Casual Friday Presents

Type 1.5 Diabetes

and support considerations pt II

A BIOGENETIX CLINICAL PRESENTATION

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CLEVELAND CLINIC JOURNAL OF MEDICINE

Latent autoimmune diabetes in adults: Not type 1, not type 2, a little of both

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Clevela

Latent autoimmune diabetes in adults (LADA) is a slowly progressive form of autoimmune diabetes that shares features of type 1 and type 2 diabetes, often leading to misdiagnosis and a delay in starting needed insulin therapy. This review summarizes LADA's presentation, diagnostic criteria, and management, emphasizing the importance of testing for antibodies early in the course of disease when patients have atypical features of type 2 diabetes.

KEY POINTS

- LADA is a slowly progressive autoimmune-mediated form of diabetes that is often misdiagnosed as type 2 diabetes.
- To detect LADA promptly, diabetes-associated antibody testing should be obtained in patients with diabetes who are lean and do not have metabolic syndrome or in those with a personal or family history of autoimmune disease.
- Noninsulin therapies can be used in the early stages, but patients eventually require insulin months to years after their diagnosis, as guided by C-peptide and hemoglobin A1c monitoring.
- Rather than waiting for noninsulin therapies to fail, proactive antibody testing and subsequent monitoring can ensure that patients with LADA benefit from the appropriate use of insulin.
- Further research is needed on beta-cell preservation and immunosuppressive therapies to slow the progression of LADA.

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How type 1.5 differs differs

Feature	Type 1	Type 2	LADA (Type 1.5)
Cause	Autoimmune	Insulin resistance	Autoimmune
Onset	Rapid (often childhood)	Gradual	Gradual (adult)
*Insulin needed	Immediately	Sometimes later	*Eventually required
Body type	Often lean	Often overweight	*Often lean or average

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Testing:

If a patient is on insulin, just run the tests.

Autoantibodies

- GAD-65 ab
- Insulin ab
- Antipancreatic Islet cell antibodes
- Zn Transporter 8 Ab (targets beta cells)

- **C-peptide levels** (to measure insulin production)

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Cheat sheet

Type 1 – fast AI
Type 1.5 – slow AI
Type 2 – insulin resistance

Case:
64 yo male
5’10” - 250 lbs
Dx: type 2 dm
RX: metformin, glipizide, insulin

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Cheat sheet

Type 1 – fast AI
Type 1.5 – slow AI
Type 2 – insulin resistance

Case:
70 yo female
5’5” - 104 lbs
Dx: type 2 dm
RX: metformin, insulin

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A1C Chart based on ADAG formula

A1C-Derived Average Glucose (ADAG) Study;
eAG in mg/dl = (28.7* hba1c)-46.7 or
eAG in mmol/l = (1.59 x HbA1c)-2.59

A1C	4.0	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	4.9	5.0	5.1
mg/dl	68	71	74	77	80	82	85	88	91	94	97	100
mmol/l	3.8	3.9	4.1	4.3	4.4	4.6	4.7	4.9	5.1	5.2	5.4	5.6
A1C	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	6.0	6.1	6.2	6.3
mg/dl	103	105	108	111	114	117	120	123	125	128	131	134
mmol/l	5.7	5.8	6.0	6.2	6.3	6.5	6.7	6.8	6.9	7.1	7.3	7.4
A1C	6.4	6.5	6.6	6.7	6.8	6.9	7.0	7.1	7.2	7.3	7.4	7.5
mg/dl	137	140	143	146	148	151	154	157	160	163	166	169
mmol/l	7.6	7.8	7.9	8.1	8.2	8.4	8.5	8.7	8.9	9.0	9.2	9.4
A1C	7.6	7.7	7.8	7.9	8.0	8.5	9.0	9.5	10.0	11.0	12.0	13.0
mg/dl	171	174	177	180	183	197	212	226	240	269	298	326
mmol/l	9.5	9.7	9.8	10.0	10.2	10.9	11.8	12.5	13.3	14.9	16.5	18.1
Super Optimal		Optimal		Normal		Pre Diabetes		Diabetes		Dangerous		

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Clinical Pearls

1. If they’re on insulin, check for type 1.5.
    - GAD65 ab, Insulin ab, pancreatic islet cell ab.
2. Correlate gi function to what you see in front of you.
3. Any other symptoms that are pertinent?
4. Onset…
5. Glucose window.
6. Treatment considerations.

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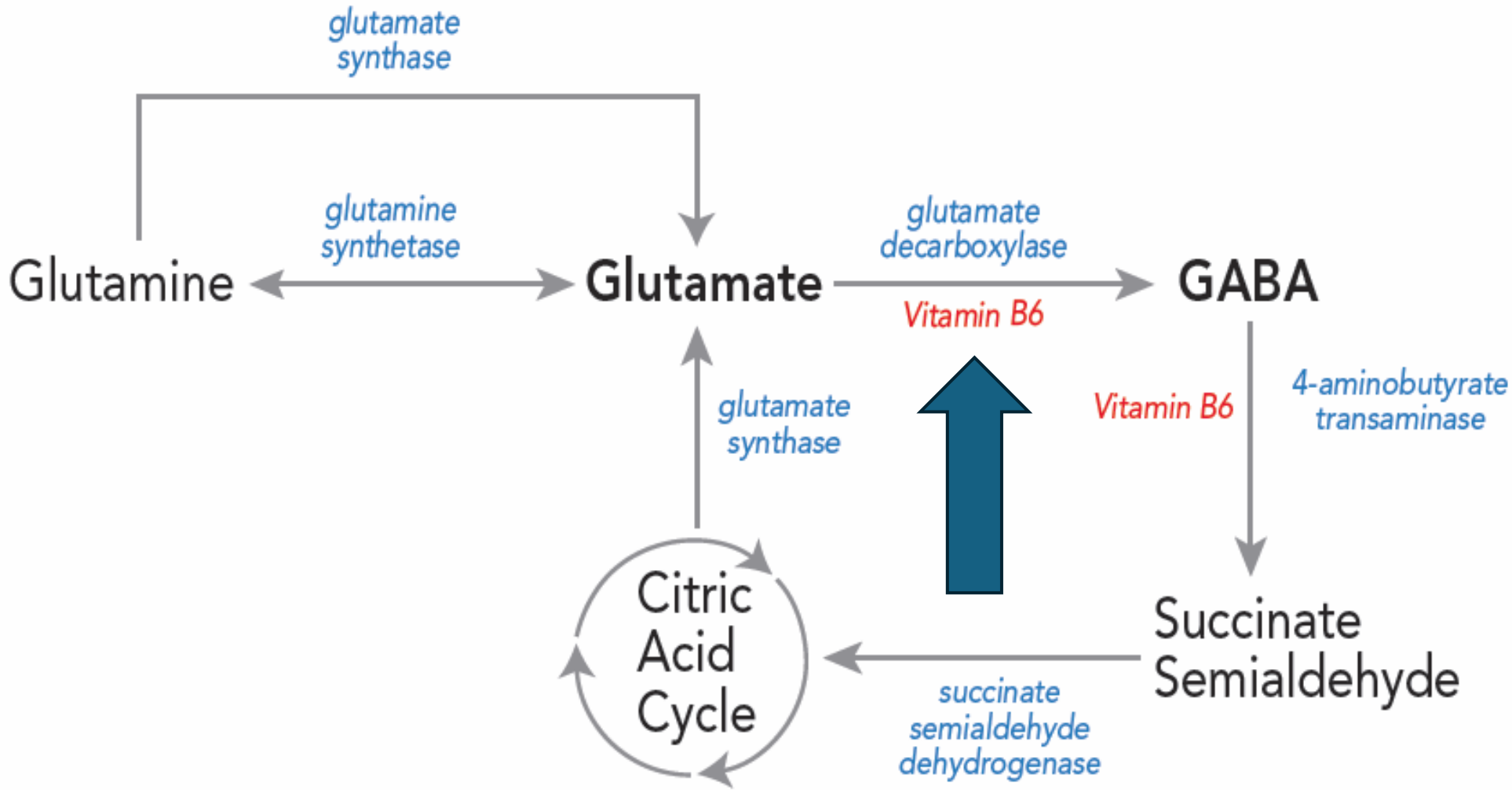

