

Casual Friday Series

# **Mycotoxins and Chronic Care Patients, Part II.**

A Biogenetix Clinical Presentation

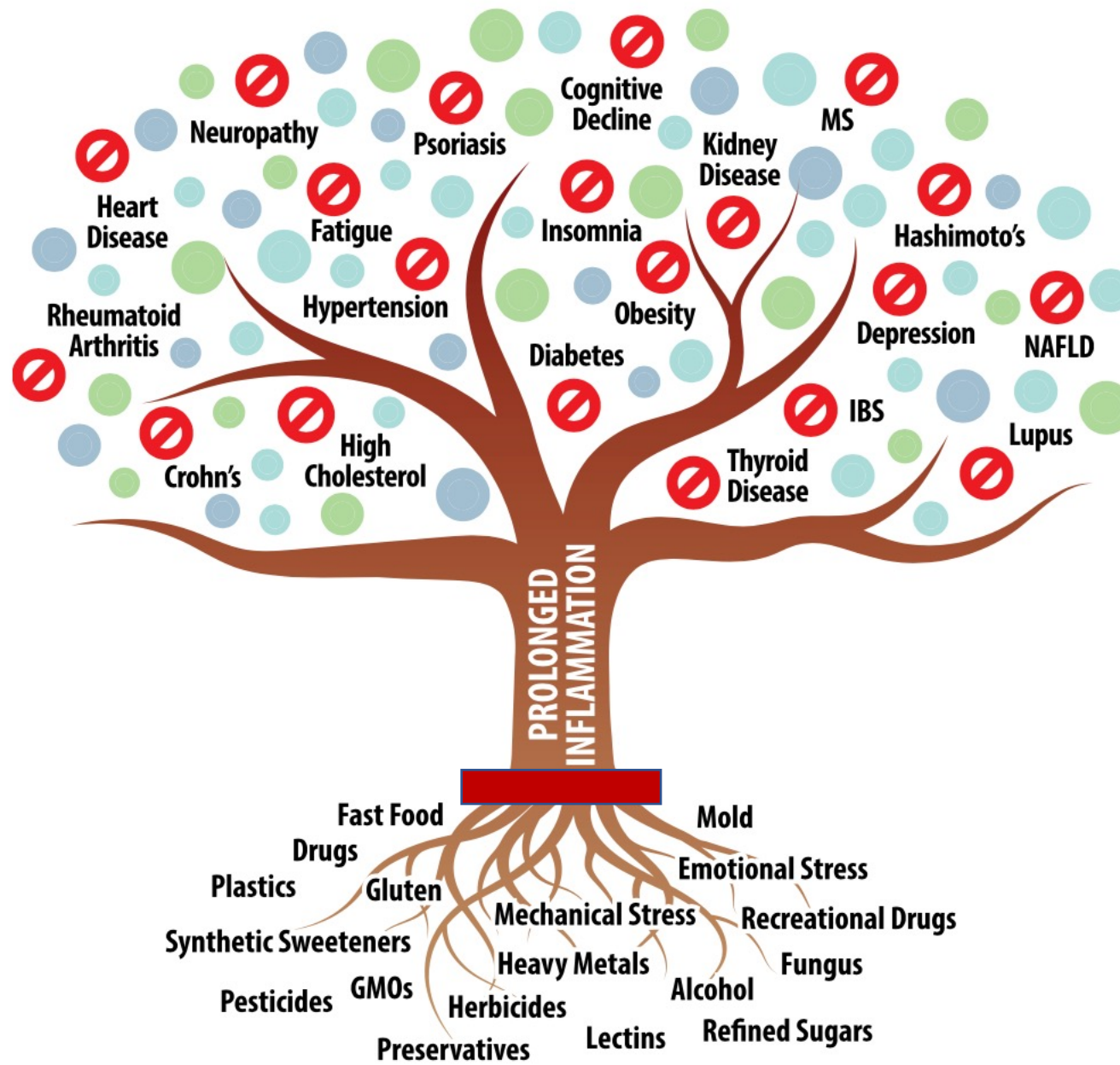
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# Disclaimer

- *Information in this presentation is not intended, in itself, to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*





# Symptoms of Mycotoxin Exposure

- Fatigue and weakness
- Chronic burning in the throat and nasal passages
- Coughing, wheezing, and shortness of breath
- Loss of balance
- Depression and/or anxiety
- Skin rashes
- Eye irritation or tearing of the eyes
- Headache and/or light sensitivity
- Hearing loss
- Heightened sensitivity to chemicals and foods
- Irregular heartbeat
- Morning stiffness and/or joint pain
- Muscle weakness
- Sleep problems
- Poor memory, difficulty finding words
- Slower reaction time
- Vision changes
- Difficulty concentrating
- Abdominal pain, diarrhea, and/or bloating
- Unusual skin sensations, tingling, and numbness
- Increased urinary frequency or increased thirst
- Disorientation and/or dizziness
- Static shocks or metallic taste in the mouth



