVERGROWTH MICROBES

DYSBIOTIC & OVERGROWTH BACTERIA	Result		Reference
Bacillus spp.	1.03e6		< 1.76e6
Enterococcus faecalis	<dl		< 1.00e4
Enterococcus faecium	<dl		< 1.00e4
Morganella spp.	<dl		< 1.00e3
Pseudomonas spp.	1.04e2		< 1.00e4
Pseudomonas aeruginosa	<dl		< 5.00e2
Staphylococcus spp.	<dl		< 1.00e4
Staphylococcus aureus	<dl		< 5.00e2
Streptococcus spp.	2.27e4	High ↑	< 1.00e3
COMMENSAL OVERGROWTH MICROBES			
Desulfovibrio spp.	7.06e8		< 7.98e8
Methanobacteriaceae (family)	6.25e9	High ↑	< 3.38e8
INFLAMMATORY & AUTOIMMUNE-RELATED BACTERIA			
Citrobacter spp.	<dl		< 5.00e6
Citrobacter freundii	<dl		< 5.00e5
Klebsiella spp.	<dl		< 5.00e3
Klebsiella pneumoniae	<dl		< 5.00e4
M. avium subsp. paratuberculosis	<dl		< 5.00e3
Proteus spp.	<dl		< 5.00e4
Proteus mirabilis	<dl		< 1.00e3
COMMENSAL INFLAMMATORY & AUTOIMMUNE-RELATED BACTERIA			
Enterobacter spp.	1.72e6		< 5.00e7
Escherichia spp.	2.33e8		< 3.80e9
Fusobacterium spp.	5.58e6		< 1.00e8
Prevotella spp.	5.46e7		< 1.00e8

FUNGI/YEAST

FUNGI/YEAST	Result	Reference
Candida spp.	<dl	< 5.00e3
Candida albicans	<dl	< 5.00e2
Geotrichum spp.	<dl	< 3.00e2
Microsporidium spp.	<dl	< 5.00e3
Rhodotorula spp.	<dl	< 1.00e3

VIRUSES

VIRUSES	Result	Reference
Cytomegalovirus	<dl	< 1.00e5
Epstein-Barr Virus	<dl	< 1.00e7

Gut Dysbiosis, SIBO, IBS/IBD
Stool Analysis

- Some bacterial are know to be associated with triggering autoimmune dysfunction in particular. There are as outlined:
  - i) Citrobacter spp.
  - ii) Citrobacter freundii
  - iii) Fusobacterium spp.
  - iv) Klebsiella spp.
  - v) Klebsiella pneumoniae
    - (1) Known for joint pain, ankylosing spondylitis, reactive & rheumatoid arthritis, as well as IBS chrones
  - vi) Mycobacterium avium
  - vii) Prevotella copri
  - viii) Proteus spp.
  - ix) Proteus mirabilis

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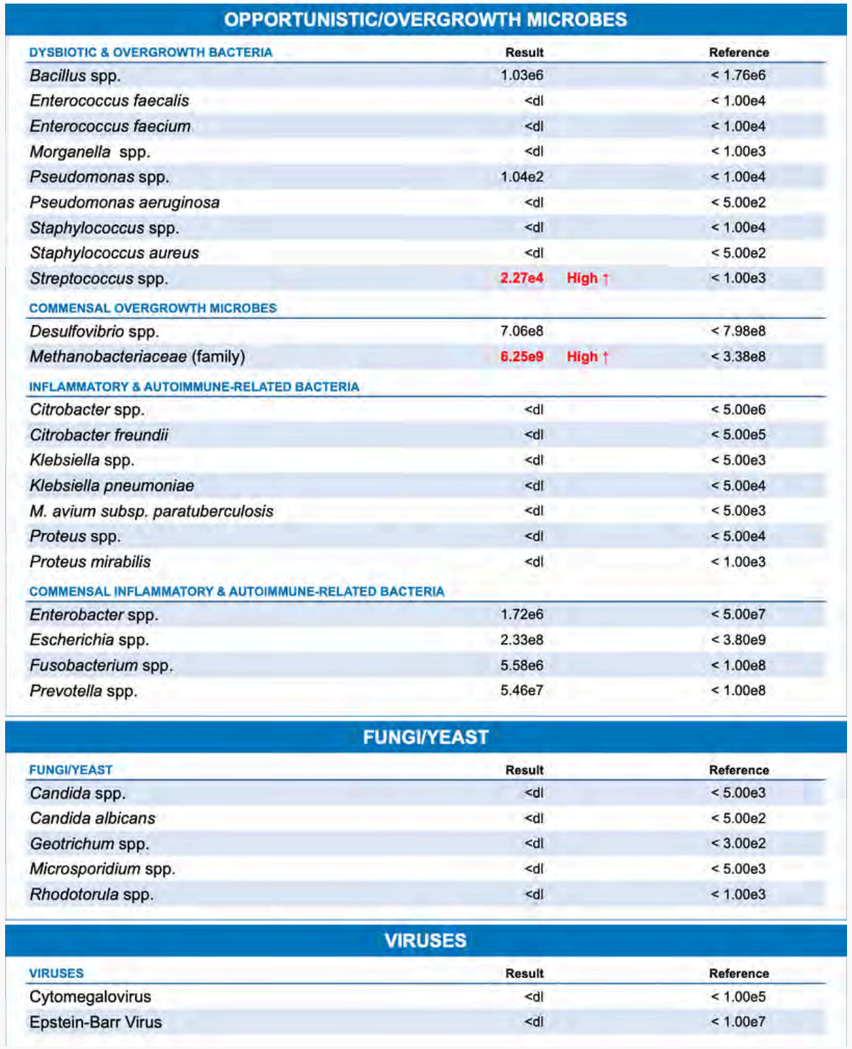
Gut Dysbiosis, SIBO, IBS/IBD
Stool Analysis

- Klebsiella pneumoniae (continued)
  - (1) Known for joint pain, ankylosing spondylitis, reactive & rheumatoid arthritis, as well as IBS chrones

AS could be a form of reactive arthritis following Klebsiella infection, especially in HLA-B27-positive individual

Elevated anti-Klebsiella antibodies have been detected in AS patients, further supporting the link between the bacteria and the disease.



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Ebringer A. (1989). The relationship between Klebsiella infection and ankylosing spondylitis. Bailliere's clinical rheumatology, 3(2), 321–338. https://doi.org/10.1016/s0950-3579(89)80024-x

Gut Dysbiosis, SIBO, IBS/IBD

Stool Analysis

- Symptoms may indicate the need to be screened for protozoans. Autoimmunity or sometimes thyroid disease may also indicate the need, besides simple GI symptoms.

PARASITES

PROTOZOA	Result	Reference
Blastocystis hominis	<dl	< 2.00e3
Chilomastix mesnili	<dl	< 1.00e5
Cyclospora spp.	<dl	< 5.00e4
Dientamoeba fragilis	<dl	< 1.00e5
Endolimax nana	<dl	< 1.00e4
Entamoeba coli	<dl	< 5.00e6
Pentatrichomonas hominis	<dl	< 1.00e2
WORMS		
Ancylostoma duodenale	Not Detected	Not Detected
Ascaris lumbricoides	Not Detected	Not Detected
Necator americanus	Not Detected	Not Detected
Trichuris trichiura	Not Detected	Not Detected
Taenia spp.	Not Detected	Not Detected

INTESTINAL HEALTH MARKERS

DIGESTION	Result	Reference
Steatocrit	<dl	< 15 %
Elastase-1	208	> 200 ug/g
GI MARKERS		
β-Glucuronidase	1722	< 2486 U/mL
Occult Blood - FIT	109 H	< 10 ug/g
IMMUNE RESPONSE		
Secretory IgA	<210 L	510 - 2010 ug/g
Anti-gliadin IgA	70	< 175 U/L
Eosinophil Activation Protein (EDN, EPX)	0.04	< 2.34 ug/g
INFLAMMATION		
Calprotectin	7	< 173 ug/g
ADD-ON TESTS		
Zonulin	260.6 H	< 175 ng/g

Gut Dysbiosis, SIBO, IBS/IBD
Stool Analysis

H. PYLORI ANTIBIOTIC RESISTANCE GENES

	Result	Reference
Amoxicillin	**Negative**	**Negative**
Genes associated with amoxicillin resistance		
PBP1A S414R	**Absent**	
PBP1A T556S	**Absent**	
PBP1A N562Y	**Absent**	

	Result	Reference
Clarithromycin	**Negative**	**Negative**
Genes associated with clarithromycin resistance		
A2142C	**Absent**	
A2142G	**Absent**	
A2143G	**Absent**	

	Result	Reference
Fluoroquinolones	**Negative**	**Negative**
Genes associated with fluoroquinolone resistance		
gyrA N87K	**Absent**	
gyrA D91N	**Absent**	
gyrA D91G	**Absent**	
gyrB S479N	**Absent**	
gyrB R484K	**Absent**	

	Result	Reference
Tetracycline	**Negative**	**Negative**
Genes associated with tetracycline resistance		
A926G	**Absent**	
AGA926-928TTC	**Absent**	

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

Bacteroidetes: Normal/OptimalRange:861B-331TUnits

- Most prominent gut microbes
- Thought to protect against microbe because they do not digest fat well
- Tends to dominate in slimmer people
- Studies in mice suggest high-fiber diet increases this microbe and were less susceptible to dust mite antigen allergies

Microbe transfer from obese humans into mice has lead to enduced obesity even with low fat (4%) and high plant diets. They also developed insulin resistance

- Whole grains promote the growth of Bacteroids
    - They contain non-digestible carbs that can promote the growth of beneficial bacteria
- Fermented Foods, avoiding artificial sweeteners, prebiotic foods, plant based

1. diets, foods rich in polyphenols (blueberries, broccoli, dark chocolate & green tea).

