Casual Friday Series

Acid Reflux and GERD

A Biogenetix Clinical Presentation

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GERD: Gastroesophageal Reflux Disease

NERD: Nonerosive Reflux Disease (simple heartburn)

https://www.ncbi.nlm.nih.gov/books/NBK441938/

Currently, there is no known cause to explain the development of GERD. Over the years, several risk factors have been identified and implicated in the pathogenesis of GERD. Motor abnormalities such as esophageal dysmotility causing impaired esophageal acid clearance, impairment in the tone of the lower esophageal sphincter (LES), transient LES relaxation, and delayed gastric emptying are included in the causation of GERD [7]. Anatomical factors like the presence of hiatal hernia or an increase in intra-abdominal pressure, as seen in obesity are associated with an increased risk of developing GERD [7]. A meta-analysis by Hampel H *et al.* concluded that obesity was associated with an increased risk of developing GERD symptoms, erosive esophagitis, and esophageal carcinoma [8]. The ProGERD study by Malfertheiner, *et al*. evaluated the predictive factors for erosive reflux disease in more than 6000 patients with GERD and noted that the odds ratio for the erosive disease increased with the body mass index (BMI) [9]. Several other risk factors have been independently associated with the development of GERD symptoms that include age ≥50 years, low socioeconomic status, tobacco use, consumption of excess alcohol, connective tissue disorders, pregnancy, postprandial supination, and different classes of drugs which include anticholinergic drugs, benzodiazepines, NSAID or aspirin use, nitroglycerin, albuterol, calcium channel blockers, antidepressants, and glucagon[10][11][12].

The pathophysiology of GERD is multifactorial and is best explained by various mechanisms involved, including the influence of the tone of the lower esophageal sphincter, the presence of a hiatal hernia, esophageal mucosal defense against the refluxate and esophageal motility.

Impaired Lower Esophageal Sphincter (LES) Function and Transient Lower Esophageal Sphincter Relaxations (TLESRs)

The LES is a 3-4 cm tonically contracted smooth muscle segment located at the esophagogastric junction (EGJ) and, along with the crural diaphragm forms the physiological EGJ barrier, which prevents the retrograde migration of acidic gastric contents into the esophagus[17]. In otherwise healthy individuals, LES maintains a high-pressure zone above intragastric pressures with transient relaxation of the LES that occurs physiologically in response to a meal facilitating the passage of food into the stomach. Patients with symptoms of GERD may have frequent transient LES relaxations (TLESRs) not triggered by swallowing, resulting in exceeding the intragastric pressure more than LES pressures permitting reflux of gastric contents into the esophagus[18]. The exact mechanism of increased transient relaxation is unknown, but TLESRs account for 48-73% of GERD symptoms[19]. The LES tone and TLESRs are influenced by factors such as alcohol use, smoking, caffeine, pregnancy, certain medications like nitrates, and calcium channel blockers [18].

Hiatal hernia

Hiatal hernia is frequently associated with GERD and can exist independently without causing any symptoms. Nonetheless, the presence of hiatal hernia plays a vital role in the pathogenesis of GERD as it hinders the LES function[20]. Patti et al. reported that patients with proven GERD with or without a small hiatal hernia had similar LES function abnormalities and acid clearance. However, patients with large hiatal hernias were noted to have shorter and weaker LES resulting in increased reflux episodes. It was also pointed out that the degree of esophagitis was worse in patients with large hiatal hernias[21]. A study evaluating the relationship between hiatal hernia and reflux esophagitis by Ott *et al.* demonstrated the presence of hiatal hernia in 94% of patients with reflux esophagitis [22].

Impaired esophageal mucosal defense against the gastric refluxate

The esophageal mucosa comprises various structural and functional constituents that function as a protective defense barrier against the luminal substances encountered with GERD [18]. This defensive barrier can be breached by prolonged exposure to the refluxate, which consists of both acidic gastric contents (hydrochloric acid and pepsin) and alkaline duodenal contents (bile salts and pancreatic enzymes) leading to mucosal damage. The influence of gastroparesis on GERD is unknown. It is believed that delayed gastric emptying contributes to GERD symptoms due to gastric distention and increased exposure to the gastric refluxate[18].

Defective esophageal peristalsis

Normally, the acidic gastric contents that reach the esophagus are cleared by frequent esophageal peristalsis and neutralized by salivary bicarbonate[23][18]. In a prospective study by Diener *et al.*, 21% of patients with GERD were noted to have impaired esophageal peristalsis leading to decreased clearance of gastric reflux resulting in severe reflux symptoms and mucosal damage[24].

The diagnosis of GERD is imprecise as there is no gold standard test available. The diagnosis of GERD is made solely based on presenting symptoms or in combination with other factors such as responsiveness to antisecretory therapy, esophagogastroduodenoscopy, and ambulatory reflux monitoring.

Proton pump inhibitor (PPI) trial

GERD can be presumptively diagnosed in most patients presenting with typical symptoms of heartburn and regurgitation [29]. Unless there are no associated alarm symptoms that include dysphagia, odynophagia, anemia, weight loss, and hematemesis, most patients can be initiated on empiric medical therapy with proton pump inhibitors(PPIs) without further investigations with a response to treatment confirming the diagnosis of GERD[29]. However, a meta-analysis published literature by Numans et al. refuted the accuracy of this empiric PPI trial diagnostic strategy[30].