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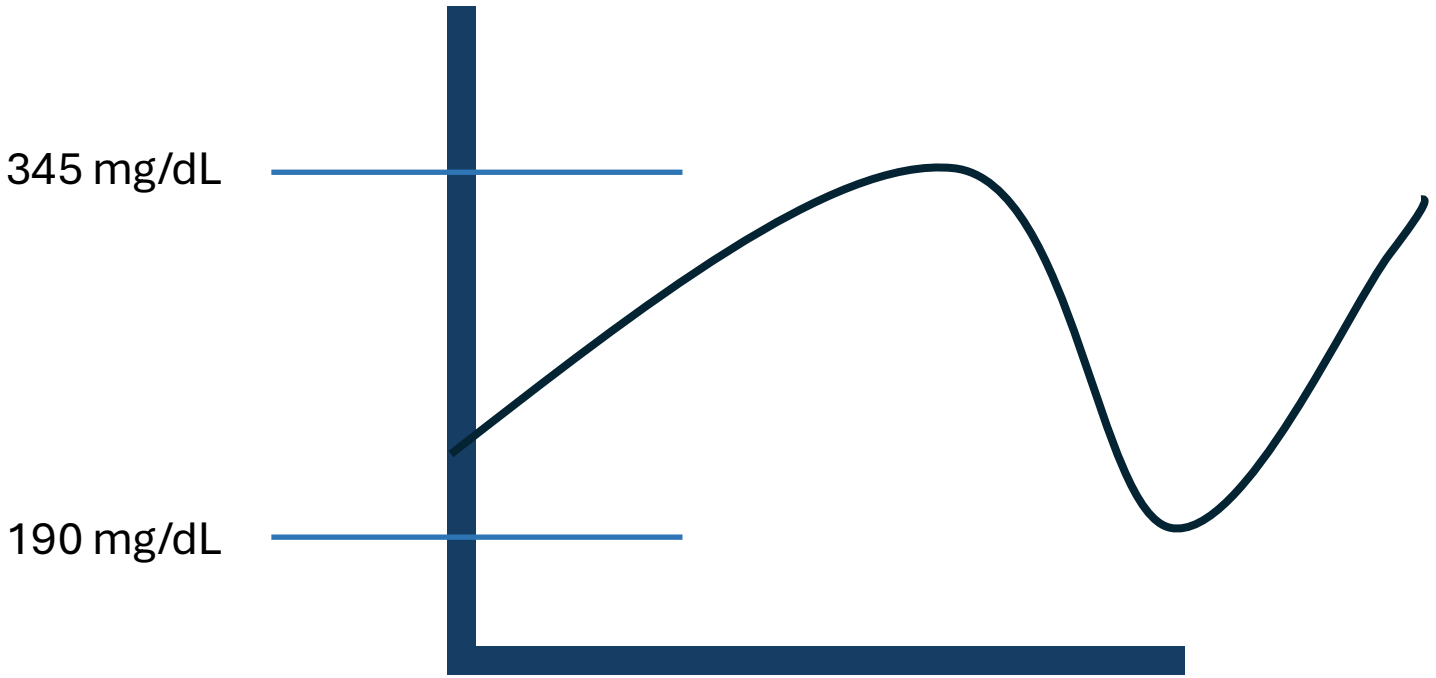
https://pmhealthnp.com/wp-content/uploads/2018/08/gaba-glutamate-synthesis.png

Glucose Window



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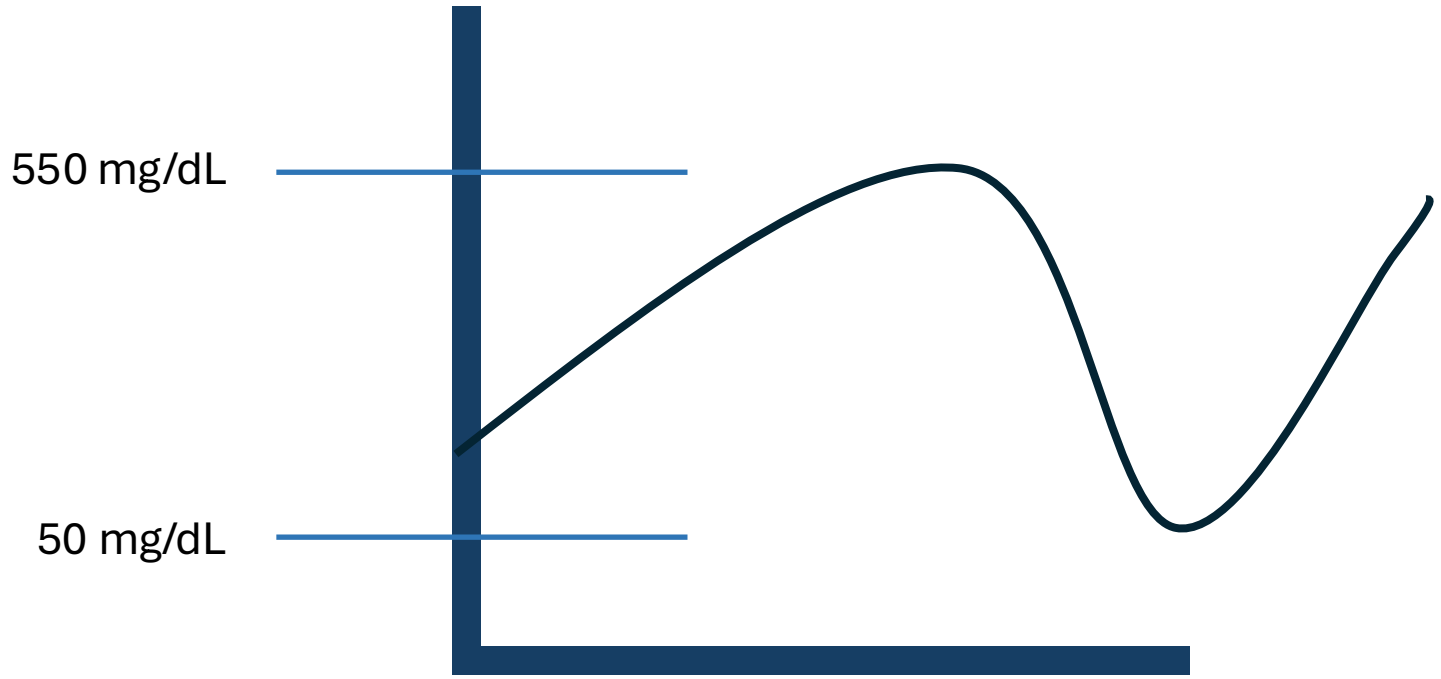
Glucose Window