## Mycotoxin: Its Impact on Gut Health and Microbiota

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► Author

in some findings. This review comprehensively discussed the role of mycotoxins (trichothecenes, zearalenone, fumonisins, ochratoxins, and aflatoxins) toward gut health and gut microbiota. Certainly, mycotoxins cause perturbation in the gut, particularly in the intestinal epithelial. Recent insights have generated an entirely new perspective where there is a bi-directional relationship exists between mycotoxins and gut microbiota, thus suggesting that our gut microbiota might be involved in the development of mycotoxicosis. The bacteria–xenobiotic interplay for the host is highlighted in this review article. It is now well established that a healthy gut microbiota is largely responsible for the overall health of the host. Findings revealed that the gut microbiota is capable of eliminating mycotoxin from the host naturally, provided that the host is healthy with a balance gut microbiota. Moreover, mycotoxins have been demonstrated for modulation of gut microbiota composition, and such alteration in gut microbiota can be observed up to species level in some of the studies. Most, if not all, of the reported effects of mycotoxins, are negative in terms of intestinal health, where beneficial bacteria are eliminated accompanied by an increase of the gut pathogen. The interactions between gut microbiota and mycotoxins have a significant role in the development of mycotoxicosis, particularly hepatocellular carcinoma. Such knowledge potentially drives the development of novel and innovative strategies for the prevention and therapy of mycotoxin contamination and mycotoxicosis.