- Too high of levels may result from constipation and animal-based diets

Gut Dysbiosis, SIBO, IBS/IBD *Labs*

- Bifidobacterium spp.
  - Present in breast milk
  - Babies become colonozed in their GI tract at vaginal birth
  - Thrives on variety of prebiotic fibers

- Gut dysfunction & inflammation can be a result in T4 not being converted into sufficient T3, which accountes for 20% of conversion (Kresser, 2022).

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Breath Test

- Patient will take a lactose challenge drink
  - ◯ A negative test will not yield excessive methane or hydrogen gases and indicates a lack of bacterial overgrowth
  - If they have high levels of bacteria in the small intestines, The bacteria will ferment the lactulose and release hydrogen and or methane gases As a by-product. This is considered a positive test for overgrowth
- 3 maintypes: (Singer, Englar, 2018)

1. Methane Dominant (CH4)t:
   - treatment: Ideal Bowl Support/L. Plantarum
     - Pt tends to be more constipated
2. Hydrogen Sulfide Dominant:
     - Treatment is Rifampin/Flagyl verses probiotics
     - Tends to be more diarrhea dominant
     - Rotten egg smell
3. Hydrogen Dominant (H2)
     - Nonspeciifc symptoms

- Elevated is considered 3 parts per million at any point during the first 120 Minutes of the test. (Based on Dr. Pimentels findings-some are more liberal with what constitutes a negative result)
- Consider the pt and whether or not they are symptomatic if results are borderline

Gut Dysbiosis, SIBO, IBS/IBD

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Gut Dysbiosis, SIBO, IBS/IBD

Low stomach acid and slow motility leads to a perfect breading ground for the wrong bacteria to proliferate

Symptoms:

- i) Contant Burping
- ii) Bloating worse throughout day (results from fermentation)
- iii) Less symptomatic on Low FODMAP
- iv) May have felt worse after taking probiotics
- v) Uncomfortable feeling of fullness/gas after eating
- vi) Loose stools

SIBO Symptoms

Causes:

- i) PPIs, Tums, Pepcid, etc.
- ii) Gastroparesis
- iii) Celiac's
- iv) Chronic Constipation/slow digestion
- v) Low stomach acid
- vi) Abdominal surgery, especially of uterus
- vii) Stress (d/t high cortisol)
- viii) Diet high in sugar, processed carbs and alcohol
- ix) H. Pylori, e. Coli, Klebsiella infection
- x) Food poisoning
- xi) hypothyroidism

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Complications

- i) Poor absorption of fats, carbs and proteins leads to malabsorption, loose stools, gas and bloat
- ii) Vitamin deficiency
- iii) Osteoporosis
- iv) Kidney stones d/t poor calcium absorption
- v) Liver toxicity & development of Non-Alcoholic Fatty Liver Disease (1) d/t elevated gut toxins increasing lipid peroxidation, TNF increase, inflammation and upregulated hepatic lipgenesis
    - Hepatic lipogenesis, the liver's synthesis of fatty acids, is a complex process regulated by hormones, nutrients, and transcription factors, primarily activated by high carbohydrate intake and insulin, contributing to triglyceride accumulation and potentially NAFLD.
- Occurs in up to 80% of pts with IBS and is often overlooked

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Tx

- May try bismuth
- Oil of oregano(Biota-Clear is a good brand) and/or garlic/peppermint Elemental diet
- Biofilm disruptor (especially important for chronic disease)
- FODMAP diet
  - Try to avoid prebiotic foods/supplements such as inulin or fructoooliogosaccharids as they tend to be high producers for hydrogen. Wait until gut health is restored
  - Triple antibiotic treatment most successful:
    - Lactobacillus and Bifidobacteria blend
    - Saccharomyces boulardii (a beneficial yeast)
    - Soil-based probiotics, usually Bacillus species

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Tx

- Implement low FODMAP diet and slowly reintroduce foods. Then eliminate foods that cause symptoms.May also try elemental diet
  - (1) More restrictive and have to drink only the elemental drinks for 2-3 weeks
    - (a) Starves out the bad bacteria
- Herbal microbials may be implemented in conjunction with
- Pts needs to be warned that possible candida will also die off (if present) and they may feel worse before they feel better and the dyeing microorganisms will release toxins. This could last up to 3-4 weeks
- Methane Dominant SIBO: Treat with Allicin (dose on next slide)
- Hydrogen Dominate SIBO: Treat with Berberine
- Methan & Hydrogen Dominant SIBO: Allicin + Berberine
- Prevention of relapse:
  - Pt needs to be on prokinetic (supplement to help motility) for at least 90 days after treatment. Important b/c slow motility allows bacteria to stay in the intestines too long

Can also include digestive enzymes and testing for hypochloridia (low stomach acid), if stomach acid levels are low

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Tx

🧄 Allicin (Typically derived from garlic extract)
Recommended Dose (SIBO — Methane-Dominant):
Enteric-coated allicin supplement:
✅ 400–450 mg, 2–3 times per day, taken with meals
Duration: 4–6 weeks, depending on clinical response
Best in combination with a comprehensive antimicrobial protocol
Notes:
Choose a standardized allicin product (e.g., Allimax or Allimed)
Avoid raw garlic alone—it doesn't reliably yield therapeutic allicin in the gut
🌿 Berberine (From plants like Berberis, Coptis, Goldenseal)
Recommended Dose (SIBO — Hydrogen-Dominant):
Berberine HCl:
✅ 300–500 mg, 2–3 times daily, with food
Duration: 4–8 weeks is common in antimicrobial protocols

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Tx

- <u>Oregano</u>
- 1. Pain-relieving and liver-protective effects have been noted. May act as an antidepressant. May also have Antibacterial effects against harmful bacillus species
- Sweet Wormwood
- Peppermint oil
  - Effective at decreasing pain and bloat associated with IBS
- Berbine
  - May inhibit dementia by being protective
  - Supports healthy glucose, cholesterol & triglyceride levels
  - May aid in decreasing risk of colorectal cancer & h. Pylori infection

Gut Dysbiosis, SIBO, IBS/IBD

SIBO Tx

Combination Options:
Often paired with oregano oil, Neem, or barberry
Can be cycled in 2-week blocks (2 weeks on, 1 week off)

Cautions:
May cause GI discomfort or constipation in sensitive individuals
Avoid in pregnancy and breastfeeding
Monitor for interactions if on medications like metformin, anticoagulants, or immunosuppressants

Gut Dysbiosis, IBS/IBD

IBS Treatment based on symptoms:

Probiotics (Grey, 2021):

a) IBS-D
    i) Saccharomyces boulardii
        (1) Is actually a yeast
        (2) Great for travellers diarhea and post-antibiotic use
            (a) Florastor Select may also be able to help pts off of PPIs

Gut Dysbiosis, IBS/IBD

b) IBS-C
    i) Bifidobacterium lactis BB-12
        (1) Most well researched strain in the genus
        (2) Helps with promoting more regular stools
    ii) Lactobacillus rhamnosus GG is another option
c) IBS-A (alternating)
    i) Lactobacillus acidophilus NCFM Plus Bifidobacterium lactis Bi-07
    ii) Lactobacillus plantarum
        (1) Are also show to reduce cholesterol levels
d) IBS-U: neither constipation or diarrhea. May be loose, watery and harder, but both less then 25% of the time.
    i) Bifidobacterium lactis HN019
e) Post-Infectious IBS
    i) Tend to me mixed stool pattern
    ii) Saccharomyces boulardii
        (1) Another yeast
f) Treatment of IBS bloating
    i) Lactococcus casei Rosell-1058 & Bifidobacterium infantis 35624
        (1) Aid in the digestion of foods like starch and lactose

Gut Dysbiosis, IBS/IBD

F) Prebiotics
   a) Can help, but can exacerbate some so keep this individualized
   b) Act as food sources for probiotics
   c) Foods naturally containing Prebiotics
      i) Bananas and plantains have prebiotic properties
      ii) Jerusalem artichokes
      iii) Garlic
      iv) Bananas
      v) Chicory
      vi) Onions
      vii) Leeks
      viii) Peas
      ix) Lentils
      x) Oats
      xi) Dandelion leaves
      xii) Unpasturized apple cider
   d) Fermented foods, onions and garlic can worsen IBS
   e) IBS-related anxiety:
      i) can be significantly improved after prebiotic galactooligosaccharide mixture

Gut Dysbiosis, IBS/IBD

G) Worsened symptoms post probiotic use (and prebiotic common; esp if SIBO)

a) Can occur if the individual has dysbios (in an extreme imbalance)

b) Should subside within 48 hours

1. i) Start low and go slow
2. ii) May start after on FODMAP for some time

Gut Dysbiosis, SIBO, IBS/IBD

ProtozoanTx

- (a) Probiotics like S. Boulardii
- (b) Lactobacillus and Bifidobacteria blend probiotic may also be tried + a healthy yeast such as Saccharomyces boulardii + a soil-based probiotic
- (c) FODMAP diet
- (d) Anti-inflammatory diet
- (e) Elemental Formula
- (f)Antimicrobial Agents: start low and go slow as the parasites die you can induce symptoms from the toxin release, such as headache (Jarisch-Herxheimer reaction (JHR) is a temporary flu-like set of symptoms that can occur after starting treatment for certain bacterial & parasitic infections)
    - (i) Wormwood
    - (ii) Oregano oil
    - (iii) Black walnut
    - (iv) Berberine
    - (v) Grapefruit seed extract
    - (vi) Papaya seed
    - (vii) Pumpkin seed
    - (viii) Garlic

Root Cause

INVESTIGATION

Functional Medicine 3 Hour Overview

- Today’s Goal: To delve into the prevalence, trends, and underlying factors contributing to the growing illnes crisis, while exploring innovative approaches, to support our patients' overall health and resilience.

