# HISTAMINE OVERLOAD

Causes, Symptoms, & Management

Histamine plays a crucial role in our body's inflammatory response, but an overload can lead to various health issues. This guide delves into the concept of histamine intolerance, its sources, and how the body processes it. It explains the mechanisms behind histamine degradation, the symptoms of histamine overload, and potential treatment strategies. By understanding the pathways and influences of histamine, we can better manage conditions related to histamine imbalance and improve overall health.

## What is Histamine?

Histamine is an inflammatory mediator. As with many substances in the body (e.g., cholesterol, estrogen, insulin), too much of a good thing can become problematic or even debilitating. Histamine overload (also often called histamine intolerance) is where the amount of histamine present outweighs the body's ability to degrade and eliminate it.

Histamine comes from many sources. Externally, we primarily get it from our foods. Internally, we produce it in response to immune threats (e.g., allergens, bacteria, fungi, viruses), and some of the microbes in our gut also produce it as part of their normal metabolism. The body degrades histamine via two pathways: DAO and HNMT.

## What is DAO?

In a healthy, balanced body, the diamine oxidase (DAO) enzyme is produced by intestinal villi in the brush border of the intestines (and, to a lesser degree, in the kidneys).

It is responsible for handling extracellular histamine from food and what is produced by our microbes. Therefore, damage to the brush border can impair DAO production. Genetic SNPs can also result in slow DAO production.

This enzyme is also called amine oxidase copper containing 1 (AOC1 gene) and, as the name implies, needs copper and activated Vitamin B6 (P5P) as a cofactor.

DAO is found in all organs but is highest in the upper portion of the small intestines (to help break down histamine in food). It is also prevalent in the kidneys, thymus, and placenta.

In fact, the placenta produces high amounts of DAO in pregnancy to protect the fetus from excess histamine. Therefore, one excellent clue about histamine intolerance is when a woman feels significant relief from her usual symptoms while pregnant.

So, for example, if a woman suffers from chronic migraines but she stops getting them during pregnancy, that is a significant clue as to the root cause of her challenges. Another great clue is if an antihistamine dramatically improves people's symptoms. For example, H1 antihistamines are often prescribed for anxiety and/or sleep (histamine promotes wakefulness and hypervigilance).



©2022 B Better Membership

# HISTAMINE OVERLOAD

Causes, Symptoms, & Management

## What is HNMT?

Histamine N-methyltransferase (HNMT) is the enzyme responsible for handling intracellular histamine. HNMT helps break down the histamine in the brain and central nervous system.

Genetic variations in HNMT however can lead to slower removal of histamine. This enzyme requires B vitamins and minerals, like molybdenum, copper, selenium, and zinc to work properly. Methylation is also required to process intracellular histamine and is also dependent on B vitamins, especially vitamins B9, B12 and B6.

When histamine is broken down with the help of the HNMT enzyme, it forms N-methylhistamine, which cannot bind to histamine receptors. A methyl group is needed in that reaction. N-methylhistamine then breaks down even further into N-methylimidazole acetaldehyde with the help of another enzyme called MAO-B.

## Histamine's Many Important Roles

Cells throughout the body have receptors for histamine, and therefore, the symptoms of histamine intolerance are widespread and vary wildly from individual to individual. It can be hard to pinpoint since symptoms can come and go and rotate.

- Receptors are found in neurons, endothelial cells, skin cells, adrenal cells, muscle cells, hepatocytes, chondrocytes, monocytes, neutrophils, eosinophils, mast cells, T cells, and B cells.
- Histamine is a potent vasodilator, meaning it helps open up tiny blood vessels to help blood circulate better and allows our white blood cells to get to where they're needed in the body. This is a useful response when the body is dealing with a threat, as long as everything is working properly. When it's uncontrolled, it can cause flushing, blood pressure fluctuations, dizziness, tissue swelling, rapid or irregular heartbeat, and more.
- Histamine plays many important roles in the brain. It helps us stay awake and alert, but too much can cause insomnia, anxiety, and/or panic attacks.
- In the stomach, histamine helps make stomach acid to digest our food well. However, too much can cause acid reflux, stomach pain, dysmotility, and/or diarrhea.
- Histamine is a critical chemical mediator of an effective immune system, but too much can create a hyperactive immune response, resulting in allergies, asthma, rashes, hives, and/or eczema.



©2022 B Better Membership

# HISTAMINE OVERLOAD

Causes, Symptoms, & Management

## Common Symptoms of Histamine Overload

| | | |
|---|---|---|
| Anxiety | Edema, flushing | Insomnia |
| Allergies, excess mucous secretion, contributing to sinus congestion, post-nasal drip, sneezing, and perhaps eustachian tube involvement, impairing hearing | Excess sweating | Mood issues, such as irritability, anxiety, depression, or panic attacks |
| Asthma, especially exercise-induced asthma | Fatigue | Motion sickness, sea sickness |
| Blood pressure swings (high or low) | Flushing | PMS or PMDD |
| Brain fog | GI issues, such as acid reflux, bloating, gas, diarrhea, early satiety, nausea, or vomiting | Skin issues such as itchiness, rashes, eczema, hives, urticaria, dermatographia, angioedema, very itchy from bug bites |
| Dizziness, fainting, or vertigo | Headaches, especially migraines | Tachycardia |

## Can histamine be tested?

Histamine can be tested in blood, but due to the fluctuating nature of histamine, one-time measurements may or may not be elevated.