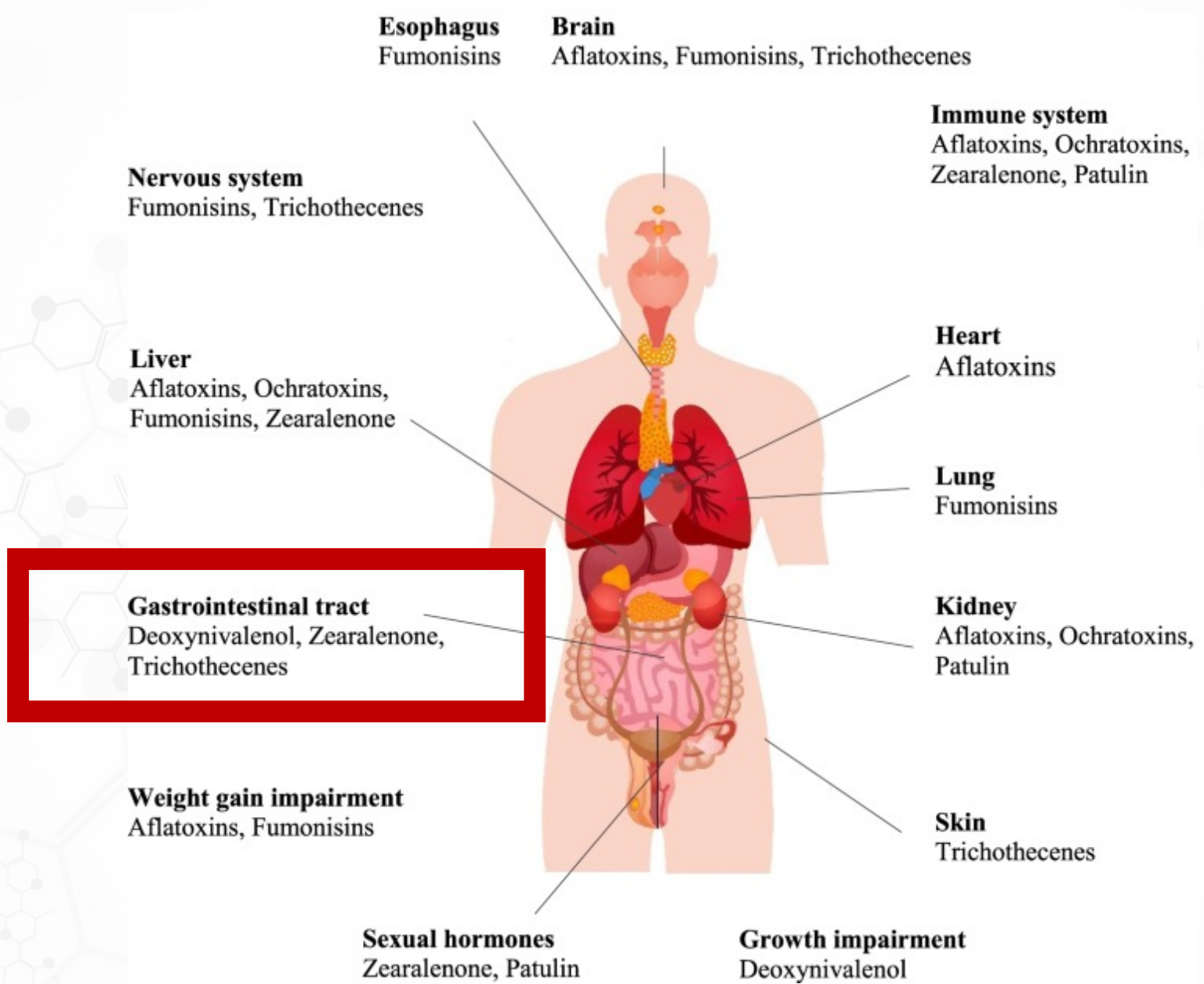


## Mycotoxin: Its Impact on Gut Health and Microbiota

Upon ingestion of contaminated food or feed, the GI tract is particularly affected by mycotoxin. Generally, intestinal barrier in the GI tract functions as a filter against harmful mycotoxins. However, some mycotoxins have been found to exert their detrimental effects in the GI tract. For example, mycotoxins can alter the normal intestinal functions such as barrier function and nutrient absorption. Some mycotoxins also affect the histomorphology of intestine. The impacts of mycotoxins include trichothecenes, zearalenone, fumonisins, ochratoxins, and AFs on general and gut health will be comprehensively reviewed.

**Trichothecenes** *Fusarium graminearum* is the main fungi species that produces trichothecenes. All trichothecenes contain an epoxide at the C12, C13 positions, which is responsible for their toxicological activity (Nathanail et al., [2015](#)). T-2 toxin (Type A) and DON (Type B) are the major mycotoxins that cause toxicity to humans and animals via oral ingestion (Nathanail et al., [2015](#)).





**My** During World War II, a biological weapon caused an acute syndrome consists of cough, sore throat, dyspnea, bloody nasal discharge, and fever was reported by Soviet scientists (Pitt and Miller, [2016](#)). Twenty years later, T-2 mycotoxin was discovered when civilians consumed wheat that was unintentionally contaminated with *Fusarium* fungi (Pitt and Miller, [2016](#)). A human toxicosis due to ingestion of moldy rice contaminated with T-2 toxin has been reported in China. According to Wang Z. et al. ([1993](#)), 65% of patients developed food poisoning symptoms such as chills, nausea, abdominal distension, dizziness, vomiting, thoracic stuffiness, abdominal pain, and diarrhea. Similar to T-2 toxicity, victims of DON outbreak suffered from vomiting syndromes (Etzel, [2014](#)). Several outbreaks of acute DON toxicity in human have been reported in India, China, and the USA (Etzel, [2014](#)).

**Win**

**Au**

Trichothecenes toxic effects in animals (dairy cattle, swines, broilers, and rats) include decreased plasma glucose, reduced blood cell and leukocyte count, weight loss, alimentary toxic aleukia, as well as pathological changes in the liver and stomach (Adhikari et al., [2017](#)). The mechanism involved in T-2 and DON toxicity is generally via oxidative stress-mediated deoxyribonucleic acid (DNA) damage and apoptosis (Wu et al., [2014](#)). Furthermore, T-2 and DON are well-known inhibitors of protein synthesis resulting from the binding of peptidyl-transferase, which is located in the 60s ribosomal subunit (Yang et al., [2017](#)).



## Mycotoxin: Its Impact on Gut Health and Microbiota

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In the GI tract, a decreased absorption of glucose was observed following T-2 and DON intoxication resulted from suppressed SGLT1 (glucose transporter) mRNA expression. Apart from the glucose absorption, SGLT1 also responsible for water reabsorption, thus reduction of SGLT1 transporter induces diarrhea as well (Grenier and Applegate, [2013](#)).