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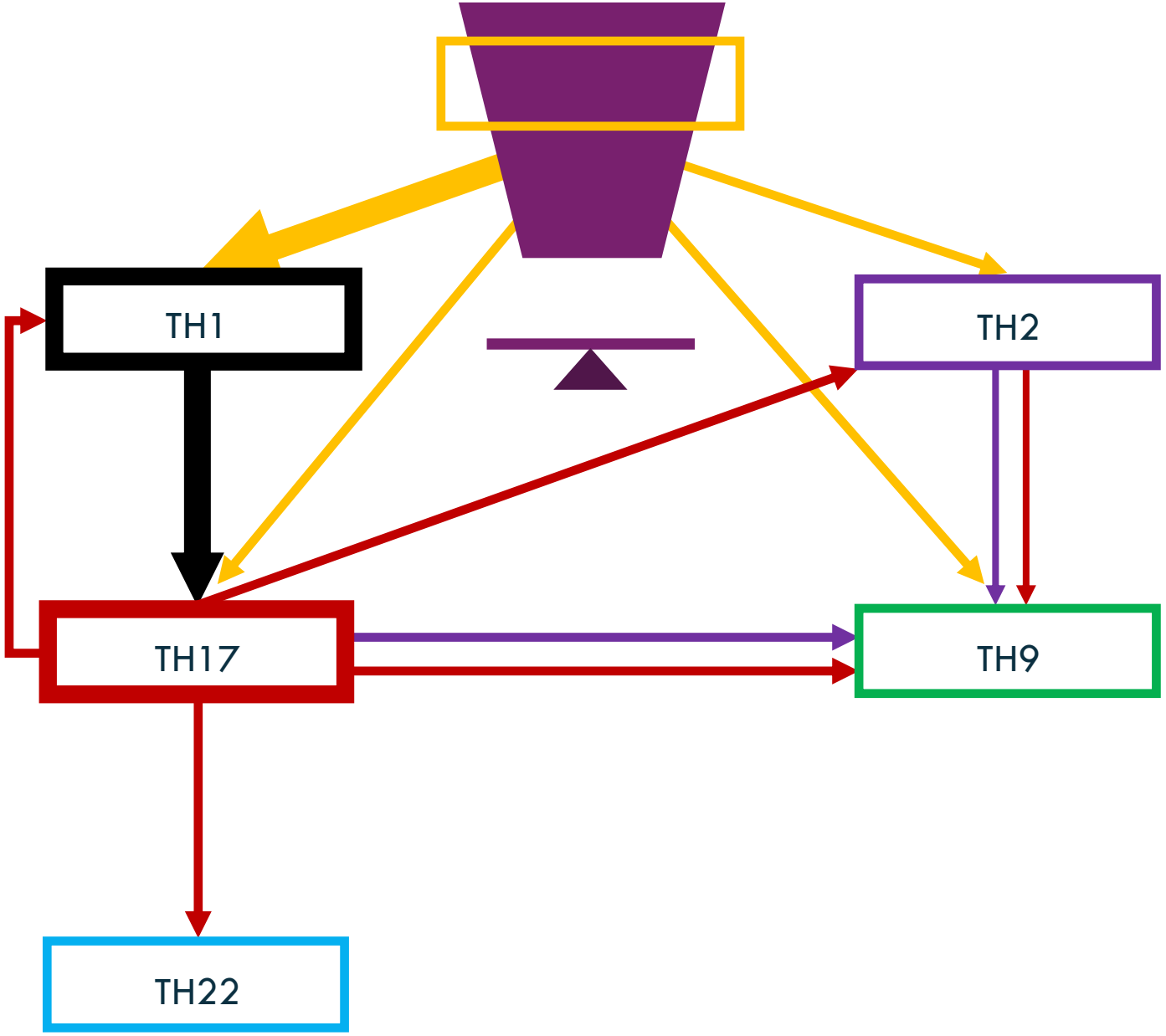

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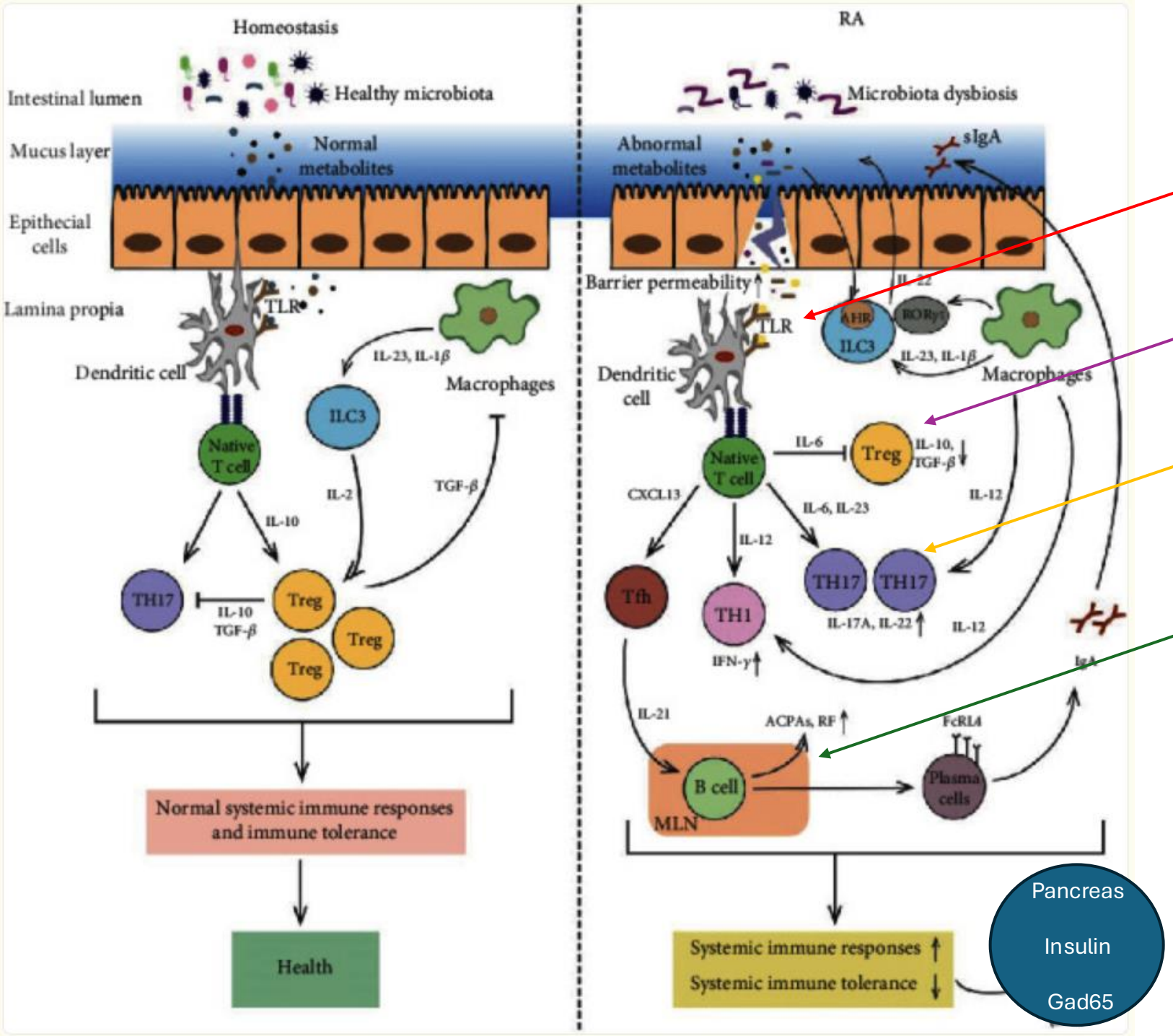
Homeostasis
Intestinal lumen
Healthy microbiota
Mucus layer
Normal metabolites
Epithecial cells
Lamina propia
TLR
Dendritic cell
IL-23, IL-1β
Macrophages
ILC3
Native T cell
IL-2
TGF-β
IL-10
TH17
IL-10 TGF-β
Treg
Treg
Treg
Normal systemic immune responses and immune tolerance
Health
RA
Microbiota dysbiosis
Abnormal metabolites
sIgA
Barrier permeability
IL-22
AHR
RORγt
ILC3
TLR
Dendritic cell
IL-23, IL-1β
Macrophages
Native T cell
IL-6
Treg
IL-10, TGF-β
CXCL13
IL-6, IL-23
IL-12
IL-12
Tfh
TH1
IFN-γ
TH17
TH17
IL-17A, IL-22
IL-12
IgA
IL-21
ACPAs, RF
FcRL4
B cell
MLN
Plasma cells
Systemic immune responses
Systemic immune tolerance
Pancreas
Insulin
Gad65