Functional Approach

Focuses on *why* illness occurs and how to help *the body* correct it, rather than just how to temporarily alleviate imbalance or symptoms.

While some providers may not fully adopt a functional medicine approach, incorporating elements of this approach in an integrative way can be beneficial in managing mental health challenges.

identifying Root Causes of Illness in Functional Medicine:

1. Chronic Inflammation

➤ Low-grade, persistent inflammation is at the root of nearly every chronic disease—from autoimmune to metabolic disorders. [4,26,30]

2. Gut Dysfunction

➤ Dysbiosis, leaky gut, infections, poor digestion—all mess with immunity, mood, hormones, and detox. [26]

3. Toxin Overload

➤ Mold, heavy metals, pesticides, plastics, and other environmental toxins overwhelm detox pathways and trigger chronic illness. Genetics is the gun, but environment pulls the trigger. [38,89]

identifying Root Causes of Illness in Functional Medicine:

4. Nutrient Deficiencies & Imbalances

➤ Even with a “good” diet, we’re often low in magnesium, B vitamins, omega-3s, and key minerals due to poor absorption, stress, or depleted soil. [26,29,31]

5. Blood Sugar Dysregulation

➤ Insulin resistance and glucose swings fuel fatigue, mood issues, hormone imbalances, and inflammation. [26]

6. Hormonal Imbalances

➤ This includes cortisol, thyroid, estrogen/testosterone, insulin—aka the hormonal soap opera playing in the background of most chronic symptoms. [115]

identifying Root Causes of Illness in Functional Medicine:

7. Mitochondrial Dysfunction

➤ When your cellular energy factories are fried from stress, toxins, and poor nutrition, everything slows down—energy, detox, immunity, brainpower. [59]

8. Stress & Nervous System Dysregulation

➤ Chronic fight-or-flight mode hijacks healing. Think: HPA axis dysfunction, vagus nerve stagnation, and burnout masquerading as illness.

9. Infections (chronic or stealth)

➤ Lyme, Epstein-Barr, Candida, SIBO, viruses that never fully cleared—these guys are like bad exes that keep popping back up. [1,58]

identifying Root Causes of Illness in Functional Medicine:

10. Epigenetics & Genetic Polymorphisms

➤ Variants like MTHFR can impact methylation, detox, neurotransmitter production—but remember: genes load the gun, environment pulls the trigger. [64]

Inflammation

Inflammation is more than we often think of...

Worldwide, 3 out of 5 people die due to chronic inflammatory diseases like stroke, chronic respiratory diseases, heart disorders, cancer, obesity, and diabetes [120]

2%

Increased Risk for Depression

FOR EVERY UNIT OF CRP THAT INCREASES [5][13]

Found to double in men with CRP >/= 3 mg/L

Also associated with increased severity of the disease and resistance to treatment [13]

Impaired Body Regulation

Necrosis: Damage to/degeneration of that tissue/cell type causes them to leak cell fragments (esp. nucleoproteins) into the blood, causing increased autoantibody formation to that cell type (esp. nucleoproteins) [122]

Immune Dysregulation

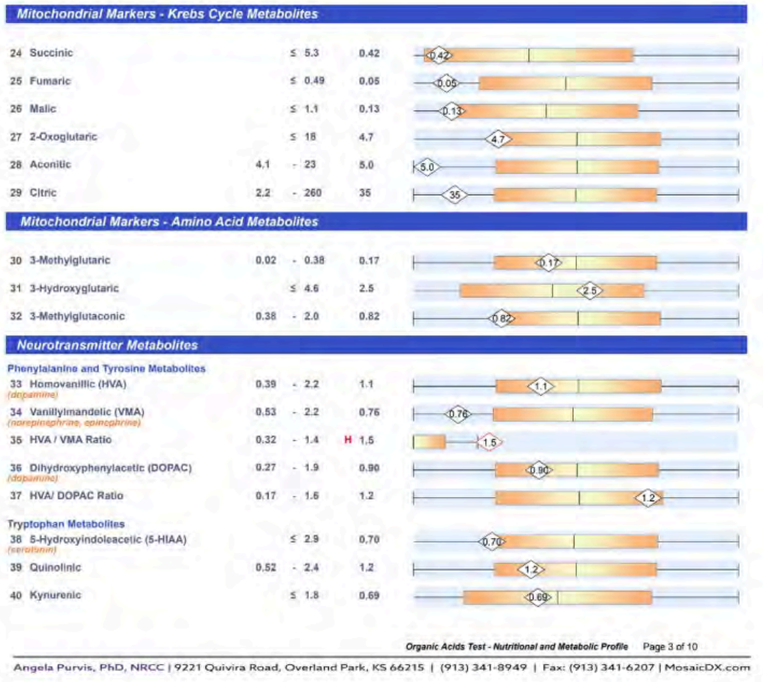
Weak innate immunity allows "stealth" or latent pathogens to linger unchallenged, leading to over-activity in the acquired immune system.

A state of immune "Danger" (high alert/reactivity), often caused by necrosis, dysbiosis, or vaccine adjuvants, which breaks down immune regulation. [122[

Measure of Neuroinflammation

- Quinolinic acid (QA) is measured on the organic acids test
  - Elevation very significantly tied to OCD [16][27]
  - Treatment for elevated QA
    - Vitamin B3 500-1000 mg TID [16]
    - Magnesium & Omega 3 (several studies on efficacy)[27][16]
    - Curcumin 1-8 g/day in divided doses [16]
      - Per Dr. Greenbalat's, MD Protocol

CRP, ESR will not always be elevated



Mitochondrial Markers - Krebs Cycle Metabolites

24	Succinic	≤	5.3	0.42	0.42
25	Fumaric	≤	0.49	0.05	0.05
26	Malic	≤	1.1	0.13	0.13
27	2-Oxoglutaric	≤	18	4.7	4.7
28	Aconitic	4.1	- 23	5.0	5.0
29	Citric	2.2	- 260	35	35

Mitochondrial Markers - Amino Acid Metabolites

30	3-Methylglutaric	0.02	- 0.38	0.17	0.17
31	3-Hydroxyglutaric	≤	4.6	2.5	2.5
32	3-Methylglutaconic	0.38	- 2.0	0.82	0.82

Neurotransmitter Metabolites

Phenylalanine and Tyrosine Metabolites

33	Homovanillic (HVA) *(dopamine)*	0.39	- 2.2		1.1	1.1
34	Vanillylmandelic (VMA) *(norepinephrine, epinephrine)*	0.53	- 2.2		0.76	0.76
35	HVA / VMA Ratio	0.32	- 1.4	H	1.5	1.5
36	Dihydroxyphenylacetic (DOPAC) *(dopamine)*	0.27	- 1.9		0.90	0.90
37	HVA/ DOPAC Ratio	0.17	- 1.6		1.2	1.2

Tryptophan Metabolites

38	5-Hydroxyindoleacetic (5-HIAA) *(serotonin)*	≤	2.9		0.70	0.70
39	Quinolinic	0.52	- 2.4		1.2	1.2
40	Kynurenic	≤	1.8		0.69	0.69