Esophagogastroduodenoscopy (EGD)

Patients presenting with typical GERD symptoms associated with any one of the alarm symptoms should be evaluated with an EGD to rule out complications of GERD. These include erosive esophagitis, Barrett's esophagus, esophageal stricture, and esophageal adenocarcinoma or rule out peptic ulcer disease. Distal esophageal biopsies are not routinely recommended to make a diagnosis of GERD as per the current American College of Gastroenterology (ACG) guidelines[29]. Patients with a high index of suspicion for coronary artery disease presenting with GERD symptoms should undergo evaluation for underlying cardiovascular disease. In contrast, patients presenting with noncardiac chest pain suspected due to GERD should have a diagnostic assessment with an EGD and pH monitoring before initiation of PPIs[31]. Current ACG guidelines recommend against screening for Helicobacter pylori infection in patients with GERD symptoms[29].

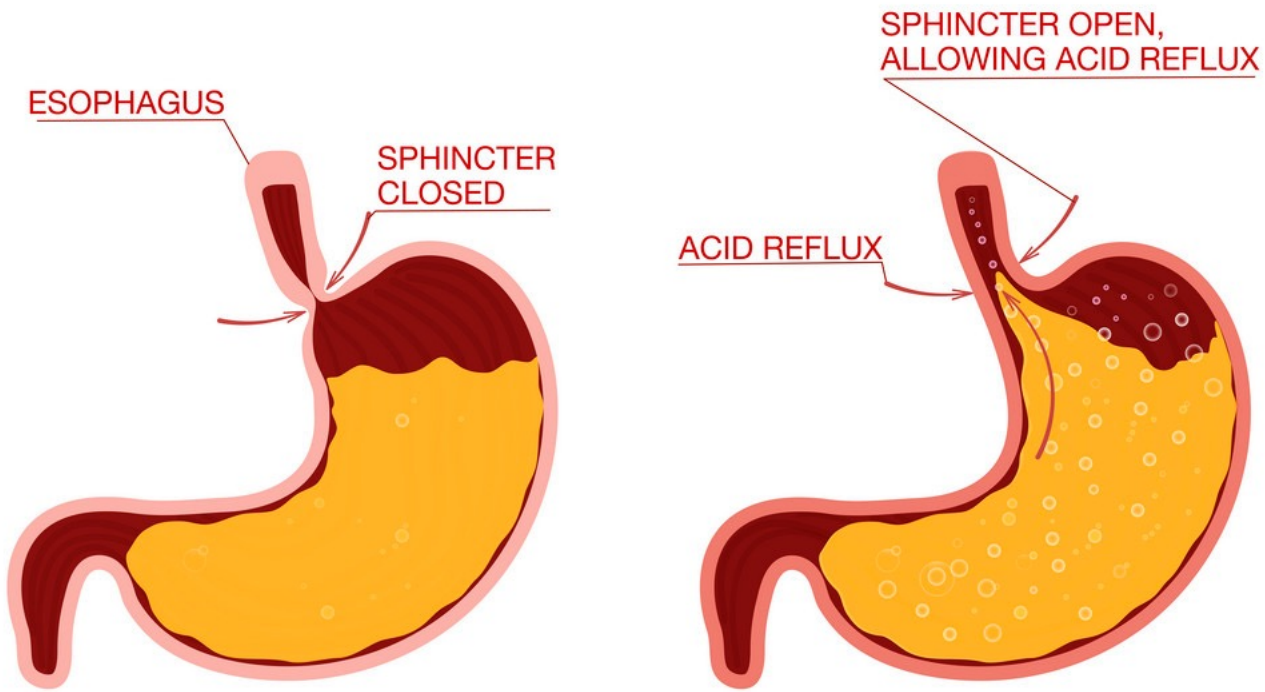
Radiographic studies

Radiographic studies like barium radiographs can detect moderate to severe esophagitis, esophageal strictures, hiatal hernia, and tumors. However, their role in the evaluation of GERD is limited and should not be performed to diagnose GERD[29].

Ambulatory esophageal reflux monitoring

Medically refractory GERD is increasingly common, and patients often have normal endoscopy evaluation as PPIs are incredibly effective in healing esophagitis caused by the refluxate. Ambulatory esophageal reflux monitoring can assess the correlation of symptoms with abnormal acid exposure. It is indicated in medically refractory GERD and in patients with extraesophageal symptoms suspicious for GERD. Ambulatory reflux (pH or in combination with impedance) monitoring employs the utility of a telemetry pH capsule or a transnasal catheter. It is the only available test that detects pathological acid exposure, frequency of reflux episodes, and correlation of symptoms with reflux episodes[29]. Current practice guidelines recommend mandatory preoperative ambulatory pH monitoring in patients without evidence of erosive esophagitis[29].

Pathological/Mechanical GERD



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The goals of managing GERD are to address the resolution of symptoms and prevent complications such as esophagitis, BE, and esophageal adenocarcinoma. Treatment options include lifestyle modifications, medical management with antacids and antisecretory agents, surgical therapies, and endoluminal therapies.