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Diabetes Care. 2021 Oct 7;44(12):2738–2746. doi: 10.2337/dc20-2975

Characteristics of the Gut Microbiota and Metabolism in Patients With Latent Autoimmune Diabetes in Adults: A Case-Control Study

Yuanyuan Fang [1], Chenhong Zhang [2], Hongcai Shi [3], Wei Wei [1], Jing Shang [1], Ruizhi Zheng [1], Lu Yu [1], Pingping Wang [1], Junpeng Yang [1], Xinru Deng [1], Yun Zhang [1], Shasha Tang [1], Xiaoyang Shi [1], Yalei Liu [1], Huihui Yang [1], Qian Yuan [1], Rui Zhai [4], Huijuan Yuan [1,✉]

OBJECTIVE

Type 1 and type 2 diabetes are associated with gut dysbiosis. However, the relationship between the gut microbiota and latent autoimmune diabetes in adults (LADA), sharing clinical and metabolic features with classic type 1 and type 2 diabetes, remains unclear. Here, we used a multiomics approach to identify the characteristics of the gut microbiota and metabolic profiles in patients with LADA.

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Amplicon sequence variants (ASV):

An amplicon sequence variant is any one of the inferred single DNA sequences recovered from a high-throughput analysis of marker genes. Because these analyses, also called "amplicon reads," are created following the removal of erroneous sequences generated during PCR and sequencing, using ASVs makes it possible to distinguish sequence variation by a single nucleotide change.

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The gut microbiota is an indispensable environmental factor for the development of T1D and T2D (5,6); the structure and composition of the gut microbiota in patients with T1D and T2D differ from those in healthy subjects. Studies in T1D animal models showed that the gut microbiota can regulate toll-like receptor 2/4 signaling, T helper type 17 cells in the intestinal mucosa, sex hormone levels, and the secretion of pancreatic antibacterial peptide, which may modulate the autoimmune targeting of β-cells (7–9). Additionally, in T2D, intestinal dysbiosis can disrupt the gut barrier function and promote chronic metabolic inflammation and the secretion of intestinal hormones, including glucagon-like peptide 1 and peptide YY, affecting insulin sensitivity and secretion (10,11). Importantly, studies have shown that dietary interventions (probiotics, dietary fiber supplements, etc.) and fecal transplants can regulate the gut microbiota; vaccines and various drugs that regulate key factors that affect intestinal barrier function can be used as novel treatment strategies (12). However, no such studies have been conducted in patients with LADA, so the relationships between the gut microbiota, metabolic profile, and LADA remain to be determined.

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Characterization of the Gut Microbiota of Patients With LADA

No differences in the richness (observed ASVs), diversity (Shannon index), and evenness (Pielou index) were found among the four groups (Supplementary Fig. 1). However, the PCoA and score plots of the PLS-DA (Fig. 1*A* and Supplementary Fig. 2) showed that the structure and composition of the gut microbiota differed significantly among the three diabetes groups and healthy group. Furthermore, the structure of the microbiota differed significantly between the LADA group and the other two diabetes groups. Clinical groups, inflammatory factors, autoantibody GADA, and medication use were significantly associated with gut microbial variations ($P < 0.1$ of permutational MANOVA) (Fig. 1*B*). As GADA is a very strong explanatory factor for variations in the gut microbiota, the classic T1D group was further divided into T1D-A (GADA-P) and T1D-B (GADA-N) groups. The microbiota structure of the T1D-A group was the most similar to that of the LADA group, whereas that of the T2D group was the most dissimilar to that of the LADA group (Fig. 1*C* and *D*). The clinical features of the LADA, T1D-A, and T1D-B groups are shown in Supplementary Table 2. The T1D-B group showed lower BMI, $AUC_{C\text{-peptide}}$, and serum LBP levels than the LADA and T1D-A groups and a longer duration of diabetes than the LADA and T1D-A groups.

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Supplementary Table 1—Clinical characteristics, autoantibodies, medication, and defecation in the studied sample

Variable	Healthy controls (n = 29)	Type 2 diabetes patients (n = 31)	LADA patients (n = 30)	Classic type 1 diabetes patients (n = 29)	*P*
RBC ($\times 10^{12}$/L)	4.70 (4.30–4.98)	4.72 (4.46–4.98)	4.56 (4.35–4.90)	4.42 (4.21–4.85)	0.28
Hemoglobin (g/L)	144.00 (127.50–152.50)	144.00 (132.00–149.00)	136.50 (126.00–149.00)	135.00 (124.50–146.50)	0.547
WBC ($\times 10^{9}$/L)	5.70 (4.68–6.40)[a,c]	7.00 (5.47–7.85)[b]	5.01 (4.41–6.47)[a]	6.36 (5.24–7.59)[b,c]	0.004
ALT (U/L)	16.80 (12.80–21.60)	19.00 (14.10–30.10)	17.00 (13.25–20.55)	15.85 (12.33–21.73)	0.300
AST (U/L)	21.15 (17.28–23.55)	19.20 (15.50–22.70)	17.80 (15.25–22.40)	18.60 (15.20–24.30)	0.469
GGT (U/L)	17.05 (13.03–21.00)[a]	23.40 (15.30–39.70)[b]	15.70 (12.30–21.40)[a]	15.20 (10.63–21.80)[a]	0.009
Creatinine (μmol/L)	60.00 (52.00–69.50)[a]	56.00 (44.00–60.00)[b]	54.00 (44.88–61.25)[b]	49.00 (42.00–59.50)[b]	0.007
Uric acid (μmol/L)	306.50 (263.50–385.75)[a]	279.00 (224.00–370.00)[a,c]	221.00 (175.00–7–272.50)[b]	263.00 (203.50–315.00)[b,c]	0.001
Autoantibodies					
GADA positive (%)	0 (0)[a]	0 (0)[a]	30 (100)[b]	18 (62.07)[c]	<0.001
IA-2A positive (%)	0 (0)[a]	0 (0)[a]	13 (43.33)[b]	7 (24.14)[b]	<0.001
Zn-T8 positive (%)	0 (0)[a]	0 (0)[a]	5 (16.67)[b]	5 (17.24)[b]	0.003
Medication					
1. Insulin (%)	0 (0)[a]	26 (83.87)[b]	27 (90.00)[b,c]	29 (100)[c]	<0.001
2. Acarbose (%)	0 (0)	6 (19.35)	3（10.00)	3 (10.34）	0.080
3. Metformin (%)	0 (0)[a]	5 (16.13)[a]	10 (33.33)[b]	1 (3.45)[a,b]	<0.001
4. DDP4 inhibitors (%)	0(0)[a]	5 (16.13)[b]	5 (16.67)[b]	0(0)[a]	0.033
5. Aspirin (%)	0 (0)	0 (0)	0 (0)	1 (3.45)	0.487
6. Lipid-lowering agents (%)	0 (0)	4 (12.90)	2 (6.67)	2 (6.90)	0.267
7. Hypotensor (%)	0 (0)	5 (16.13)	2 (6.67)	2 (6.90)	0.132
8. Levothyroxine (Euthyrox) (%)	0 (0)	0 (0)	3 (10.00)	0 (0)	0.041

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Remarkably, the gut microbiota of patients with LADA showed distinctive characteristics (e.g., significantly decreased abundance of *Faecalibacterium* spp., *Roseburia* spp., and *Blautia* spp.) compared with the other groups. These are short-chain fatty acid (SCFA)–producing bacteria. SCFA-producing bacteria are known to positively affect glucose metabolism; they strengthen the gut barrier function, reduce chronic inflammation, and modulate intestinal hormones to improve insulin sensitivity and reduce pancreatic autoimmunity (27–29). The structure and composition of the gut microbiota in patients with T1D and T2D are different from that in healthy subjects, with a decrease in the abundance of SCFA-producing bacteria (9,30). Our study found that patients with LADA show a severe deficiency in SCFA-producing bacteria compared not only with healthy subjects but also with patients with classic T1D and T2D. Accordingly, the severe SCFA-producing bacterial deficiency in the guts of patients with LADA may contribute to the occurrence and progression of the disease. However, further studies are needed to identify the key microbiota players and investigate their disease-linked mechanisms of action.