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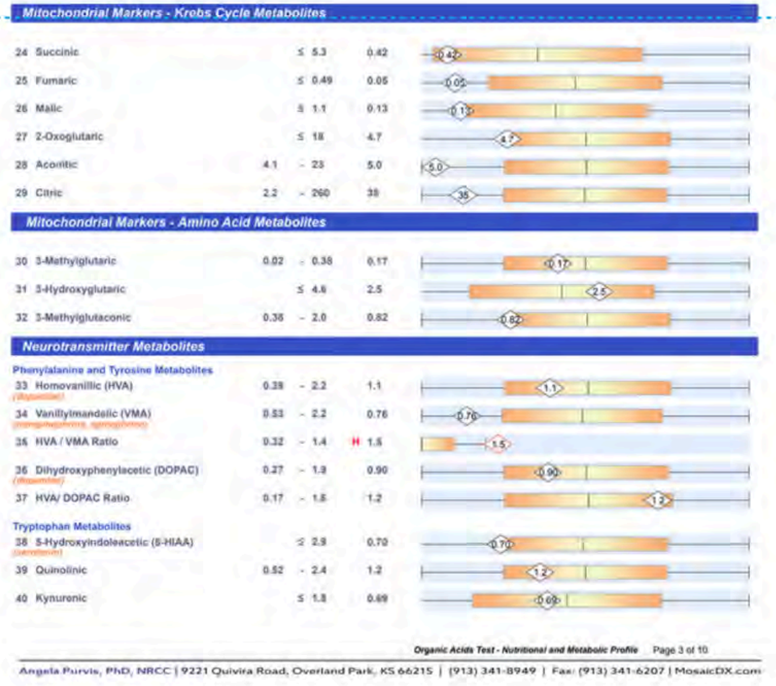
Role of Vitamin D

- It regulates inflammation
- Deficiency related to elevated TNF-a, IL-6, and CRP [28][29]
- Parker et al. found depressed individuals are 65% more likely to have vitamin D deficiency [30]
- Improvement in depression scores with supplementation [31]
- Several studies now available for effects of preventing development of depression in adolescents with vitamin D supplementation [29].
- Risks for deficiency:
  - Diet, inhibited gut absorption, ozone, sunscreen, etc. Vitamin D genetic polymorphisms and absorption rates [29]



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Dysbiosis

Gastrointestinal Dysfunction

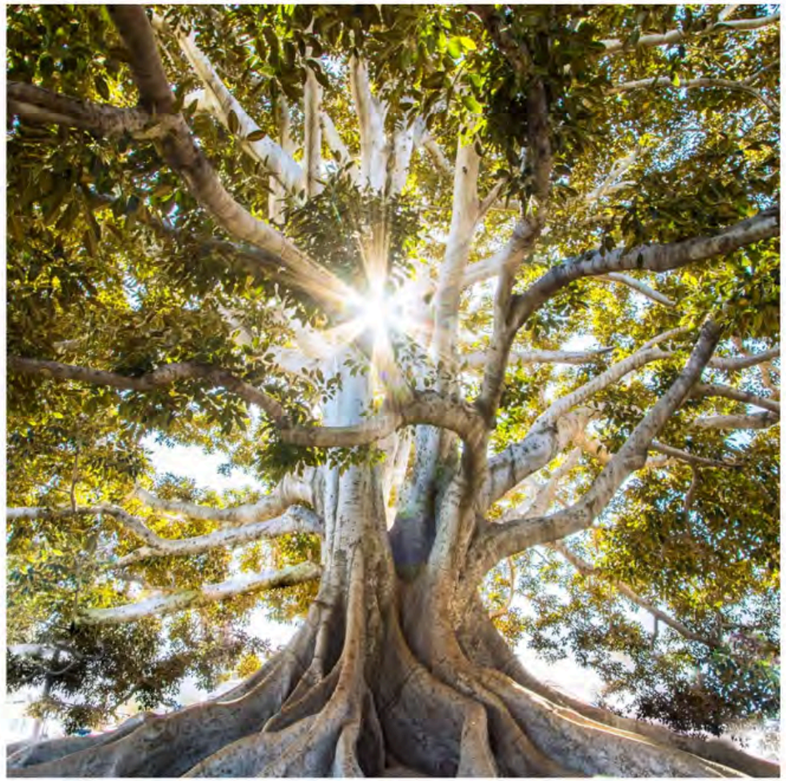
Gastrointestinal Dysfunction:
Dysbiosis (depleted healthy flora, excess pathogens) leading to the "danger" state & overactivity in the acquired immune system

Leaky Gut: intestinal hyperpermeability, leading to foreign proteins & pathogens entering the blood and leading to cross-reactivity through molecular mimicry. [63]

Increased Permeability (Leaky Gut):

- Leaky gut syndrome is a clinical theory that suggests the presence of increased intestinal permeability including symptoms of gastrointestinal issues & an inflammatory response. [44] [95]
- Cleveland Clinic recognizes intestinal permeability, or "leaky gut," as a real phenomenon, but is unclear whether it qualifies as a standalone disease or directly leads to other illnesses.
- Not officially recognized as an medical diagnosis at this time.

Microbiota Alternations



Exploring Root Cause (non-exhaustive)

- Environment/Geographical/Sterilized Environments [87]
- Other Medications:
  - PPIs/antacids
  - oral contraceptives (studies at 1 and 6 months contradictory) [91][92][93]
    - Increased risk of increased intestinal permeability, IBS and IBD [94]
- Past infections (viral and bacterial) [87][88]

Microbiota Alterations

Exploring Root Cause

- Mother's diet and flora during pregnancy and lactation influences the quantity of her microbiota, influences the microbiome of her kids during pregnancy and their young life [87]
- Antibiotic use [87]
- Whether or not a child is breast fed or vaginally delivered changes the child's the gut flora. [87]
- Nutrition makes an strong impact (MOs need fiber) and many food are natural pro/prebiotics [88].
- Vaccinations are known to alter gut flora by decreasing the variation of species.
  - How the effective a vaccination is, is related to the diversity and health of the persons flora [87][88]
  - Gut microbiota thought to prompt immune cells to release certain cytokines, influencing the host's linear growth [88][89][90]

Gut Microbiome and Mood Regulation

Gut microbiome influences neurotransmitter production

Gut bacteria produce neurotransmitters like serotonin and dopamine, affecting mood and behavior [20][96][97][98][116].

Microbiome-gut-brain communication

The gut microbiome communicates with the brain via the vagus nerve and modulates brain function and mood.

Dysbiosis linked to mood disorders

Alterations in gut microbial composition (dysbiosis) has been associated with depression, anxiety, and other mood disorders [1][20][96][97][98].

The gut microbiome profoundly influences mood and mental health through various pathways, highlighting the importance of maintaining a balanced gut ecosystem.

Toxic Exposure

Exposure to Heavy Metals

What Heavy Metal Toxicity Does in the Body:

Heavy metals like mercury, lead, arsenic, and cadmium don't just sit quietly in the body. They accumulate and disrupt normal biochemistry by:

1. Mitochondrial Dysfunction
   - They interfere with the electron transport chain, reducing ATP (energy).
   - Translation: fatigue, brain fog, and low energy despite rest.
2. Oxidative Stress
   - Generate free radicals that damage cell membranes, DNA, and proteins.
   - Leads to chronic inflammation, premature aging, and higher cancer risk.
3. Enzyme Disruption
   - Many metals mimic or bind to essential minerals like zinc, magnesium, and selenium.
   - This causes nutrient deficiencies even with a good diet.
4. Immune Dysregulation
   - Chronic exposure can weaken immune defenses or trigger autoimmunity.
   - Associated with conditions like Hashimoto's thyroiditis and rheumatoid arthritis.

Exposure to Heavy Metals

What Heavy Metal Toxicity Does in the Body:

Heavy metals like mercury, lead, arsenic, and cadmium don’t just sit quietly in the body. They accumulate and disrupt normal biochemistry by:

5. Neurotoxicity
   - Metals cross the blood-brain barrier, disrupting neurotransmitters and myelin.
   - Can cause anxiety, depression, ADHD-like symptoms, memory problems, and even Parkinsonian features. [9]
6. Hormone Disruption
   - Interferes with thyroid function, adrenal resilience, and sex hormones.
   - Leads to infertility, irregular cycles, low libido, and hypothyroid symptoms.

Exposure to Heavy Metals

Heavy Metal Detox Protocol

1. Reduce Exposure

- Remove/replace old amalgam fillings (only with a biological dentist trained in safe removal).
- Filter water (look for filters rated for lead, arsenic, mercury).
- Limit high-mercury fish (shark, swordfish, king mackerel, tuna).

Exposure to Heavy Metals

2. Strengthen the Body's Detox Foundations [2]

- Hydration: 2–3 L/day of clean, filtered water.
- Diet: Emphasize cruciferous veggies (broccoli, kale, cauliflower), garlic, onions, cilantro, parsley.
- Fiber: 30–40g/day to bind toxins in the gut and support elimination.
- Minerals: Ensure adequate magnesium, zinc, selenium—these compete with heavy metals for binding sites.
- Protein: Adequate amino acids for glutathione production (e.g., N-acetyl cysteine, whey, sulfur-rich foods).
- Milk Thistle
- Sulforaphane (from broccoli, cauliflower, and sprouts)

Exposure to Heavy Metals

3. Support Antioxidant & Detox Pathways [61]

- Glutathione (or NAC): Protects against oxidative stress, enhances detox.
- Vitamin C: 2–3g daily divided doses; reduces oxidative burden.
- Alpha Lipoic Acid (ALA): A gentle chelator and antioxidant (use cautiously, always alongside binders).