Lifestyle Modifications

Lifestyle modifications are considered to be the cornerstone of any GERD therapy. Counseling should be provided about the importance of weight loss given that underlying obesity is a significant risk factor for the development of GERD, and studies have shown that weight gain in individuals with a normal BMI has been associated with the development of GERD symptoms [32]. Individuals should also be counseled about avoiding meals at least 3 hours before bedtime and maintaining good sleep hygiene as it has been shown that minimal disturbances in sleep are associated with suppression of TLESRs, resulting in decreased reflux episodes[27][33]. Studies have also shown improvement in GERD symptoms and pH monitoring studies with the elevation of the head end of the bed. Diet modification with the elimination of chocolate, caffeine, and spicy foods, citrus, and carbonated beverages in GERD is controversial and is not routinely recommended as per current ACG guidelines[29].

Medical Therapy

Medical therapy is indicated in patients who do not respond to lifestyle modifications. Medical therapy is comprised of antacids antisecretory agents like histamine (H2) receptor antagonists (H2RAs) or PPI therapy and prokinetic agents. Currently, there are two US Food and Drug Administration (FDA) approved H2RAs (famotidine and cimetidine) available in the US and are available over-the-counter. The other commonly used H2RA known as ranitidine has been recalled as a potential health hazard or safety risk due to an unexpected impurity in the active ingredient. The less commonly known prescription-only H2RA nizatidine has also been recalled as well due to similar concerns. In the US, there are six PPIs that are currently available, of which three (omeprazole, lansoprazole, and esomeprazole) are available over-the-counter, and the remaining three (pantoprazole, dexlansoprazole, and rabeprazole) are prescription-only medications. Of the available medical options, PPI therapy is considered to be the most effective for both erosive and non-erosive GERD based on multiple large-scale studies. These studies have also shown improved symptom control, healing of underlying esophagitis, and decreased relapse rates compared to H2RAs [34][35]. ACG guidelines recommend PPI therapy be initiated at once a day dosing before the first meal of the day[29]. Patients with incomplete responses to once-daily dosing can be treated with twice-daily dosing or adjustment of dose timing, specifically in patients with nighttime symptoms [29]. As needed, bedtime administration of H2RAs is recommended for individuals with nighttime symptoms not optimized with maximal PPI therapy[29]. The role of prokinetic agents such as metoclopramide and domperidone in GERD is limited due to lack of data and also due to their profound adverse effects on the central nervous system and cardiovascular system.

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Complications:

Erosive Esophagitis (EE)

EE is characterized by erosions or ulcers of the esophageal mucosa[28]. Patients may be asymptomatic or can present with worsening symptoms of GERD. The degree of esophagitis is endoscopically graded using the Los Angeles esophagitis classification system, which employs the A, B, C, D grading system based on variables that include length, location, and circumferential severity of mucosal breaks in the esophagus [40].

Esophageal Strictures

Chronic acid irritation of the distal esophagus can result in scarring of distal the esophagus leading to the formation of a peptic stricture. Patients can present with symptoms of esophageal dysphagia or food impaction. ACG guidelines recommend esophageal dilation and continue PPI therapy to prevent the need for repeated dilations [29].

Barrett Esophagus

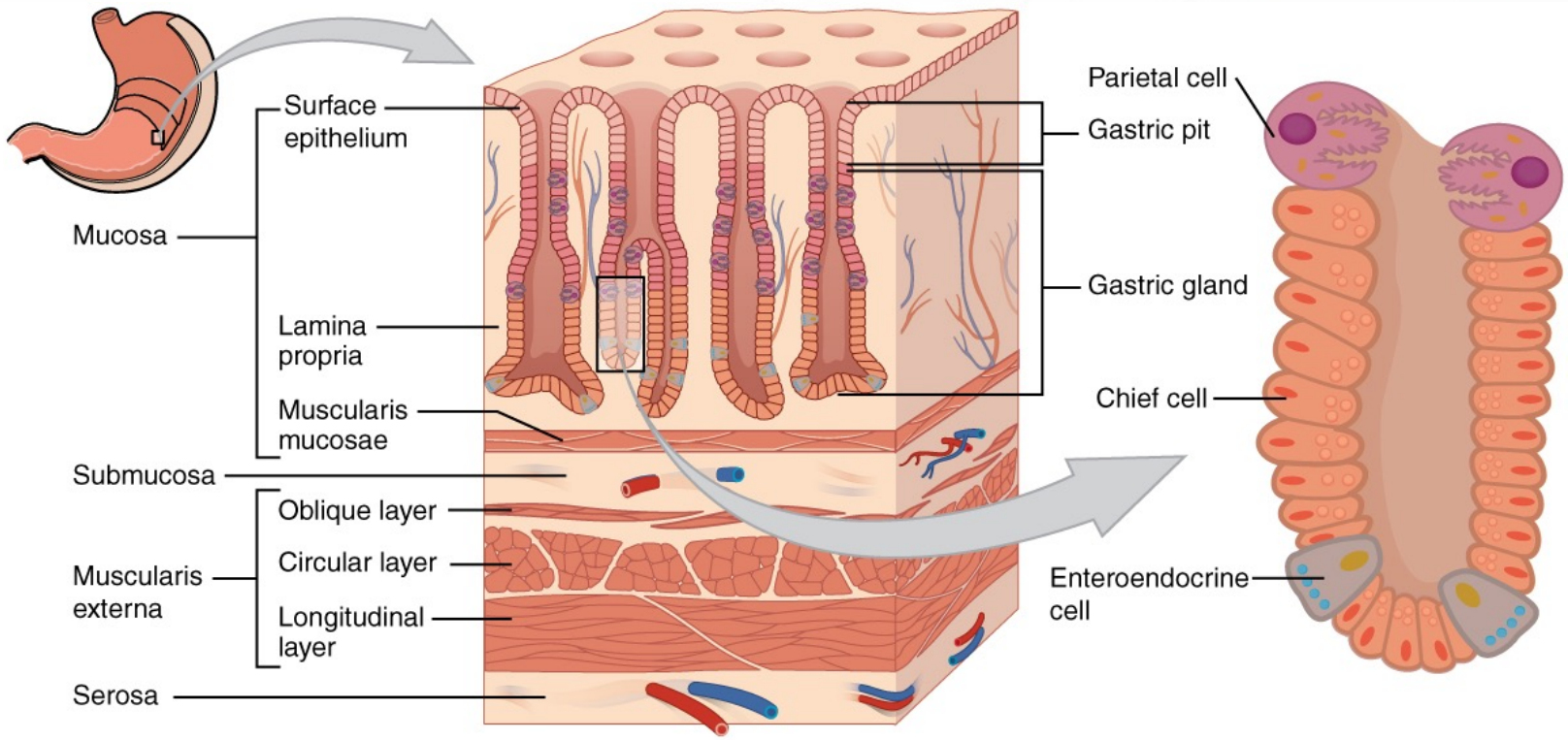
This complication occurs as a result of chronic pathological acid exposure to the distal esophageal mucosa. It leads to a histopathological change of the distal esophageal mucosa, which is normally lined by stratified squamous epithelium to metaplastic columnar epithelium. Barrett's esophagus is more commonly seen in Caucasian males above 50 years, obesity, and history of smoking and predisposes to the development of esophageal adenocarcinoma[28]. Current guidelines recommend the performance of periodic surveillance endoscopy in patients with a diagnosis of Barrett's esophagus[41].

