

HCI – HISTAMINE CLEARANCE INDEXTM

The Histamine Clearance Index evaluates the efficiency of histamine clearance, which can provide insight into diamine oxidase (DAO) activity and inhibition.

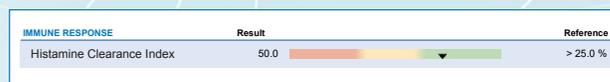


Figure 1. Histamine Clearance Index Sample

Results are reported as a percentage within a 5% to 95% range.

- Lower values (< 25%) = reduced histamine clearance¹
- High values (> 40%) = increased histamine clearance

NOTE: High doses of biotin may interfere with results. Individuals supplementing with more than 5 mg of biotin per day are generally advised to discontinue biotin supplementation for at least 24 hours prior to blood collection.

WHAT IS HISTAMINE?

Histamine is a bioactive amine derived from the amino acid histidine.² It is primarily produced in mast cells and basophils and released into surrounding tissues upon degranulation.³ Beyond endogenous production, dietary sources and microbial metabolism in the gut can substantially influence total histamine load.

Histamine receptors are widely distributed throughout the body, including on neurons, parietal cells, epithelial cells, and lymphocytes.^{3,4} As a result, histamine plays a role in numerous physiological processes, including vasodilation, inflammatory and allergic responses, smooth muscle contraction, gastric acid production, and gastrointestinal motility. Histamine also functions as a neurotransmitter in the central nervous system.^{2,4,5}

DAO and histamine N-methyltransferase (HNMT) enzymes are responsible for the breakdown of extracellular and intracellular histamine, respectively. DAO is predominantly expressed in the small intestine, ascending colon, liver, and kidneys.^{2,3,6} Within the small intestine, DAO is localized to the brush border, with activity increasing from the duodenum to the ileum.^{2,3}

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HISTAMINE-RELATED REACTIONS

When histamine levels exceed the body’s capacity for breakdown and clearance, patients may experience symptoms of what is commonly referred to as histamine intolerance.¹ This term is used to describe a non-IgE mediated sensitivity associated with increased histamine burden. This may be due, in part, to reduced or impaired DAO activity.^{7,8} Clinical presentations can be diverse and multisystemic.

Although histamine intolerance and IgE-mediated allergies may present with similar symptoms, the underlying mechanisms differ.

The IgE Allergy Explorer™ can help identify sensitization to specific allergens and may be useful in determining whether immune-mediated allergy is contributing to a patient’s symptoms.

SYMPTOMS OF HISTAMINE INTOLERANCE

- **Gut-Related Symptoms^{2,3,8,9}**
 - » Abdominal pain
 - » Bloating
 - » Postprandial fullness
 - » Diarrhea
 - » Constipation
- **Extraintestinal Symptoms^{2,3,8,9}**
 - » Headaches
 - » Dizziness
 - » Palpitations
 - » Sneezing
 - » Congestion
 - » Asthma
 - » Eczema
 - » Swelling
 - » Flushing
 - » Pruritus
 - » Urticaria

SOURCES OF HISTAMINE

Dietary intake can represent a significant source of histamine exposure. Histamine content varies widely in foods and beverages.

SOURCES OF DIETARY HISTAMINE ^{6,8,10,11}

Alcohol <i>(particularly red wine and beer)</i>	Canned fish	Peanuts, walnuts, cashews
Cured meats	Soy products <i>(soy sauce, tofu, etc.)</i>	Licorice
Aged cheeses	Vegetables <i>(tomatoes, eggplant, spinach)</i>	Leftovers
Fermented foods <i>(sauerkraut, kimchi, yogurt, etc.)</i>	Fruit <i>(avocado, pineapple, banana, papaya, kiwi, strawberries, citrus fruits)</i>	
Pickled or vinegar-based foods <i>(pickles, olives, mustard, etc.)</i>	Chocolate	

Histamine is also produced by specific bacteria, many of which are included on the **GI-MAP**®.^{2,12-16} Evaluating both dietary patterns and gut microbial activity can offer valuable insights into overall histamine burden.

HISTAMINE-PRODUCING BACTERIA ON GI-MAP

- *Lactobacillus* spp.
- *Enterococcus* spp.
- *Morganella* spp.
- *Pseudomonas* spp.
- *Citrobacter freundii*
- *Klebsiella* spp.
- *Klebsiella pneumoniae*
- *Proteus* spp.
- *Proteus mirabilis*
- *Enterobacter* spp.
- *Escherichia* spp.
- *Fusobacterium* spp.

DAO INHIBITION AND DEFICIENCY

DAO activity can be influenced by a variety of factors, including genetics, gastrointestinal conditions, and medication use.^{1,2} More than 50 genetic single nucleotide polymorphisms (SNPs) have been identified that influence DAO function.⁵

Conditions such as inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), celiac disease, nonceliac gluten sensitivity, gastroenteritis, and lactose intolerance may compromise DAO activity by affecting the integrity of the intestinal mucosa.^{6,13} Dysbiosis can exacerbate this process through its impact on mucosal inflammation and intestinal barrier dysfunction.^{3,13}

Additionally, alcohol and certain medications are known to interfere with histamine metabolism.^{2,6} Other dietary and gut-derived biogenic amines, such as cadaverine, tyramine, and putrescine, can competitively inhibit DAO activity, further impairing histamine clearance.^{2,6,12}

CLINICAL CONSIDERATIONS AND THERAPEUTIC APPROACHES

Common therapeutic considerations to address histamine overload may include:

- **Low Histamine Diet:** Temporarily remove high-histamine foods to reduce overall histamine burden, followed by a structured and symptom-guided reintroduction to assess individual tolerance.²
- **DAO Enzyme Support:** Supplemental DAO taken with meals to aid in the breakdown of dietary histamine.^{3,9}
- **Nutrient Support:** DAO activity depends on adequate availability of key micronutrient cofactors, including vitamin B6, vitamin C, copper, and zinc.¹ Assess micronutrient status via plasma testing or the **Organic Acids Profile**™ using urine metabolites. Consider mast cell stabilizers such as quercetin, nettles, omega-3 fatty acids, resveratrol, etc.¹⁷
- **Gut Health:** Assessing underlying gastrointestinal factors such as inflammatory dysbiosis and compromised mucosal integrity may help reduce histamine production and improve tolerance.
- **GI-MAP Testing:** The **GI-MAP** can provide additional context related to microbial imbalances, histamine-producing organisms, immune activity, and the overall gut environment.

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LEARN MORE



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