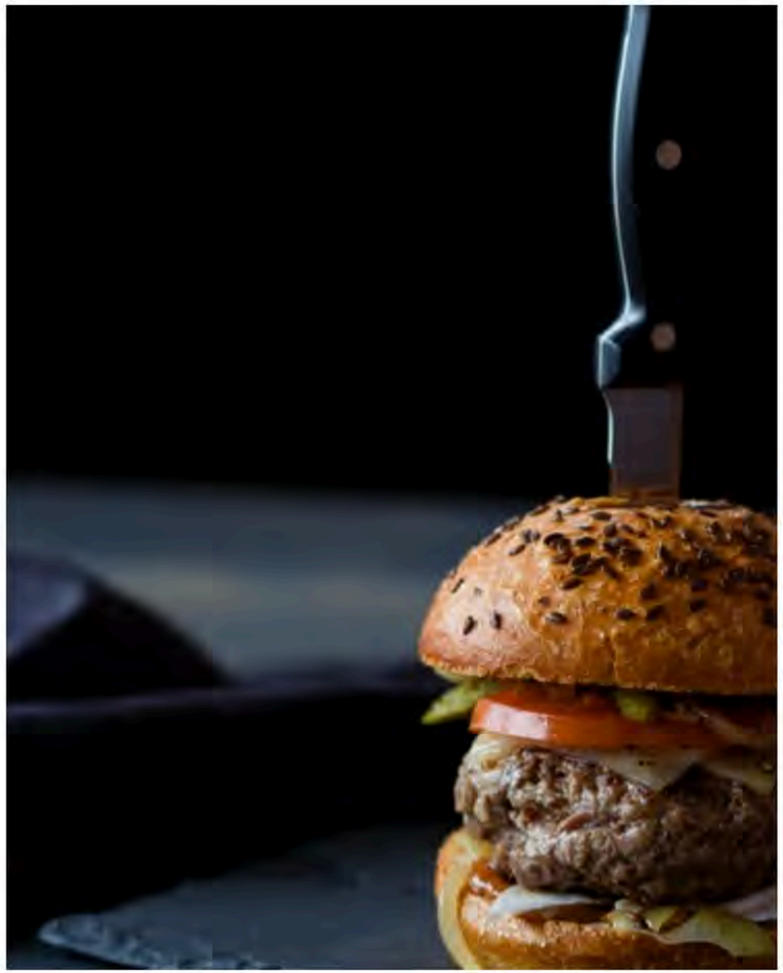
Exposure to Heavy Metals

4. Bind & Eliminate [65]
   - Gentle binders (start slow, titrate):
     - Chlorella (3–5g/day, if tolerated).
     - Activated charcoal, bentonite clay, or modified citrus pectin.
   - These help “catch” metals in the gut and prevent recirculation.
   - Ensure healthy bowel movements

5. Promote Safe Excretion
   - Sweating: Sauna or exercise 3–4x/week.
   - Regular bowel movements: Daily elimination is crucial (fiber, magnesium if needed).
   - Kidney support: Hydration + herbs like dandelion or nettle tea.

Exposure to Heavy Metals

6. Advanced Options (Only Under Practitioner Supervision)
   - IV chelation (EDTA, DMPS, DMSA) if high burden documented.
   - Targeted nutraceutical protocols tailored to specific metals.
   - Ongoing monitoring of minerals, kidney/liver function, and symptom progression.
7. Lifestyle & Environment
   - Sleep: at least 7–8 hours for repair/detox.
   - Stress reduction: meditation, prayer, deep breathing—stress impairs detox capacity.
   - Movement: improves circulation and lymphatic clearance.
   - Lymphatic Drainage



The Role of Ultra-Processed Foods

The consumption of ultra-processed foods, such as soft drinks, chips, and cookies, has been linked to a higher risk of memory and thinking problems.

American Children's diets consists of 70% of this type of food.

May of 2024: The American Academy of Neurology released a study with over 30,000 participants aged 45 and older [8].

- It was found that a 10% increase in the amount of ultra-processed foods eaten was associated with 16% higher risk of cognitive decline.
  - Results were after adjusting for HTN and other factors that could affect dementia [8]
  - MANY are advertised towards children.
  - 18% of American teens with fatty liver disease
  - Young adult cancers are up over 70%
  - *Type sub bullet*

Gluten in Non-Celiacs

- The inflammatory effects of gluten may not be limited to the gastrointestinal system. **Increased intestinal permeability leads to the entry of toxic** digestive metabolites, bacteria, and bacterial toxins into the bloodstream which may eventually reach the central nervous system
  - Benefits are found to be highest in Schizophrenic and ASD [38][36]
  - Broken down into gliadorphin, in individuals with enough DPP-IV (dipeptidyl peptidase) enzyme[16][40][53]

Gluten in Non-Celiacs

- Most studies are done on Celiac patients and it is widely acknowledged that these patients do have neurological and psychiatric symptoms when exposed to gluten [107].
- 3 Randomized-controlled trials and 10 longitudinal studies comprising of 1139 participants demonstrated that a GD diet linked deterioration of their depressive like symptoms [106].
- Sourdough is better option as is more natural forms of gluten and chemical free breads.

Testing for Gluten Sensitivity

- The Celiac & Gluten Sensitivity profile helps differentiate between celiac disease and gluten sensitivity by evaluating the serum titers of IgA and IgG for gliadin peptide, and gluten.
  - The Celiac & Gluten Sensitivity profile (Rupa) helps differentiate between celiac disease and gluten sensitivity by evaluating the serum titers of IgA and IgG for deamidated gliadin peptide, gliadin, and gluten [35,77.99]
- Obtained via blood spot or serum sample
- If DGP (Deamindated gliadin) IgA/IgG antibodies are present consider Celiac
- If Gliadin IgA/IgG/Gluten IgG antibodies are positive consider gluten sensitivity
- "Carboholics" tend to be higher risk in my experience. [14]

Prevention Continued: Avoiding Casein (Milk)

- Broken down into Casomorphin [40][52][16] Sounds like morphine b/c they are most chemically similar
- A root cause for food addiction
  - In a normal process, it is further broken down with DPP-IV (sitting in the intestinal cells) into Amino Acids
  - If a client has inactive or deficient DPP-IV or increased permeability of intestines, it is not broken down and crosses the BBB, altering behavior [40]
  - Except in mice studies when given an opioid blocker (proving its psychoactive effects) [16].
    - In the same way, morphine demonstrates a wide range of conflicted SEs (sedation versus anxiety or tachycardia versus bradycardia), casomorphin effects are individualized [40]
    - Tx: Avoidance and DPPIV supplementation for unknown exposure (Kirkman w/ ISOGEST)

Direct Effect of Environmental Exposures of Hormones On Gut-Brain Axis

- Xenoestrogens are a group of synthetic chemicals that mimic estrogen and can have adverse effects on human health. [3]
  - BPA
  - phaltes
  - Plastics
  - Pesticides
- Can bind to estrogen and testosterone.
- Test Sex Hormone Binding Globulin
  - High indicates less of free testosterone is available

Biochemical Toxins: Mold

Mycotoxins and their metabolites easily cross the blood-brain barrier (BBB) allowing for the infection of astrocytes and microglia. This leads to neuronal and brain damage as described below. [66][67]

School Mold.

Overactivation of glial cells (neuronal immune system) can lead to severe brain disease.

This activation and proliferation of glial cells is proven to influence the microenvironment of nerve tissue repair following **insult or ischemia.**

Overactivation of astrocytes and microglial cells, **forms a glial scar and oppresses the microvessels,** leading to the secretion of harmful cytokines, which affect nerve regeneration.

This process is known to occur in the development of Alzheimer, Huntington's dance, demyelinating disease, and brain trauma

Being pro-inflammatory, inducing calcium imbalance, mitochondrial damage, and the accumulation of **oxidative stress** further leads to neuronal death.

Healthy amounts of glutamate are necessary. However, **excessive glutamate (not glutamine) build-up around the brain** can cause brain cell damage or death. Mycotoxins are known to induce glutamate build-up.

Treatment May Include:

Eliminating exposure, anti-inflammatory & organic diet, air purification, Activated Charcoal, Bentonite Clay, Cholestyramine, Milk Thistle, NAC, Dandelion room, Vitamins C, Glutathione, Probiotics, Methylation support, stress reduction

Detox from Mold Exposure

1. Reduce Exposure (Non-negotiable)
   - Environment: Identify/remove water-damaged items, fix leaks, and run HEPA filtration.
   - Testing: Consider ERMI/HERTSMI-2 home testing to quantify mold load.
   - Avoidance: Sometimes requires temporary relocation if exposure is severe.
   - (You can’t out-supplement a moldy house.)

Detox from Mold Exposure

2. Stabilize & Support the Body

- Hydration: Clean filtered water, 2–3 L/day to flush kidneys.
- Diet: Low-mold diet—limit processed foods, alcohol, coffee, corn, peanuts, and aged cheeses (common mycotoxin sources). Focus on fresh, organic proteins, vegetables, and healthy fats.
- Minerals: Magnesium, zinc, selenium to support detox enzymes.
- Antioxidants: Vitamin C, NAC, glutathione (oral or liposomal).