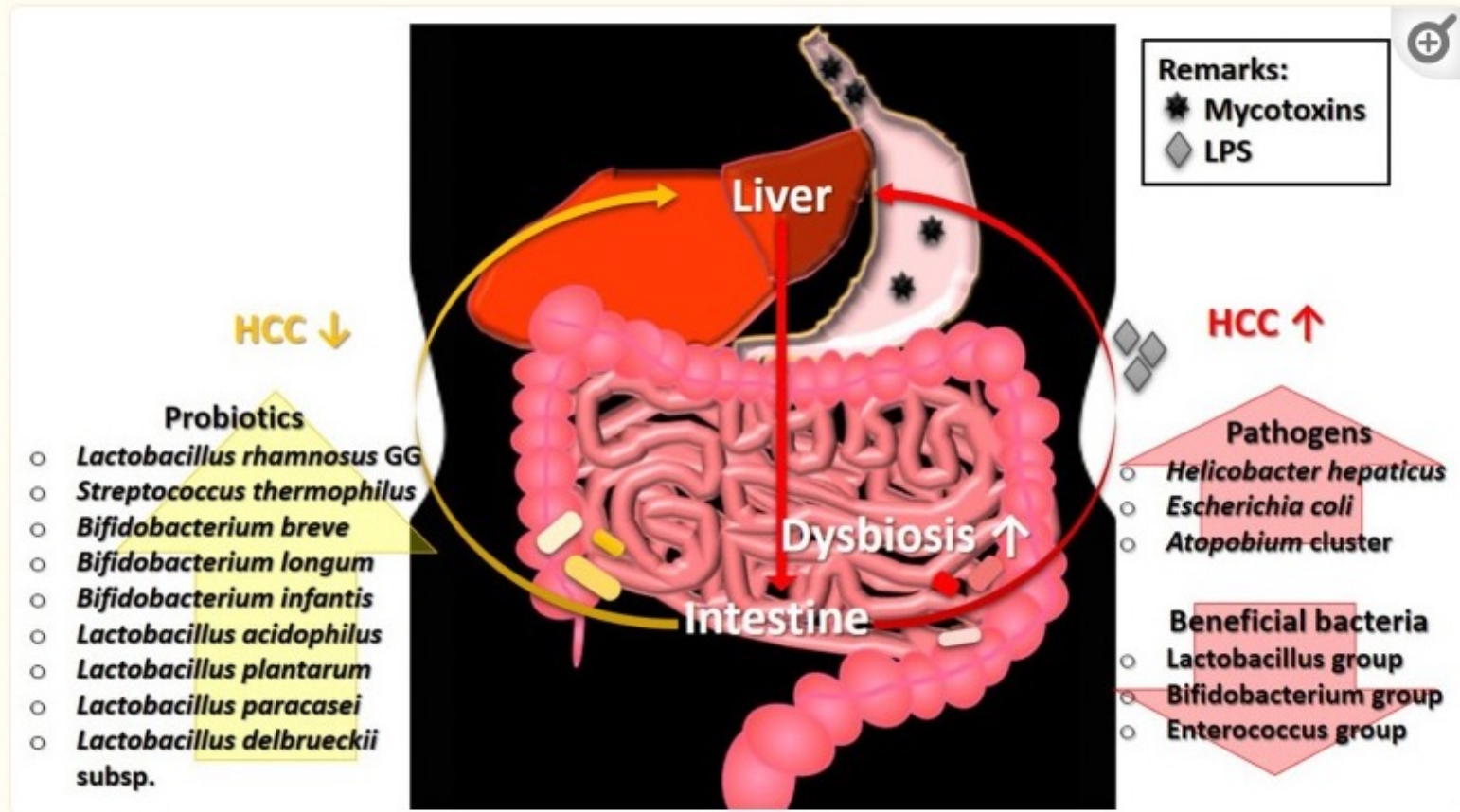
## Mycotoxin: Its Impact on Gut Health and Microbiota

Win

▶ A

Using animal models, trichothecenes was found to induce necrotic lesions in the GI tract (Kolf-Clauw et al., [2013](#)). A shortening of villi height was also observed in trichothecenes-treated animals (swine, poultry, and rat model). The changes on villi were due to activation of the apoptotic pathway by trichothecenes, which in turn leads to nutrition malabsorption (Alizadeh et al., [2015](#)). Furthermore, results obtained from *in vivo* and *in vitro* studies showed that trichothecenes increased intestinal permeability. Using porcine epithelial cell, trichothecenes increased the intestinal permeability by lowering tight junction proteins expression (Osselaere et al., [2013](#)). In addition, previous studies revealed a significant ( $P < 0.05$ ) decreased in the number of goblet cells that secrete mucin in trichothecenes-treated animals. Mucin is primarily involved in the gut barrier function (Pinton and Oswald, [2014](#)). The disruption in the integrity of intestinal epithelium allows the entry of the pathogen into the gut lumen (Lessard et al., [2015](#)). Besides, trichothecenes have been linked with a decreased level of IL-8 in the intestine, which is responsible for pathogen removal (Kadota et al., [2013](#)). Overall, trichothecenes exert negative impacts on GI tracts specifically on the gut absorption, integrity, and immunity.





**Figure 1**

The involvement of gut microbiota in the pathogenesis of HCC. Ingestion of mycotoxin-contaminated foods induces HCC, which eventually leads to the intestinal dysbiosis. The perturbation of microbial balance in the intestine causes a decrease of beneficial gut bacteria. Without the protection from beneficial bacteria, the growth of pathogens will expand rapidly and produce high level of LPS. The presence of LPS exacerbates the condition of HCC. Restoration of gut microbiota balance via intake of probiotics can alleviate the tumorigenic effects in HCC. HCC, hepatocellular carcinoma; LPS, lipopolysaccharide.



## Toxins Summary

		Current	Previous Result
Environmental Toxins	Organochlorine pesticides		
	Organophosphate pesticides		
	Other pesticides/herbicides		
	Phthalate Metabolites		
	Parabens	Propylparaben ●	
	Acrylic Metabolites		
	Other Metabolites	Tiglylglycine (TG) ●	
	Alkylphenol	Bisphenol A (BPA) ●, Triclosan ●	
	Volatile Organic Compounds (VOCs)	2-Methylhippuric Acid (2MHA) ●	
	Urine Creatinine		
Mycotoxins V2	Aflatoxin	Aflatoxin G1 ●	
	Other	Ochratoxin A ●, Zearalenone ●	
	Trichothecenes	Verrucarin A ●, Roridin A ●, Satratoxin H ●	
	Urinary Creatinine		
Heavy Metals	Heavy Metals (Creatinine)	Barium ●, Nickel ●	