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Additionally, we found that the autoantibody GADA strongly associates with the structure and composition of the microbiome but negatively correlates with SCFA-producing bacteria. GADA is one of the most potent autoantigens involved in β-cell–specific autoimmunity. LADA is defined as a heterogeneous disease with respect to susceptibility genes, effects on autoimmunity, and phenotype. The potential causes of LADA involve heterogeneous pathways in the initiation of islet autoimmunity and heterogeneity in cellular responses (31). Interestingly, animal studies found that the SCFAs acetate and butyrate produced by gut microbes protected nonobese diabetic mice from insulitis and slowed the progression of diabetes, whereas butyrate in the diet improved regulatory T cell count and enhanced regulatory T cell function (32). Additionally, several cross-sectional studies have shown that the GADA titer correlates with the phenotypic heterogeneity of autoimmune diabetes, particularly in patients with LADA (33,34). Importantly, in the current study, the findings were similar. Therefore, we hypothesized that the gut microbiota may significantly affect the clinical classification and therapy of autoimmune diabetes. Our understanding of these diseases is insufficient and needs further exploration, and the gut microbiota may provide new insights.

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We also identified specific metabolites in the feces and blood, such as BCAAs and AAAs produced by gut bacteria, that were different in patients with LADA versus others with diabetes. Of note, they correlated with glucose metabolism. Other studies have found that BCAAs and AAAs are associated with insulin sensitivity/resistance (35). Large human population studies found that a high intake of dietary BCAAs increases the risk of T2D (36,37). Conversely, animal studies demonstrated that a diet specifically enriched in leucine (BCAA) could improve glucose homeostasis (38). Moreover, lowering dietary BCAAs has been shown to improve insulin sensitivity and increase energy expenditure (39). The mechanism is probably related to the activation of mammalian target of rapamycin, affecting insulin sensitivity (40). Therefore, BCAAs and AAAs might affect glucose metabolism and sensitivity and promote autoantibody expression in patients with LADA.

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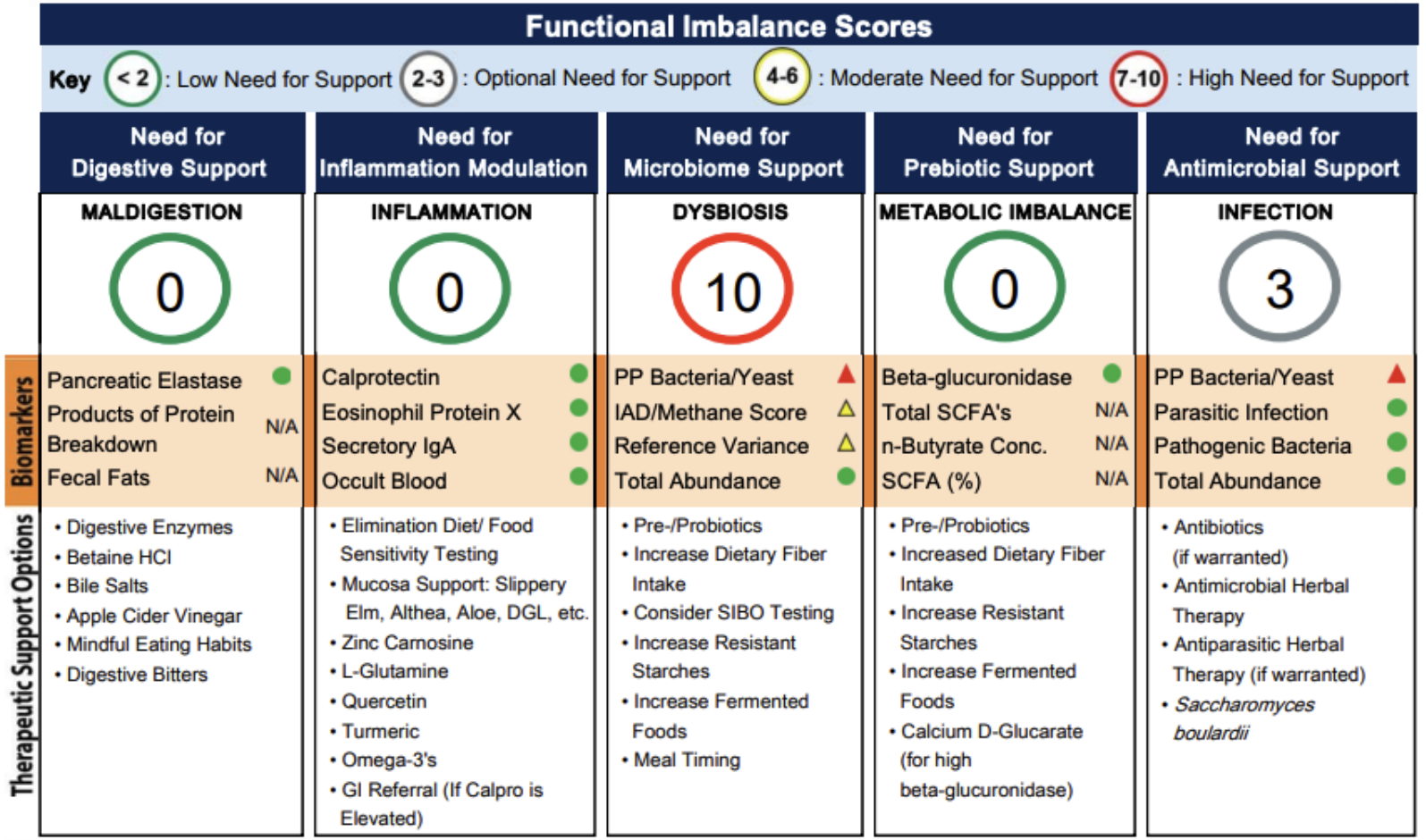
Functional Imbalance Scores
Key
< 2 : Low Need for Support
2-3 : Optional Need for Support
4-6 : Moderate Need for Support
7-10 : High Need for Support
Need for Digestive Support
Need for Inflammation Modulation
Need for Microbiome Support
Need for Prebiotic Support
Need for Antimicrobial Support
MALDIGESTION
0
INFLAMMATION
0
DYSBIOSIS
10
METABOLIC IMBALANCE
0
INFECTION
3
Biomarkers
Pancreatic Elastase
Products of Protein Breakdown
N/A
Fecal Fats
N/A
Calprotectin
Eosinophil Protein X
Secretory IgA
Occult Blood
PP Bacteria/Yeast
IAD/Methane Score
Reference Variance
Total Abundance
Beta-glucuronidase
Total SCFA's
N/A
n-Butyrate Conc.
N/A
SCFA (%)
N/A
PP Bacteria/Yeast
Parasitic Infection
Pathogenic Bacteria
Total Abundance
Therapeutic Support Options
• Digestive Enzymes
• Betaine HCl
• Bile Salts
• Apple Cider Vinegar
• Mindful Eating Habits
• Digestive Bitters
• Elimination Diet/ Food Sensitivity Testing
• Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc.
• Zinc Carnosine
• L-Glutamine
• Quercetin
• Turmeric
• Omega-3's
• GI Referral (If Calpro is Elevated)
• Pre-/Probiotics
• Increase Dietary Fiber Intake
• Consider SIBO Testing
• Increase Resistant Starches
• Increase Fermented Foods
• Meal Timing
• Pre-/Probiotics
• Increased Dietary Fiber Intake
• Increase Resistant Starches
• Increase Fermented Foods
• Calcium D-Glucarate (for high beta-glucuronidase)
• Antibiotics (if warranted)
• Antimicrobial Herbal Therapy
• Antiparasitic Herbal Therapy (if warranted)
• Saccharomyces boulardii