Partially digested proteins triggers gastrin release from G cells of the antrum of the stomach and the duodenum.

Gastrin triggers HCL production from parietal cells.

HCL enhances food degradation.

High HCL turns off gastrin.



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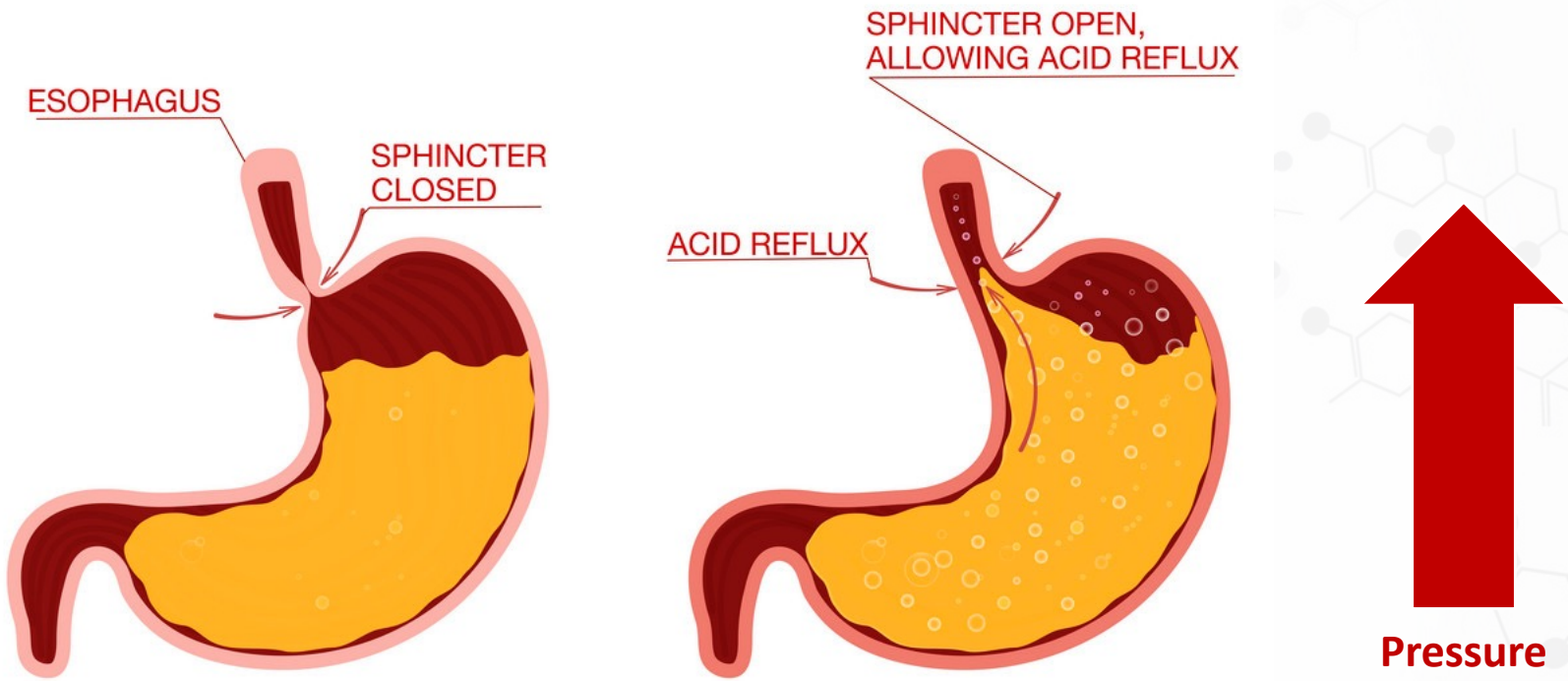
Functional Mechanisms of GERD