### **Verrucarin A**

Verrucarin A is macrocyclic trichothecenes are produced largely by *Myrothecium*, *Stachybotrys* and *Fusarium*. This toxin has a wide range of antiviral, antifungal and antibacterial activity. Trichothecenes are generally produced on many different grains like wheat, oats or maize. In early days, these macrocyclic trichothecene compounds structures were modified to create new anticancer agents.<sup>7</sup>

### **Satratoxin H**

Satratoxin H is a trichothecene mycotoxin that have been recognized as one of the potential etiologic agents in outbreaks of sick building syndromes. satratoxin H, potently inhibit protein synthesis and thymocyte proliferation and also can cause diseases such as an immune dysfunction and idiopathic pulmonary hemorrhage in infants. Recent studies have shown a possible relationship between trichothecenes and disorders of central nervous system including severe neuronal death.<sup>22</sup>

### **Roridin A**

Roridin A mycotoxin is one of the important macrocyclic trichothecenes, produced on foodstuffs such as corn, rice, wheat and other crops. Trichothecenes mycotoxins prevent polypeptide chain initiation or elongation and interact with the enzyme peptidyl transferase. Both human and animal suffer from several pathologies due to intoxication after consumption of foodstuffs contaminated with trichothecenes and the conditions have been named differently according to the causative fungus.<sup>24</sup>



Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ <b>Glucose</b> <sup>01</sup>	<b>339 High</b>		mg/dL	65-99
BUN <sup>01</sup>	12		mg/dL	8-27
Creatinine <sup>01</sup>	0.62		mg/dL	0.57-1.00
eGFR	101		mL/min/1.73	>59
BUN/Creatinine Ratio	19			12-28

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Lipids <sup>01</sup>				
▲ <b>Cholesterol, Total</b> <sup>01</sup>	<b>209 High</b>		mg/dL	100-199
▲ <b>Triglycerides</b> <sup>01</sup>	<b>300 High</b>		mg/dL	0-149
HDL Cholesterol <sup>01</sup>	58		mg/dL	>39
▲ <b>VLDL Cholesterol Cal</b>	<b>50 High</b>		mg/dL	5-40
▲ <b>LDL Chol Calc (NIH)</b>	<b>101 High</b>		mg/dL	0-99
T. Chol/HDL Ratio	3.6		ratio	0.0-4.4