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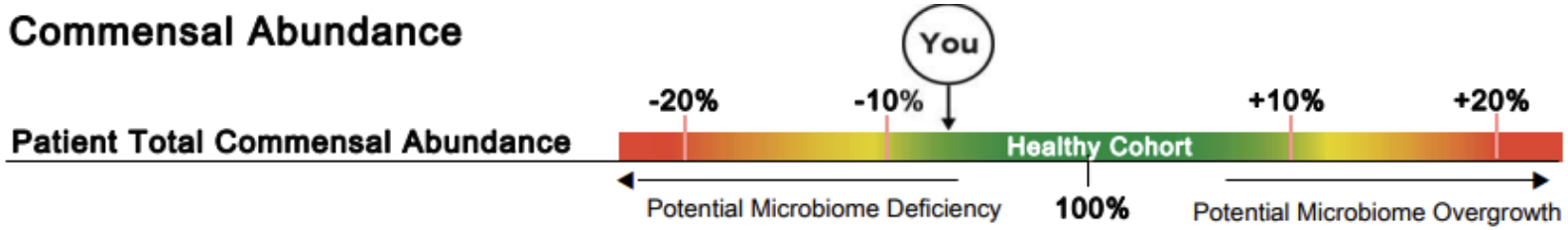
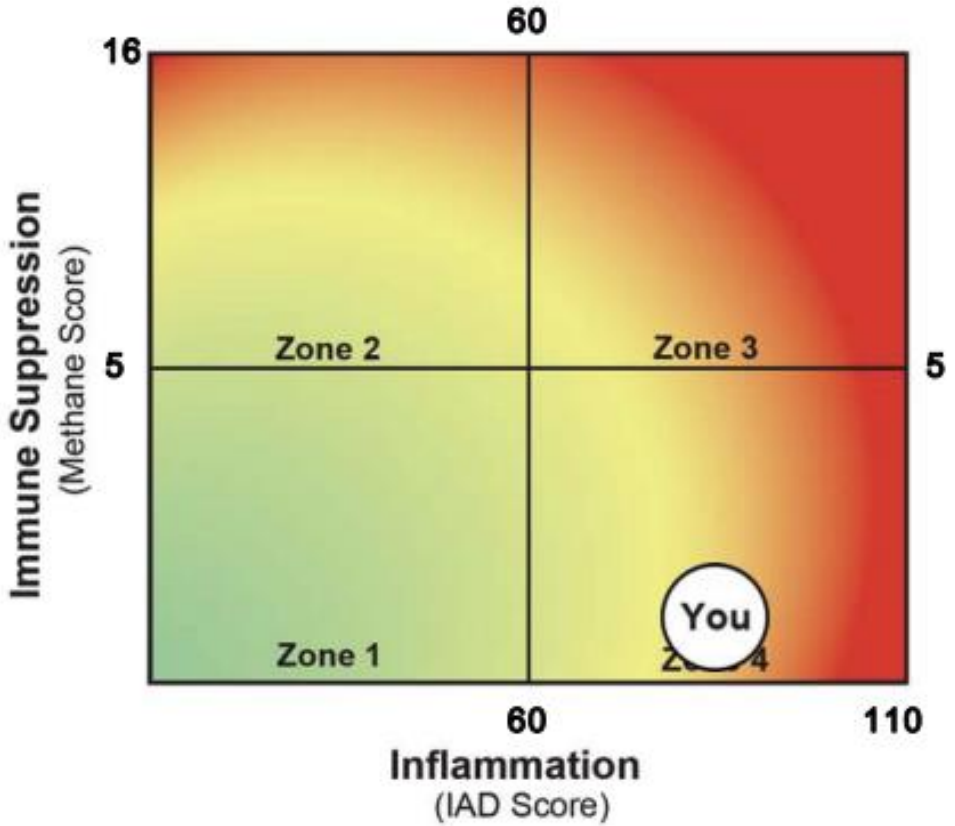
Commensal Abundance





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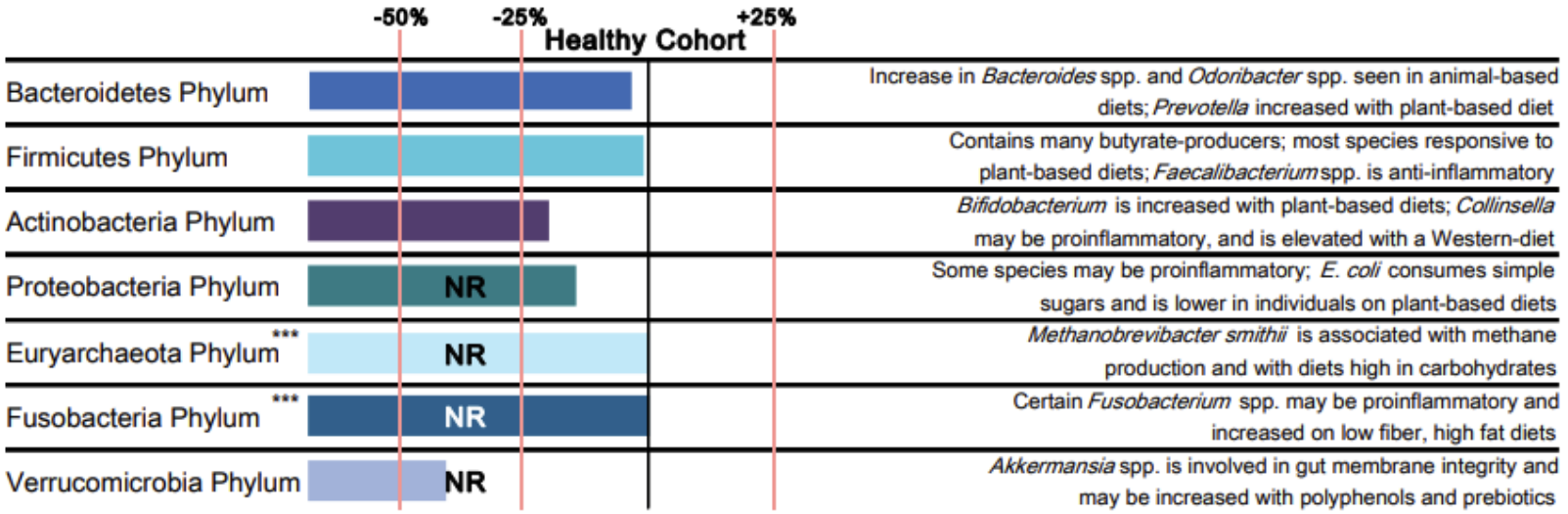
1