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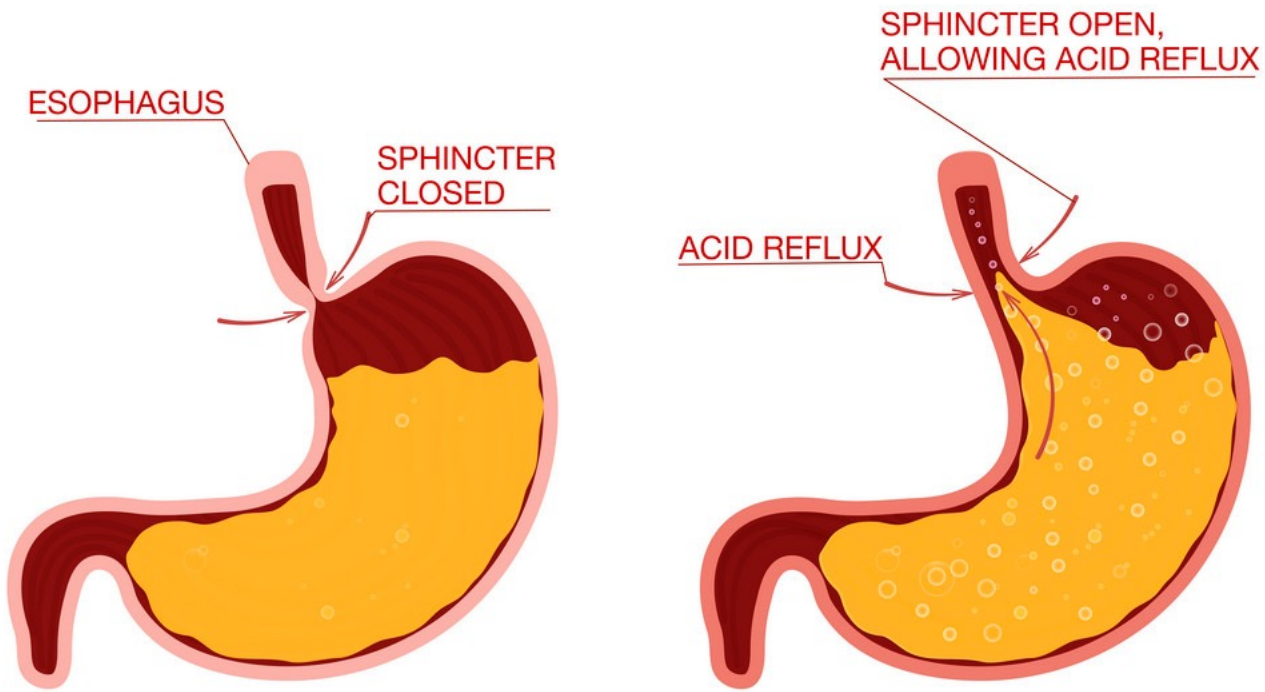
Functional Mechanisms of GERD



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Compounding Acids: organic x inorganic

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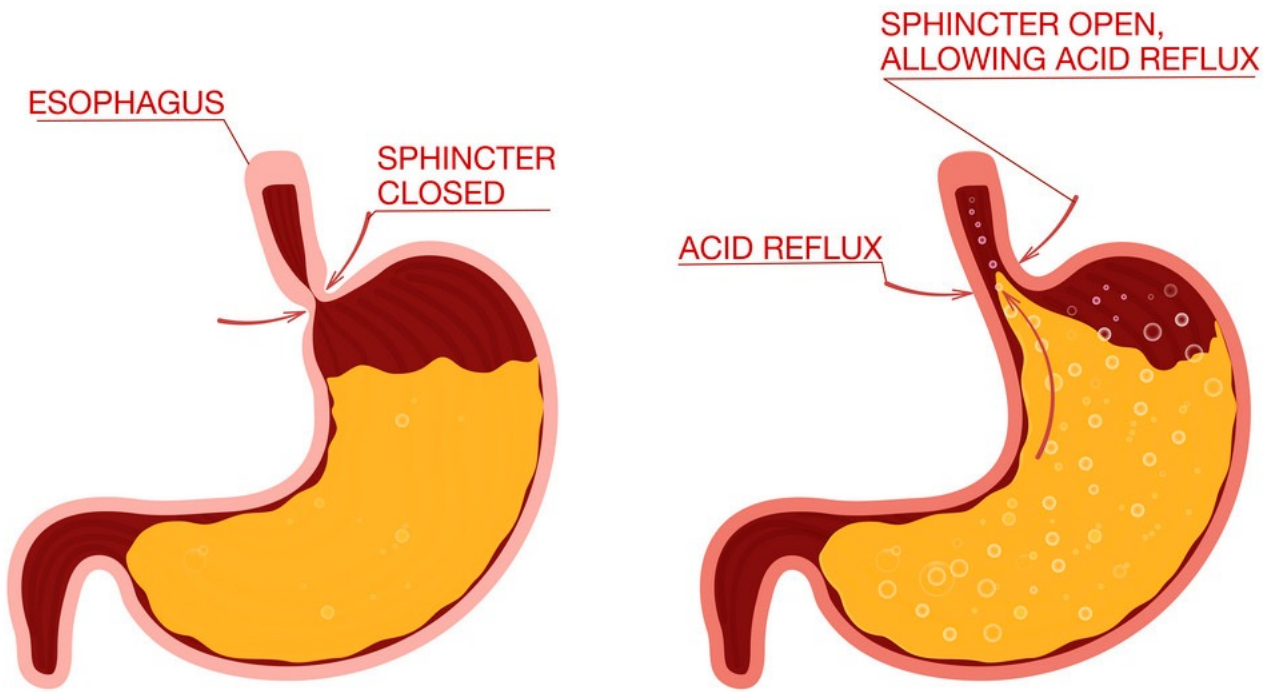
Functional Mechanisms of GERD