Please Note:<sup>01</sup>

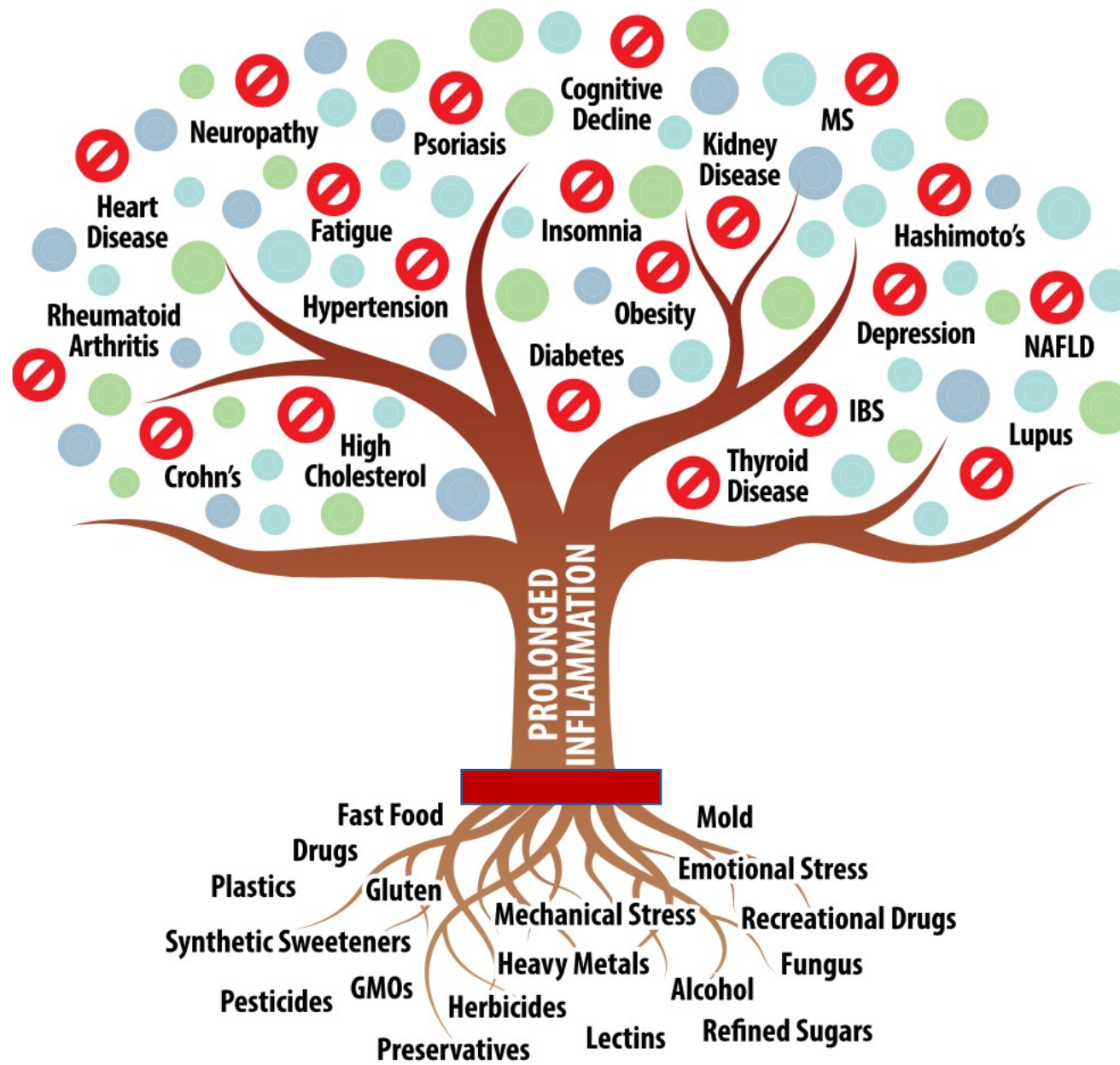


Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
TSH <sup>01</sup>	4.430		uIU/mL	0.450-4.500
Thyroxine (T4) <sup>01</sup>	8.6		ug/dL	4.5-12.0
T3 Uptake <sup>01</sup>	28		%	24-39
Free Thyroxine Index	2.4			1.2-4.9

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ Hemoglobin A1c <sup>01</sup>	10.6 High		%	4.8-5.6
Estim. Avg Glu (eAG)	258		mg/dL	

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ Ferritin <sup>01</sup>	642 High		ng/mL	15-150







## 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
<b>MALDIGESTION</b> <b>10</b>	<b>INFLAMMATION</b> <b>0</b>	<b>DYSBIOSIS</b> <b>10</b>	<b>METABOLIC IMBALANCE</b> <b>0</b>	<b>INFECTION</b> <b>2</b>
Pancreatic Elastase ▼ Fecal Fats ▲ Products of Protein Breakdown ●	Calprotectin ● Eosinophil Protein X ● Secretory IgA ● Occult Blood ●	IAD/Methane Score ▲ PP Bacteria/Yeast ▲ Reference Variance ▲ Total Abundance ▲	n-Butyrate Conc. ▼ SCFA (%) ▼ Total SCFA's ● Beta-glucuronidase ●	PP Bacteria/Yeast ▲ Total Abundance ▲ Parasitic Infection ● Pathogenic Bacteria ●
<ul style="list-style-type: none"> <li>• Digestive Enzymes</li> <li>• Betaine HCl</li> <li>• Bile Salts</li> <li>• Apple Cider Vinegar</li> <li>• Mindful Eating Habits</li> <li>• Digestive Bitters</li> </ul>	<ul style="list-style-type: none"> <li>• Elimination Diet/ Food Sensitivity Testing</li> <li>• Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc.</li> <li>• Zinc Carnosine</li> <li>• L-Glutamine</li> <li>• Quercetin</li> <li>• Turmeric</li> <li>• Omega-3's</li> <li>• GI Referral (If Calpro is Elevated)</li> </ul>	<ul style="list-style-type: none"> <li>• Pre-/Probiotics</li> <li>• Increase Dietary Fiber Intake</li> <li>• Consider SIBO Testing</li> <li>• Increase Resistant Starches</li> <li>• Increase Fermented Foods</li> <li>• Meal Timing</li> </ul>	<ul style="list-style-type: none"> <li>• Pre-/Probiotics</li> <li>• Increased Dietary Fiber Intake</li> <li>• Increase Resistant Starches</li> <li>• Increase Fermented Foods</li> <li>• Calcium D-Glucarate (for high beta-glucuronidase)</li> </ul>	<ul style="list-style-type: none"> <li>• Antibiotics (if warranted)</li> <li>• Antimicrobial Herbal Therapy</li> <li>• Antiparasitic Herbal Therapy (if warranted)</li> <li>• <i>Saccharomyces boulardii</i></li> </ul>