Relative Commensal Abundance



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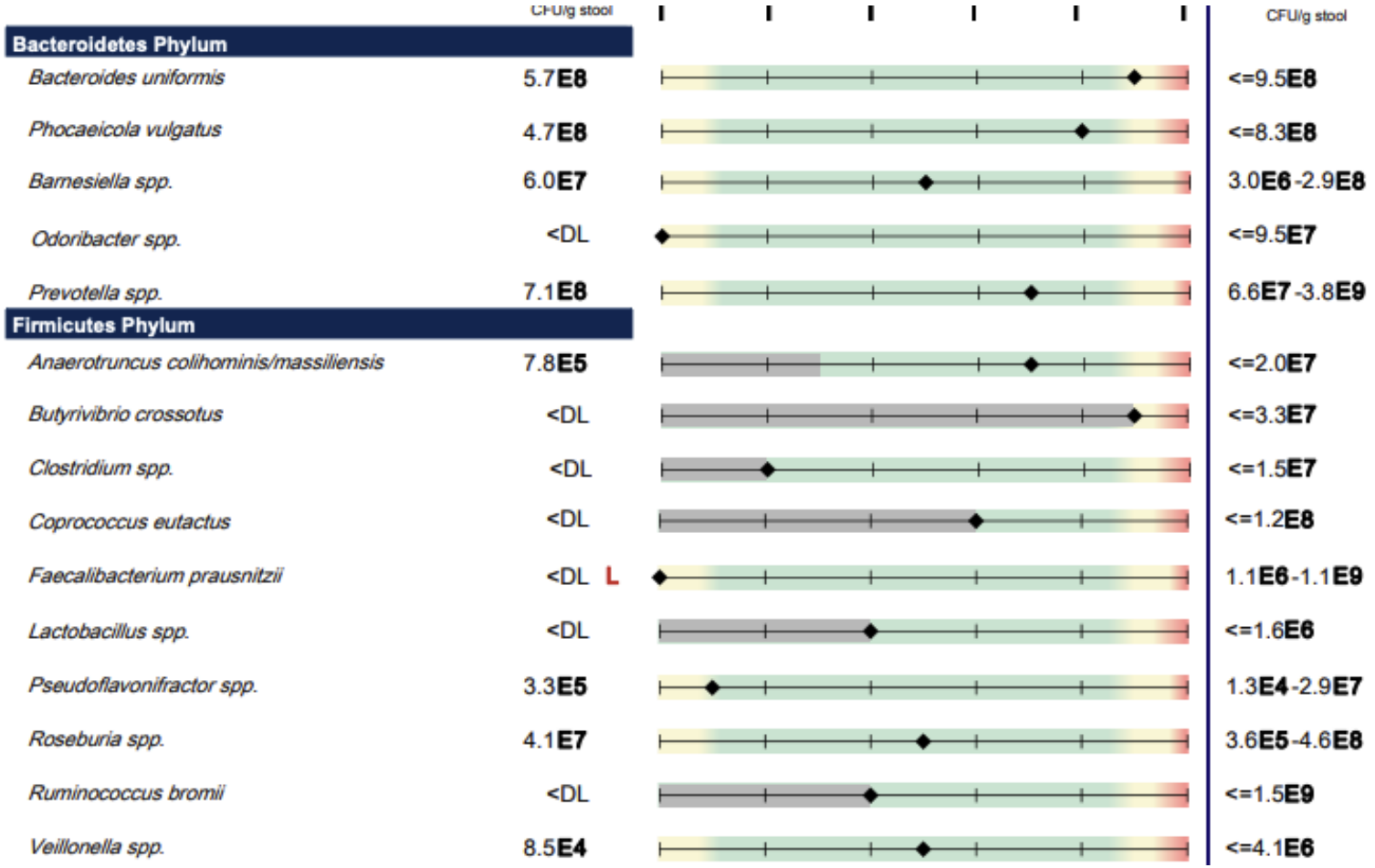
1



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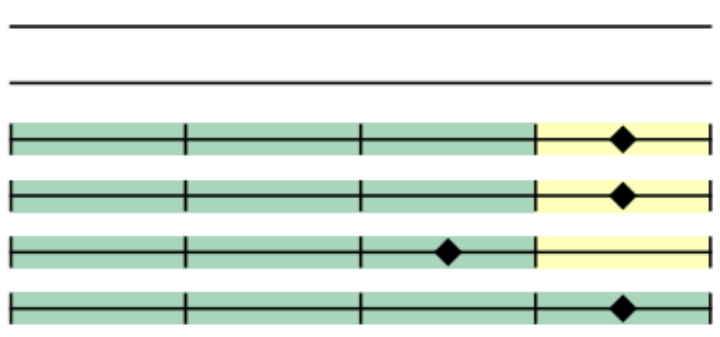
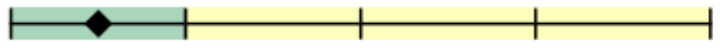
Additional Bacteria

Salmonella spp.		NG	
Shigella spp.		NG	
Klebsiella pneumoniae	4+	PP	
Citrobacter amalonaticus	4+	PP	
Pseudomonas aeruginosa	3+	NP	
Enterococcus faecium	4+	NP	



Mycology (Culture)

Candida albicans/dubliniensis	1+	NP	



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GUT DIVERSITY

1.4	0.48
Shannon's Index	**Simpson's Index**
Scale:0-4	Scale:0-1
Ref Range: ≥2.5	Ref Range: ≥0.75

Shannon's Index: Higher values indicate evenness
Simpson's Index: Higher values indicate richness

PHYLA

Proteobacteria:16.4%
Actinobacteria:2.3%
Fusobacteria:0.6%
Bacteroidetes:40.5%
Firmicutes:40.1%
Euryarchaeota:0.0%
Verrucomicrobia:0.1%

KEY RATIOS

RATIO	CURRENT	REF RANGE	PREVIOUS
F/B	1.0	≤0.9	
P/B	0.54	≥0.48	

F/B: Higher risk for obesity, metabolic disorders and inflammation.

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2

Virus	Current Result	Result	Ref Range	Prev	Result
Adenovirus F40/41	<1e2	---	≤5e2		
Astrovirus	<1e2	---	≤5e2		
Norovirus GI	<1e1	---	≤5e2		
Norovirus GII	9.8e3 H	✓	≤5e2		
Sapovirus I	<1e2	---	≤5e2		
Sapovirus II	<1e2	---	≤5e2		
Sapovirus IV	<1e2	---	≤5e2		
Sapovirus V	<1e2	---	≤5e2		
Epstein Barr virus	<1e2	---	≤1e3		
Rotavirus A	<1e2	---	≤5e2		

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INFLAMMATION MARKERS

Test Name	Current	Ref Range	Prev	Comments
Beta defensin 2	49.9 H	≤34.9		Beta-defensin 2 is an antibiotic peptide locally regulated by inflammation in humans. It is produced by a number of epithelial cells and exhibits potent antimicrobial activity against Gram-negative bacteria and Candida, but not Gram-positive bacteria. It has been speculated that beta-defensin 2 may contribute to the infrequency of Gram-negative infections on skin and lung tissue.
Lysozyme	205.7	≤575.0		
MMP 9	0.2	≤0.2		
S100A12	27.4	≤50.0		
Calprotectin	54.5 H	≤50.0		Five polyphenols in particular have evidence of benefit in treating gut inflammation: resveratrol, epigallocatechin, curcumin, quercetin, and Boswellia.
Fecal lactoferrin	15.4 H	≤6.4		Lactoferrin is a glycoprotein released by a type of white blood cell called neutrophil. Fecal lactoferrin is a biomarker of serious gastrointestinal inflammation. Gastrointestinal inflammation is associated with increased infiltration of activated neutrophils into the mucosa and increased release of lactoferrin into the gut. Clinical studies have shown that fecal lactoferrin levels of healthy persons are similar to irritable bowel syndrome (IBS) patients, but markedly increased in patients with active inflammatory bowel disease (IBD). Fecal lactoferrin levels are helpful in monitoring disease activity and efficacy of treatment for IBD.
Fecal Eosinophil Protein X	3.9	≤4.8		