HCL/Gastrin Balance

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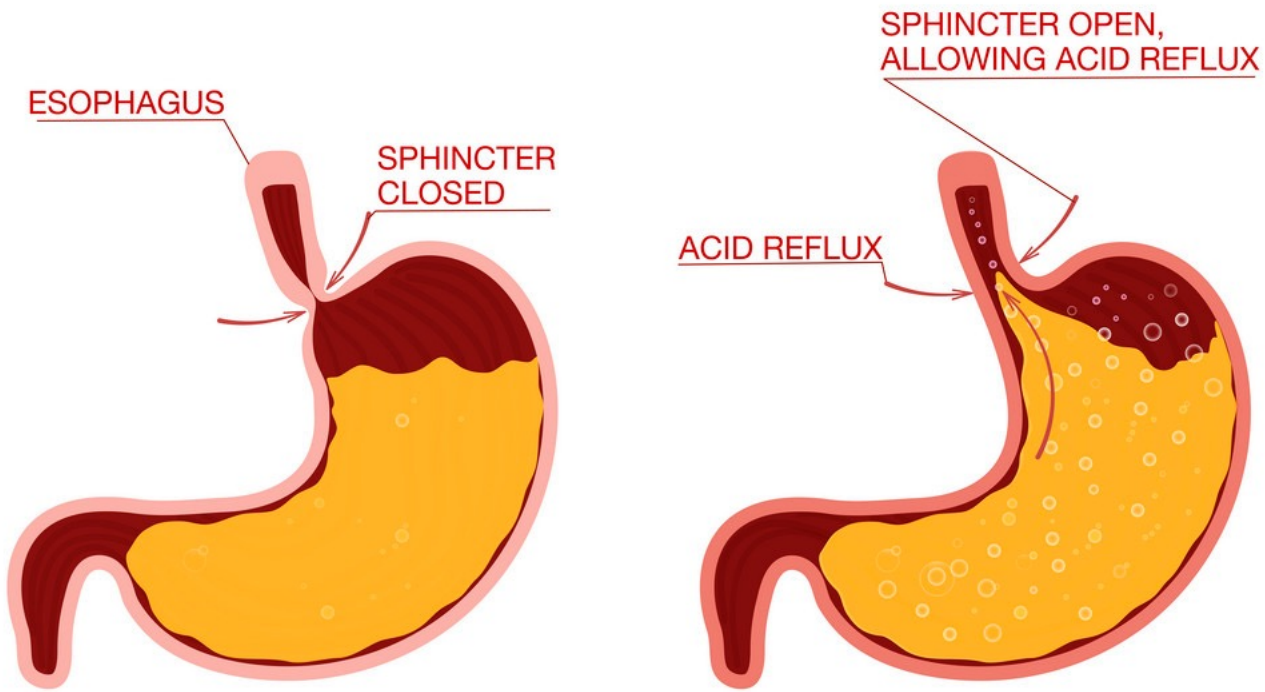
Functional Mechanisms of GERD