Interpretation At-a-Glance									
Commensal Bacteria	Patient Results Out of Reference Range	Genova Diagnostics Commensal Bacteria Clinical Associations*							
		IBS	IBD	Metabolic Syndrome	Chronic Fatigue	Auto-immune	Type 2 Diabetes	High Blood Pressure	Mood Disorders
<b>Bacteroidetes Phylum</b>									
<i>Bacteroides-Prevotella</i> group		↑	↑	↑	↑	↑	↑	↑	↑
<i>Bacteroides vulgatus</i>	H	↑			↑	↑		↑	↑
<i>Barnesiella</i> spp.									
<i>Odoribacter</i> spp.									
<i>Prevotella</i> spp.		↑		↑	↑	↑		↑	↑
<b>Firmicutes Phylum</b>									
<i>Anaerotruncus colihominis</i>		↑	↑	↑	↑	↑	↑	↑	↑
<i>Butyrivibrio crossotus</i>	L								
<i>Clostridium</i> spp.									
<i>Coprococcus eutactus</i>		↑			↑	↑		↑	↑
<i>Faecalibacterium prausnitzii</i>	H	↑				↑			↑
<i>Lactobacillus</i> spp.									
<i>Pseudoflavonifractor</i> spp.	H	↑	↑	↑	↑	↑	↑	↑	↑
<i>Roseburia</i> spp.			↓						
<i>Ruminococcus</i> spp.		↑↑	↓	↓	↓	↑↑	↑↑	↑↑	↑↑
<i>Veillonella</i> spp.		↑	↑	↑	↑	↑	↑		↑
<b>Actinobacteria Phylum</b>									
<i>Bifidobacterium</i> spp.									
<i>Bifidobacterium longum</i>									
<i>Collinsella aerofaciens</i>		↑↑	↑↑	↓	↑↑	↑↑	↑↑	↑↑	↑↑
<b>Proteobacteria Phylum</b>									
<i>Desulfovibrio piger</i>									↑
<i>Escherichia coli</i>		↑	↑	↑	↑	↑	↑	↑	↑
<i>Oxalobacter formigenes</i>	H	↑		↑	↑				↑
<b>Euryarchaeota Phylum</b>									
<i>Methanobrevibacter smithii</i>	H	↑				↑			↑