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DIGESTIVE INSUFFICIENCY AND MALABSORPTION MARKERS

ENZYME INSUFFICIENCY	Current	Ref Range	Prev	Comments
Pancreatic elastase 1	109.6 L	≥200.0		Consider digestive support with betaine HCL. Consider pepsin, plant or pancreatic enzyme supplements, digestive herbs, bile salts, and taurine. Micronutrient evaluation recommended, especially for fat soluble vitamins A, D, E, and K.
DIETARY FIBER MARKERS	**Current**	**Ref Range**	**Prev**	**Comments**
Meat fiber	NOT DETECTED	-		
Vegetable fiber	NOT DETECTED	-		
FAT MALABSORPTION	**Current**	**Ref Range**	**Prev**	**Comments**
Total Fecal Fat	56.3 H	2.9-37.5		This test measures the amount of fat in a stool sample. Excess fecal fat (termed steatorrhea) in stool is indicative of malabsorption disorder. The absorption of fat can be varied by production of bile in the gallbladder or liver, production of digestive enzymes in the pancreas, and normal functioning of the intestines. Decreased absorption of fat can be a sign of many different illnesses, including celiac disease, crohn's disease, cystic fibrosis, pancreatitis, etc.
Total Fecal Triglycerides	1.0	0.3-2.5		
Long chain fatty acids	15.8	0.9-28.1		
Total Cholesterol	15.8 H	0.5-5.3		Total Cholestrol subfraction
Total Phospholipids	22.5 H	0.3-6.4		Total Phospholipid subfraction

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Total Short chain fatty acids	32.2 L	45.4-210.1		SCFA supplements are most commonly found as butyric acid salts. Herbal medicines that can affect SCFA levels include berberine, passiflora edulis, Chinese Yam, trametes versicolor extract, lotus seed resistant starch, xylooligosaccharides from corn cobs, coptis chinensis, Reishi mushroom, Poria mushroom, Lingzhi mushroom, Daikenchuto.

OTHER MARKERS

Test Name	Current	Ref Range	Prev	Comments
Fecal Zonulin	350.9 H	25.1-160.8		Fecal zonulin measurement may be advantageous, compared to serum zonulin when assessing intestinal permeability, as serum zonulin may constitute secretion not only from intestinal cells, but also from extraintestinal tissues such as the liver, heart and brain. Stool may therefore present a more appropriate specimen for analyzing only intestinal production of zonulin. Elevated fecal levels of zonulin have been associated with metabolic syndrome, obesity, and healthy cigarette smokers. High fecal zonulin levels in smokers irrespective of IBD point to the significant and undesirable up-regulation of gut permeability in cigarette smokers.
pH	6.5	6.1-7.8		
sIgA	1886.5 H	426.0-1450.0		Secretory IgA is the primary antibody that is protecting us from pathogens and toxins from penetrating mucosal surfaces. Its role is crucial in protecting the integrity of the intestinal epithelium. The antibody blocks the access to the epithelial receptors and traps pathogens and toxins in the mucus which are then excreated by peristaltic movements. SIgA has been identified to potentially neutralize virulence factors, modulate intestinal microbiota by Fab-dependent and -independent mechanisms, promote dendritic cell (DC) recruitement across the epithelial barrier and also down-regulate pro-inflammatory responses normally associated with the uptake of highly pathogenic bacteria and potentially allergenic antigens. Multiple cytokines, including IL-4, TGF-β, IL-5, IL-6, IL-10 are instrumental in intestinal stimulating SIgA production. A subset of these cytokines, notably TGF-β and IL-10, are also required for maintaining mucosal tolerance, thus establishing one of the many links between SIgA production, immunity and intestinal homeostasis.

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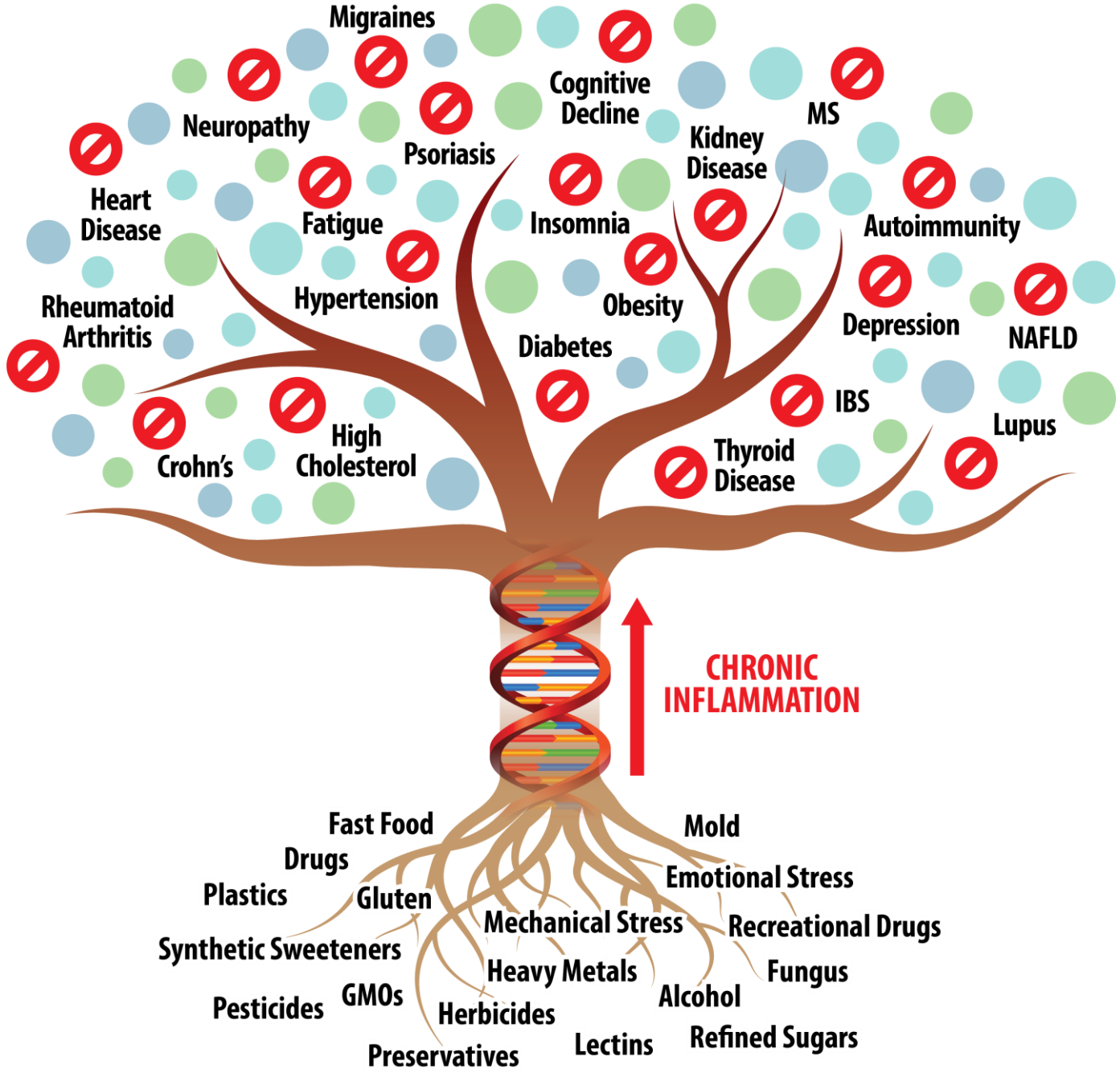
Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Autoimmunity
Rheumatoid Arthritis
Hypertension
Obesity
Depression
NAFLD
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Drugs
Plastics
Gluten
Synthetic Sweeteners
Pesticides
GMOs
Herbicides
Preservatives
Lectins
Refined Sugars
Heavy Metals
Mechanical Stress
Alcohol
Mold
Emotional Stress
Recreational Drugs
Fungus

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