AI Parietal cell dysfunction

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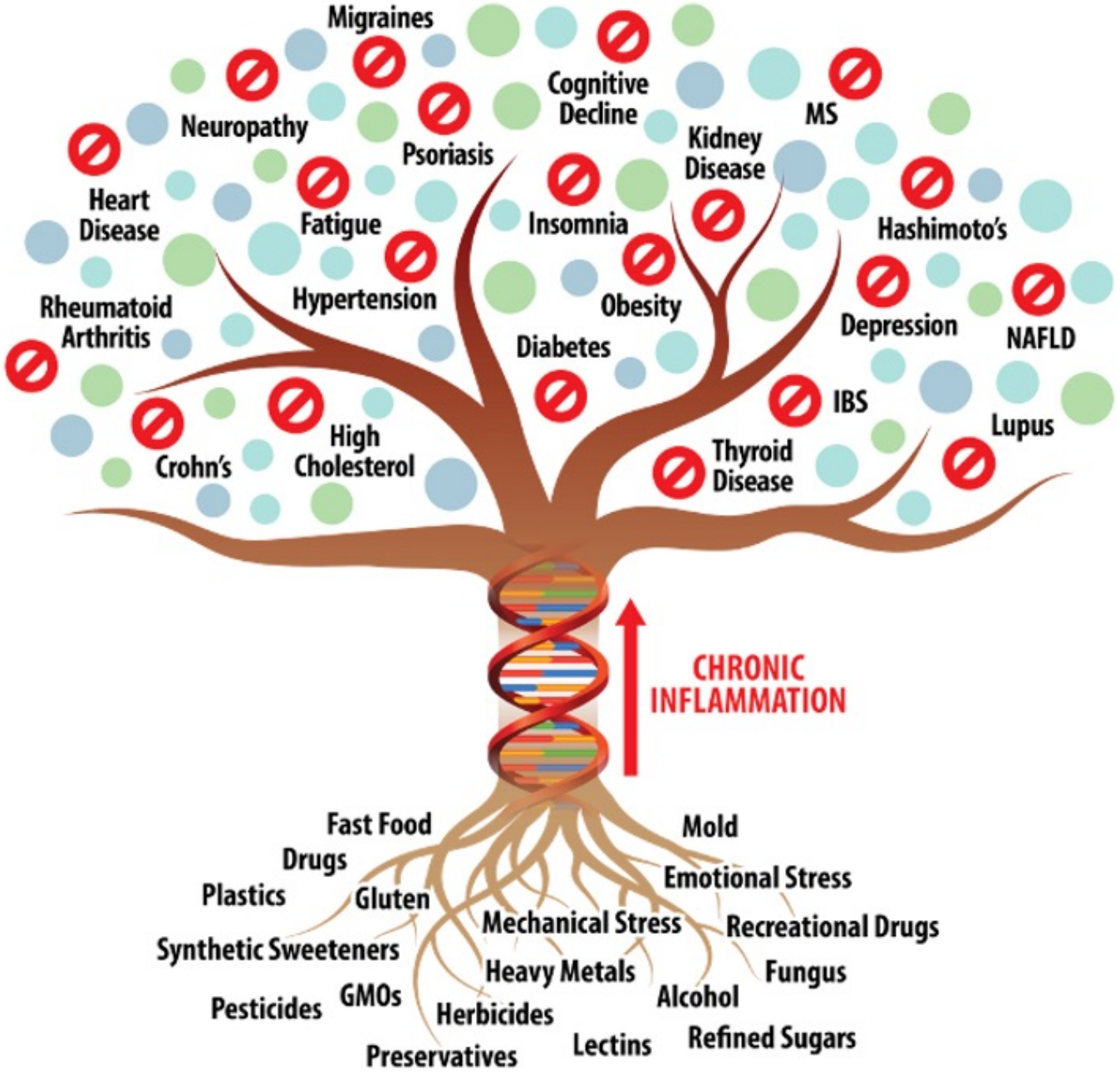
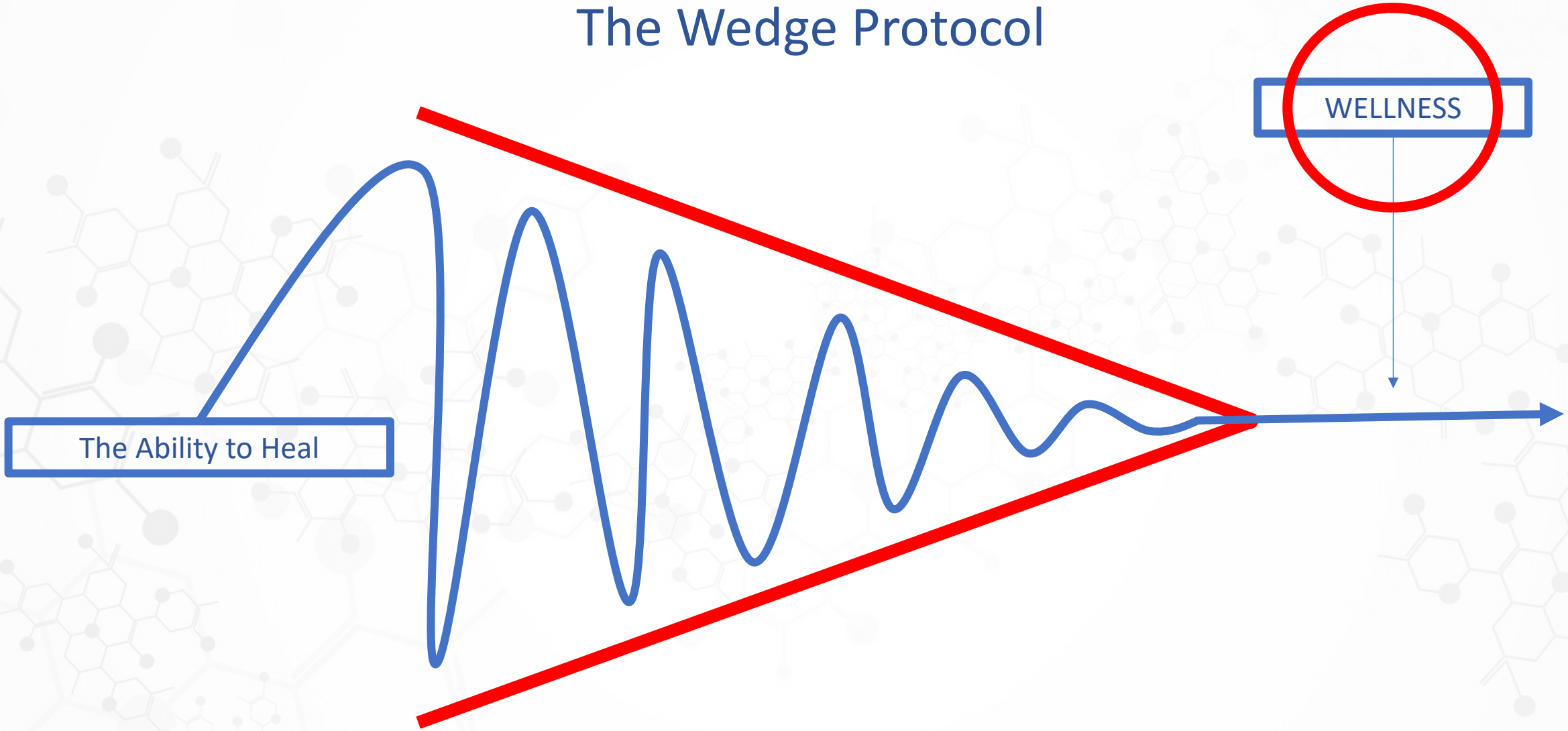
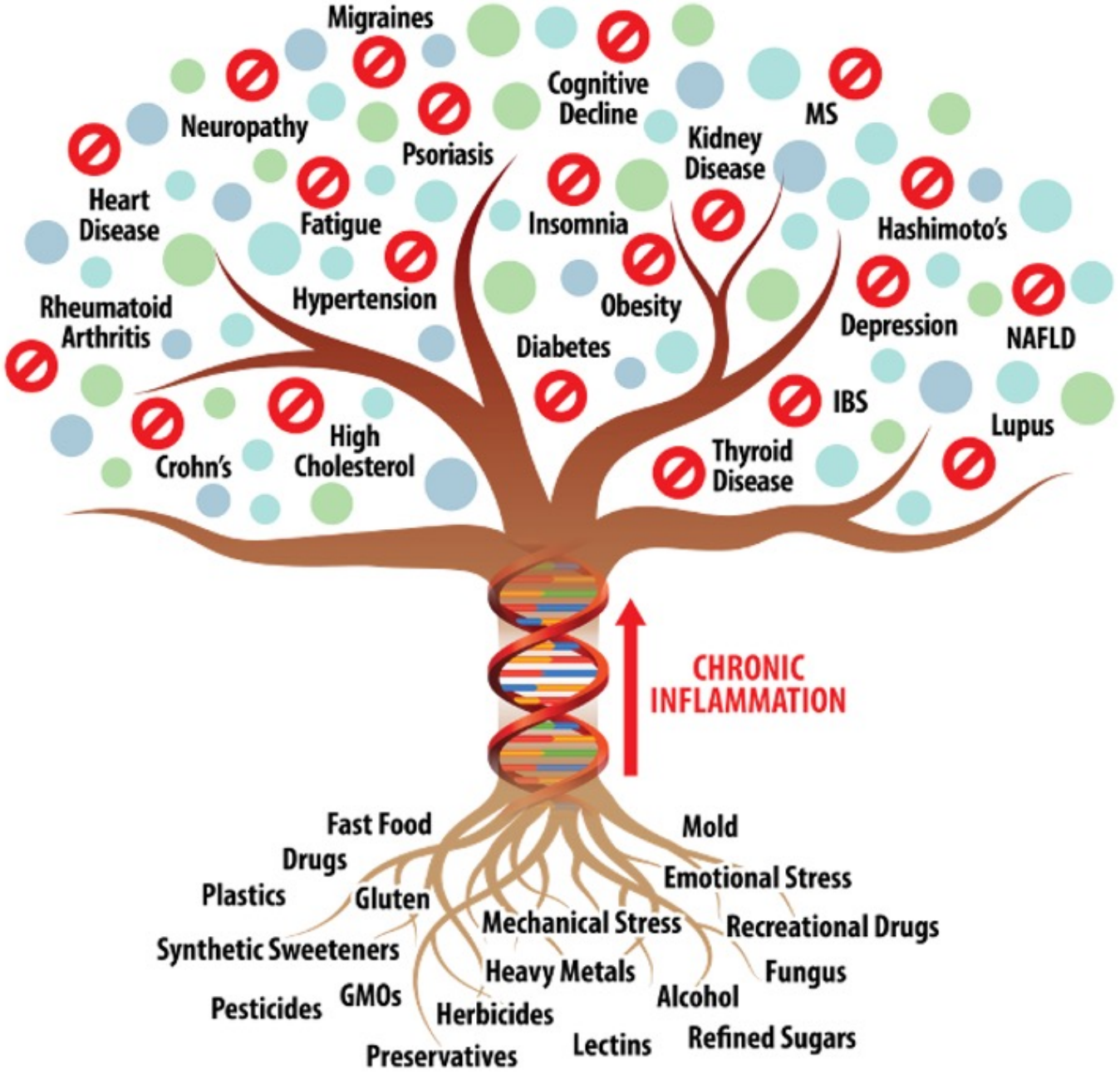

Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten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

The Wedge Protocol

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