## Toxins Summary

Blank Cell - Low

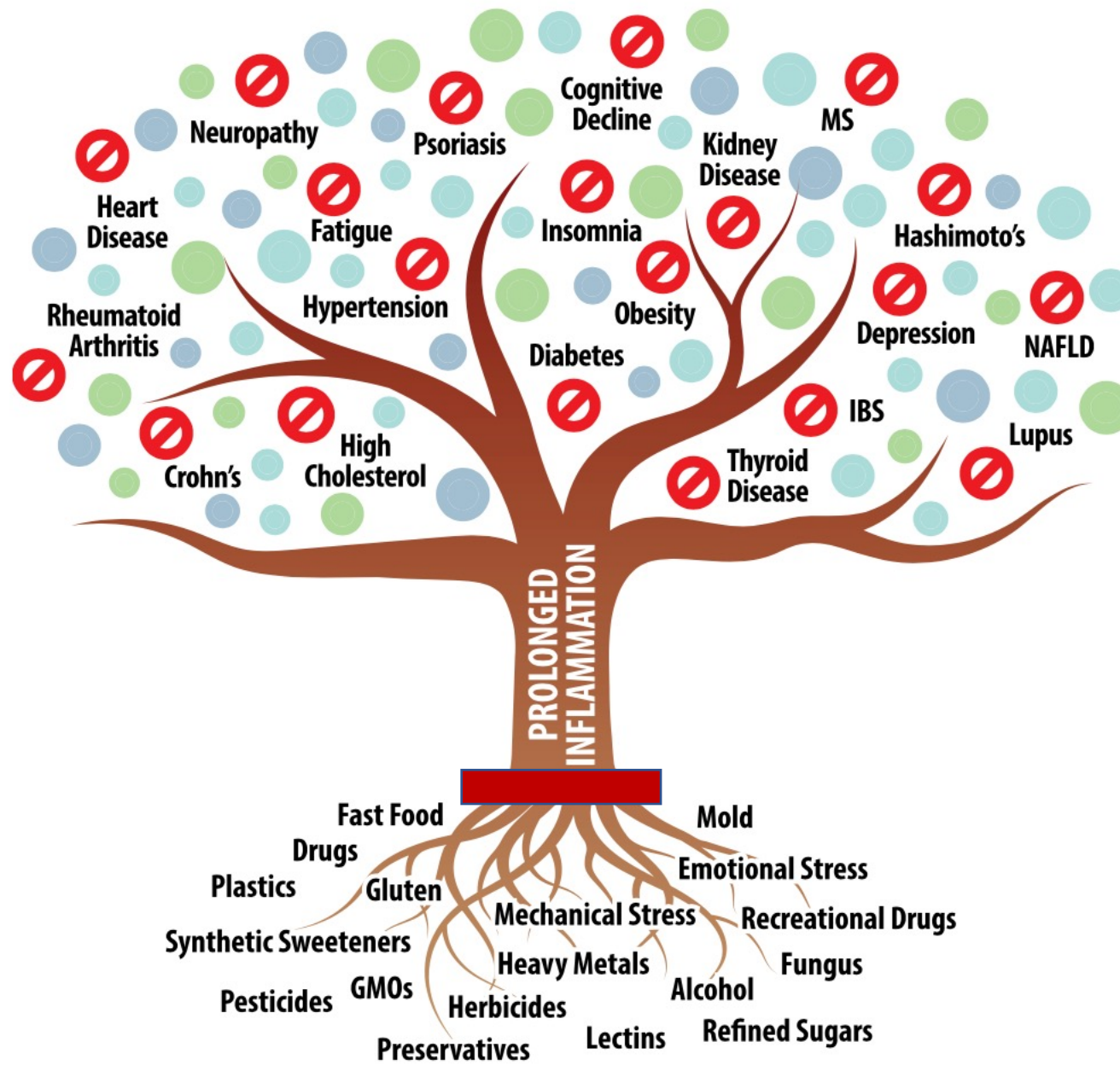
● High

● Moderate

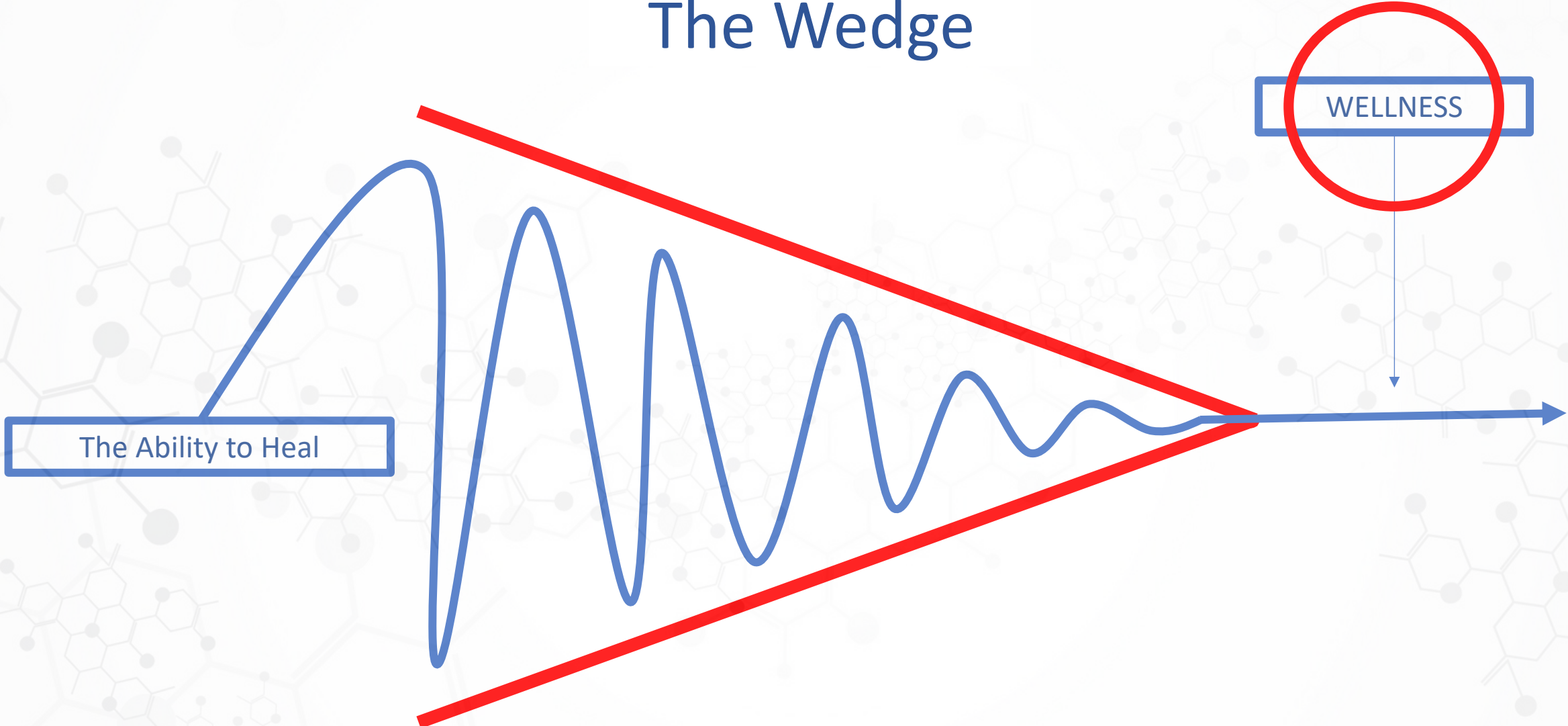
- Not Ordered or N/A

		Current	Previous Result
Environmental Toxins	Organochlorine pesticides		
	Organophosphate pesticides	Diethyldithiophosphate (DEDTP) ●, Atrazine mercapturate ●	
	Other pesticides/herbicides	Glyphosate ●	
	Phthalate Metabolites	Mono-ethyl phthalate (MEtP) ●	
	Parabens	Methylparaben ●	
	Acrylic Metabolites		
	Other Metabolites		
	Alkylphenol	Bisphenol A (BPA) ●	
	Volatile Organic Compounds (VOCs)		
	Urine Creatinine		
Mycotoxins V2	Aflatoxin	Aflatoxin B2 ●, Aflatoxin G1 ●	
	Other	Dihydrocitrinone ●	
	Trichothecenes	Roridin A ●	
	Urinary Creatinine		
Heavy Metals	Heavy Metals (Creatinine)		





# The Wedge



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