Detox from Mold Exposure

4. Drainage & Elimination Support
   - Bowel movements: Aim for daily elimination (fiber, magnesium citrate, or gentle herbal support).
   - Sweating: Sauna therapy or exercise 3–4x/week helps excrete toxins through skin.
   - Kidneys & Lymph: Herbal teas (dandelion, nettle), gentle rebounding, dry brushing.
5. Reduce Inflammation & Repair
   - Omega-3 fatty acids: Anti-inflammatory support for brain and tissues.
   - Curcumin, resveratrol, quercetin: Help calm cytokine storms.
   - Nasal health: Saline rinses with xylitol or antimicrobial sprays (especially if MARCoNS present).

Detox from Mold Exposure

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Even Good Food

Food is a common contributor to allergic symptoms.

Food reactions are common and present in a range of ways. Be sure to differentiate between:

- food allergy
  - food-specific IgE levels,
- food intolerance,
  - Can be r/t severe underlying causes, notably gut dysbiosis
  - Can even lead to autoimmune disease that can actually be CORRECTED as opposed to suppressed
- and a food sensitivity
  - IgG or IgG4a
- is crucial for appropriate treatment. [8,29]

Leaky Gut/Increased Permeability

Avoid Triggers :

MSG

- Alters the gut microbiome [45]
- Average american intake is 3-4 G/day
- Additional data demonstrates that it increases risk for metabolic syndrome, hypertension relative to each addoional gram ingested [45]
- Possibility associated with the increases in demonstrated increase firmicutes and decrease bifidobacterium Directly associated with the onset and progression of psychiatric symptoms such as depression and anxiety in mice and human studies [48][49]
- Preliminary research suggests MSG restrictions are beneficial for somatic symptoms and chronic pain syndroms [48]

Sugars, additives, ultra-processed foods [44][50]

Interesterified Palm Oil

Increases intestinal permeabilityPromotes bacterial translationAlters inflammatory parameters and tight-junctions [46]Palm oil that is not interesterified, has been shown as protective against gut disease [47]

Binders

For Example: xanthan gum: mixed reviews, between no effect and negative effects [51]

Emotional Stress

Emotional and cognitive stress: Fight or flight reaction (Sympathetic System) shunts focus from digestion and healing of cells.

This leads to hormonal dysregulation, elevated cortisol, and other etiologies for chronic illness [123].

Nutritional Deficiencies

Is vitamin deficiency that big of a deal?

- Pellagra used to be a leading cause of death until it was pushed near eradication from Vitamin B 3 (niacin) supplementation.
- The Four D's:
  - Dermatitis
  - Dementia
  - Diarrhea
  - Death [34]
    - The cure was discovered by Dr. Joseph Goldberger, in a group of inmates with simply included more meat and vegetables into their diet. [16]

The Argument of Supplements Being a Waste of Time

- No affects on the improvement of anxiety and depression with probiotic treatment alone [144]. Same is often found in nutrient supplements.
- There is some truth to this.
  - We cannot have a "Copy and Paste/One Protocol Fits All Expectation" in Functional Medicine

Nutrient Deficiencies: B3 (niacin) Deficiency

- Pellagra (Dementia, Dermatitis, Diarrhea, & Death) [34]
- Parkinson's Disease: vitamin B3 is a promising preventive and therapeutic factor as it can alleviate certain types of early-onset PD symptoms [84]

  Supplementing niacin aids in increasing dopamine synthesis to restore the optimal NAD+/NADH ratio needed for the activity of the mitochondrial complex necessary for that to occur.

  Also being researched at as a piece of the puzzle for schizophrenia

Nutrient Deficiencies Impact on Mental Health: Vitamin B3 (Niacin) Deficiency

- **How this indirectly, but powerfully correlates to the gut-brain axis:**

  Bacteroides fragilis, Prevotella copri, and Ruminococcus lactaris synthesize vitamin B3 through a biosynthesis pathway. [35]

  Both human and mouse colonic epithelial cells feature a well-developed, specific, and controlled mechanism for absorbing vitamin B3. Vitamin B3 inversely plays a key role in supporting the nourishment of local colonocytes and preserving the structure of intestinal stem cells and overall mental health. [35]

  There is a direct relationship between lack of microbiome diversity and Vitamin B3 deficiency [16][35]

B3 (niacin) Treatment Precautions

- Treatment in Deficiency: Vitamin B3 500 mg TID [16]
- Monitor labs to prevent toxicity

Potential Side Effects: flushing, itching, nausea, headache, vomiting, light-headedness, and epigastric pain

QT prolongation risk and can become hepatoxic

Monitor toxicity, rare but possible: 2018 report from the American Association of Poison Control Center's National Poison Data System reported 792 exposures (248 age 5 or less) [85].

227 treated in hospital

71 without any problems

255 with minor toxicity

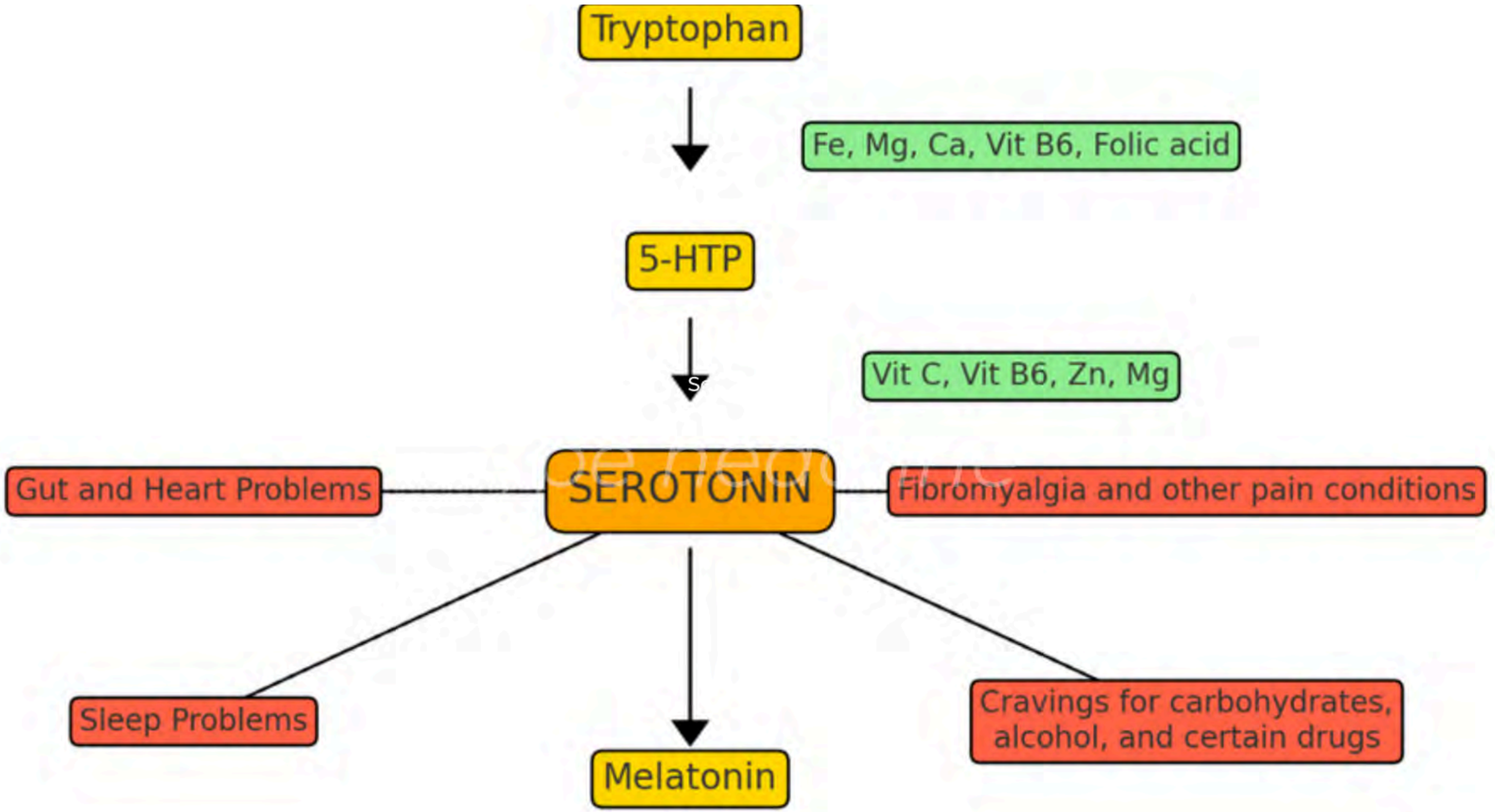
61 sustained moderate toxicity

1 significant reaction

1 death

Fiber feeds good gut bacteria

A high fiber diet provides nutrients for healthy gut bacteria.



An Example of Importance

Vitamin B6 (Pyridoxal phosphate)

It's is a cofactor for various enzymes involved in the synthesis of neurotransmitters, including dopamine. It is required for the activity of enzymes such as tyrosine hydroxylase.

Nutrient Deficiencies Impact on Health: B12 (cobalamin) Deficiency

- Sufficient B12 intake is associated with lower rates of depression and behavior problems[16] [83]

  Essential for the production of the monoamine NT [83]

  Found to aid in preventing depression [16][83]

  Deficiency is known to cause irritability and psychological disturbances such as change in personality and memory loss and exacerbate depression by increasing the accumulation of homocysteine [83]

- It is additionally necessary in the formation of RBCs, CNS development, DNE and an essential cofactor for MTHFR methylation reactions [83]

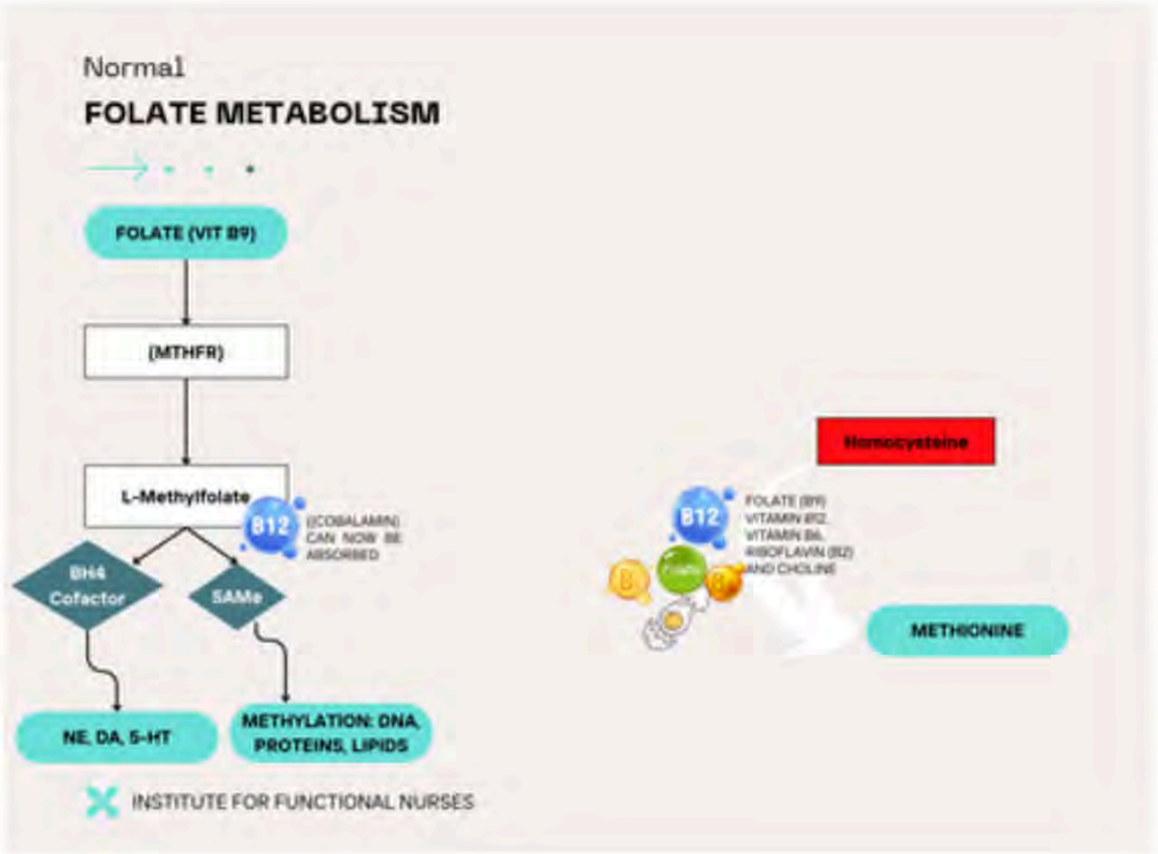
  Summarize the project and include challenges

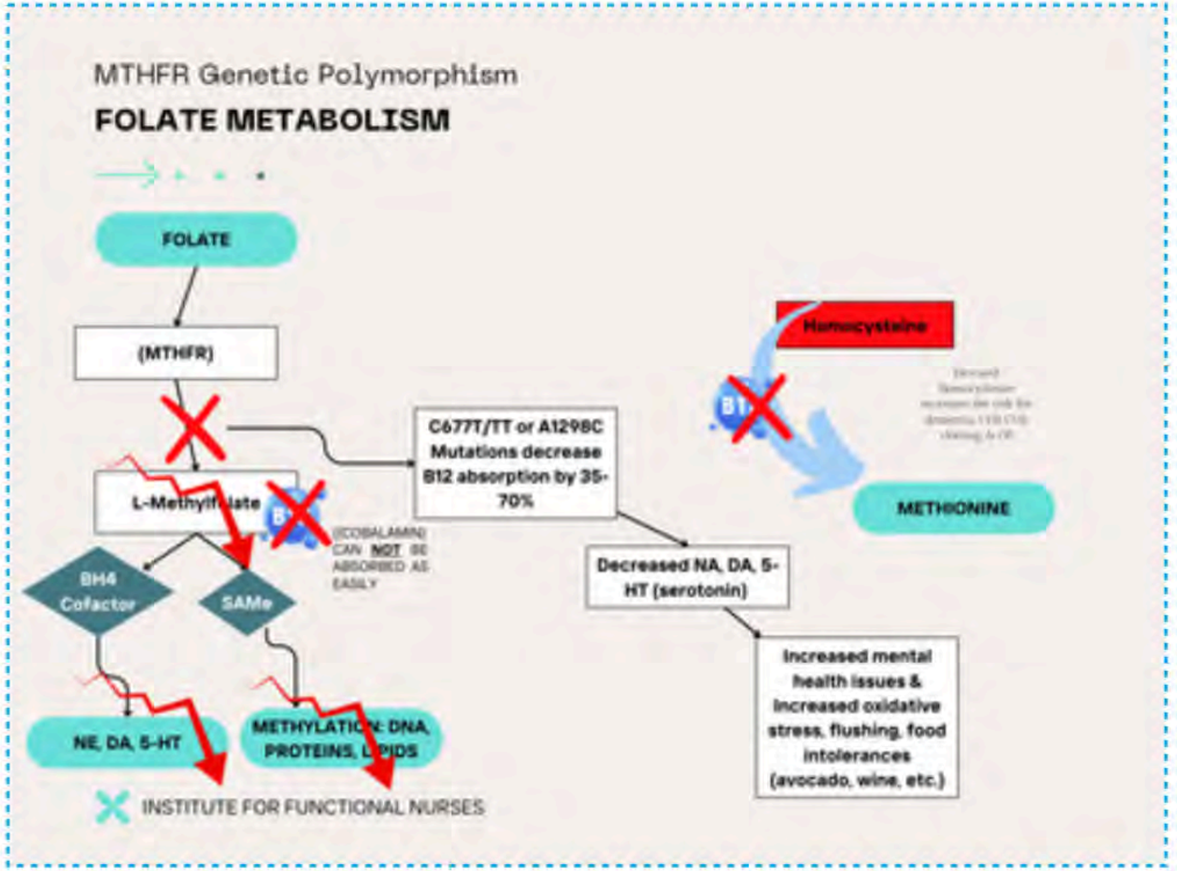
Causes of B12 Deficiency [112]

- Pernicious anemia (autoimmune disease)
- Gluten intolerance suspected to be a factor
- Bariatric surgery (Should stay on supplementation indefinetly)
- Metformin
- PPI's
- H2 Blockers for at least 3 months
- Dietary deficiency (tea & toast diets/vegan)
- ETOH Abuse
- Age >75

MTHFR Genetic Polymorphism

- L-Methylfolate is essential for the formation of neurotransmitters that are essential to mental health. [16]

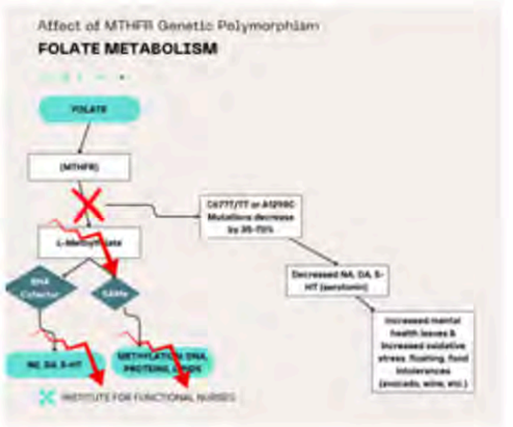




MTHFR Genetic Polymorphism

MTHFR genetic polymorphism will significantly impact B12 absorption

- Increased occurance in depression, OCD and anxiety [86][16]
- Increased oxidative stress [86]
- Inhibited DNA repair
- CC is normal
- Daily requirement of 400 ug folic acid [16]
- CT is heterozygous polymorphism (accounts for 47% of population)20-30% decreased [16]
  - Daily requirement of 80 ugTT is homozygous polymorphism (accounts for 11% of population)
- T is for “trouble”Significant decrease in folate to L-methylfolate (~66-70% decreased)[16]
  - Daily requirement of 1,200 ugTwice the risk of being TT if history of depression



MTHFR Genetic Polymorphism

- **CC (Normal)**: Individuals with this genotype have the standard version of the MTHFR gene, leading to normal enzyme activity, and usually no increased risk of health issues associated with this gene.

- **CT (Heterozygous)**: This genotype represents one normal allele and one mutated allele (C677T). These individuals may have mildly reduced MTHFR enzyme activity and a slightly increased risk of conditions like hyperhomocysteinemia, though the impact is generally mild.

- **TT (Homozygous)**: Individuals with two copies of the C677T mutation often experience a significant reduction in MTHFR enzyme activity. This can lead to higher levels of homocysteine, which is linked to an increased risk of cardiovascular diseases, pregnancy complications, and certain cancers.
  - **Folate**: Individuals with the CT or TT genotype may benefit from increased intake of folate in its active form (methylfolate) since their ability to convert folic acid into its active form is compromised.
  - **Homocysteine Levels**: Elevated homocysteine levels, a common consequence of reduced MTHFR activity, can contribute to inflammation and endothelial dysfunction, increasing the risk of cardiovascular diseases.is for Trouble

MTHFR Genetic Polymorphism

Genotype	Polymorphism (C677T)	Enzyme Activity	Possible Health Implications	Prevalence
CC (Normal)	No mutation	100%	Normal folate metabolism and homocysteine levels.	Common in most populations.
CT (Heterozygous)	One copy of the mutation	~65%	Mildly reduced enzyme function, slight risk for elevated homocysteine, and related conditions.	30-40% in various populations.
TT (Homozygous)	Two copies of the mutation	~30%	Significantly reduced enzyme function. Higher risk for elevated homocysteine, cardiovascular issues, neural tube defects, and other conditions.	10-15% in European and American populations.

MTHFR Genetic Polymorphism

- T is for Trouble
- Associated with increased risk for depression (especially in Asian populations) [110] [111]
- MTHFR A1298C polymorphism particularly significant in women of white populations [110].
- Treatment with L-methylfolate with SSRI over SSRI with placebo significantly improved results in treatment-resistant patients [110]
- Metanalysis of 91 published studies found MTHFR C677T polymorphism is significantly related to schizophrenia and major depression in the overall population [111].

B-12 Supplementation

- Absorption is about 2% at doses of 500 mcg daily

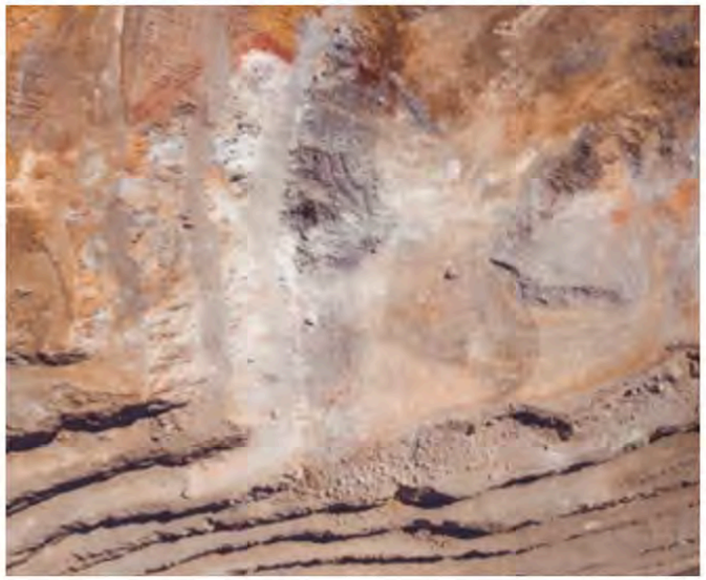
  Sublingual or PO1,000 to 2,000 mcg QD X 1-2 Weeks

  Maintenance: 1,000 mcg/day for life [112]

- Prescription Medications: Cyanocobalamin (not recommended) versus hydroxocobalamin or methylcobalamin IM, PO, or nasal gel, spray [113]
  - 100-1,000 mcg QD or EOD x 1-2 weeks
  - Maintenance: 100-1,000 mcg every 1-3 months
- Bioavailability was found to be similar between IM and PO
- Optimal range: >500-600 [41]

Zinc Deficiency

- An essential nutrient found in various plants, animal foods, and supplements
- Supplementation in deficiency is show to decrease anxiety by acting on γ-aminobutyric acid (GABA), glutamatergic, serotonergic, neurogenesis, and immune systems. [114]
- **Major part of immune regulation**



Causes of Decreased Amino Acids

Poor Intake

SAD diet [16]

Vegetarian at increased risk [16] (relative to how attentive they are to their diet)

Tryptophan Specifically:

Meat has highest amounts (chicken & turkey) but tofu still has significant amounts [33]

Fish is also high in it. Edamame, oatmeal and eggs are sufficient. [33]

Poor Digestion from Low Gastric Acid

- chronic antacid use
- Increased age (40% decrease from teenage to 30s and another 50% decline by age 70). [33]
  - HCL triggers the entire digestive cascade that starts with Pepsinogen into pepsin and then protein and AAs [33]
  - Free-form AAs are however readily absorbed without HCL or digestive enzymes [33]
    - Treatment: Provide 5 HTP 50-200 mg daily divided BID-TID [16]
      - SE: GI upset possible

Hormonal Imbalance

Sex Hormone Restoration

- Letting the body heal
- Sex hormones are like children
  - if you have others and one requires too much attention, the others don't get the attn they need
  - The 1st hormone to become depleted tends to be progesterone, which leads to estrogen dominance
    - progesterone is a calming hormone

Estrogen Dominance

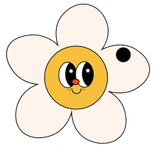
Significant driver and why 80% of AD are women

- In men low testosterone is a driver for chronic disease and can in itself lead to back and neck pain

3 estrogens & 2 types of estrogen receptors in breast tissue

- Receptors A and B
  - Think A= accelerator (bad for breast tissue health)
  - B= brake
- Estradiol
  - lowers CVD risk and helps improve bone health
    - but can easily convert to estrone

  - 1:1 ratio of A to B stimulation



- Estriol stimulates A & B receptors at a 1:3 ratio
  - More "brake" on the accelerator

- Estrone stimulates at 5:1 ratio
  - 5x more accel than break

Estrogen Dominance

Reblanacing Estrogen Dominance [3, 115]

- Calcium-D-Glucarate
  - promotes phase 2 glucuronidation biotransformation to help make molecules more water-soluble
  - also, a beta-glucuronidase inhibitor blocks the reabsorption of detoxified estrogens by binding it up and allowing it to be excreted
- Diindolylmethane (DIM)
  - make in the body from plans such as cruciferous vegetables
  - helps to metabolize estrogen
    - may help destroy cancer cells and reduce inflammation
- Glutathione & promoters
  - removal of free radicals
  - N-Acetyl-L-Cysteine (NAC) and resveratrol
    - important antioxidants to reduce the formation of estrogen
- Vitamin D for ingibitits breast cancer cell growth

Toxic Stress

The body is not intended to be a hazmat dump

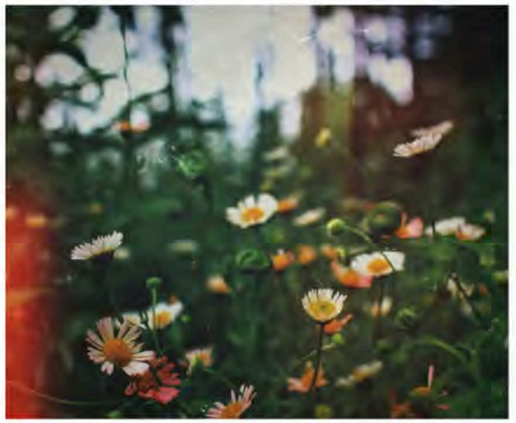
- Heavy Metals
- petrochemicals
- endocrine disruptors
- food additives, food colorings, sweeteners, sugar
- herbicides, pesticides, fungicides, volatile organic compounds (VOCs)
    - glade plug-ins, dryer sheets, etc.; tons of them
- Commercial cleaning products.
- Methylation improvement and boost of glutathione.

- One final note: much of the damage in autoimmunity is often not able to be replaced. Important to take action ASAP!

Role of Hormones On Gut-Brain Axis

- 5-HT, γ-aminobutyric acid (GABA), and tryptophan metabolites are synthesized and released by the gut microbes.
  - *Candida* and *Escherichia* utilize tryptophan from food tp produce 5-HT
  - *Bacillus* produces dopamine

- Progesterone could promote the growth of oral *Bacteroides* species and *Prevotella intermedius*.



The Estrobolome

- **Estrogen promotes the activity of serotonin and dopamine in the brain, which encourages emotions of happiness and motivation.**
- The Estrobolome is a collection of microbial bacteria that are capable of metabolizing and modulating reactions involving estrogens [133]
- microbial β-glucuronidase (GUS) enzymes are found to be a part of the system
- One study found the the ability of 35 human gut microbial GUS enzymes to reactivate two distinct estrogen molecules [133]

Direct Effect of Environmental Exposures of Hormones On Gut-Brain Axis

- Xenoestrogens are a group of synthetic chemicals that mimic estrogen and can have adverse effects on human health. [3]
  - BPA
  - phaltes
  - Plastics
  - Pesticides
- Can bind to estrogen and testosterone.
- Test Sex Hormone Binding Globulin
  - High indicates less of free testosterone is available