This functional urine panel measures histamine and DAO, and this blood test measures histamine, DAO, zonulin, and LPS antibodies.

Serum DAO has been shown to be a valid marker to help diagnose histamine intolerance. Keep in mind, however, that some individuals struggle with histamine overload due to notably high exposure and production of histamine, while others struggle due to poor degradation and clearance of histamine. Please consider both!

In conventional lab work, you can look for higher percentages of eosinophils and basophils in a Complete Blood Count (CBC). Both of these white blood cells (WBCs) secrete histamine. In a healthy, relaxed immune system, eosinophils are usually very low (<3% of WBCs), and basophils will be zero or close to zero. Basophils are particularly strong secretors of histamine, so basophils over 1% are a strong clue.

Another lab that can be helpful is a total IgE antibody level in the blood, an indication of the body's immune defenses being armed to secrete histamine.

Again, histamine levels can be high due to strong sensitivity (high release) and/or poor detoxification ability (where it builds up over time). Suboptimal Vitamin D and zinc (ideally measured through RBC zinc) can also contribute to immune system dysregulation. Consider testing those too.

©2022 B Better Membership

# HISTAMINE OVERLOAD

Causes, Symptoms, & Management

## A Simpler, Less Invasive Test: Experiment!

The easiest way to determine if you're struggling with histamine overload is to do an experiment. First implement a low-histamine diet for two weeks and take DAO supplements before meals for support. If histamine overload is a primary disease dynamic in your case, you should experience significant relief.

### Foods high in histamine are typically aged or fermented in some way. They include:

- Dairy foods, especially aged or fermented dairy such as kefir, yogurt, sour cream, and aged cheeses
- Processed meats, such as deli meat, bacon, or sausage
- Fermented alcohol, such as beer and wine (especially red wine)
- Foods made with yeast, such as bread
- All fermented/cultured foods, such as vinegar (and condiments made with vinegar, such as salad dressing and ketchup), sauerkraut, kimchi, miso, kombucha, and soy sauce
- Canned fish (e.g., anchovies, sardines, tuna)
- Fruit juice and dried fruit
- Bone broth
- Leftovers (which increase in histamine the longer they are "leftover")
- Some foods not fermented or aged are still high in histamine, including avocado, eggplant, cooked tomatoes, and spinach in large quantities

### Some foods promote histamine release without having high levels themselves. These include:

- Alcohol, chocolate, eggs, bananas, and many citrus fruits
- Diets very high in protein can also be part of the problem, as mast cells use the enzyme histidine decarboxylase (HDC) to make histamine out of the amino acid histidine.

A low-histamine diet can be challenging, but it doesn't have to be 100%. A significant reduction in histamine along with DAO supplementation should be sufficient for a trial.



©2022 B Better Membership

# HISTAMINE OVERLOAD

Causes, Symptoms, & Management

## Helpful Supplements & Strategies

If the experiment confirms histamine overload, supplements and strategies that may be helpful include:

- **Gut healing supplements to heal the brush border and improve DAO enzyme secretion**
  - Quercetin (also a natural antihistamine)
  - L-glutamine
  - Zinc carnosine
  - Combination formulas, such as Design for Health's GI Revive
- **Address any pathogens or overgrowths that may be histamine-secretors (see here and here).**
- **Cofactors for DAO and HNMT synthesis**
  - Methylated B-complex (critical for methylation to break down excess histamine internal to our tissues)
  - Copper
  - Molybdenum
- **Immune system balancing nutrients**
  - Vitamin D3 (test and aim for 50 ng/ml)
  - Zinc (test RBC and aim for the upper third of the reference range)
  - Vitamin A
  - Vitamin C
- **DAO enzymes** can help supplement what the body may not be making on its own (e.g., Seeking Health Histamine Digest). These can be taken 10-15 minutes before meals containing histamine. In some cases, they may be taken before bedtime to help with sleep (for example, if elevated gut microbe histamine secretion is suspected).
- **Natural antihistamines and mast cell stabilizers**
  - Quercetin (also helpful for healing enhanced intestinal permeability)
  - Vitamin C
  - Green tea and L-theanine
  - Stinging Nettle
  - Bromelain
  - Pycnogenol
  - Combination formulas may be best for some (e.g., Metagenics Sinuplex)



©2022 B Better Membership

- **Probiotic supplements can contain species that produce histamine, so those should be avoided. These include:**
  - L. casei, except L. casei shirota
  - L. delbrueckii subs. Bulgaricus TISTR 895 (formerly L. Bulgaricus)
  - L. fermentum
  - L helveticus - depends on the strain, low evidence
  - Streptococcus thermophilus - can produce histamine, depending on the strain, low evidence
  - L. reuteri ATCC PTA 6475
  - B. licheniformis

- **Probiotics that may be helpful include:**
  - *Lactobacillus rhamnosus*
  - *Lactobacillus plantarum*
  - *Bifidobacteria*
  - *Saccharomyces boulardii*

In addition to gut health, genetics, poor methylation, nutrient deficiencies, and histamine-producing gut bugs (all discussed above), some other upstream root causes that can increase histamine levels include:

- Chronic anti-histamine drug use
- Chronic NSAID use (due to its effect on the intestinal brush border)
- Estrogen (a clue is if a woman struggles with hormonal migraines or other symptoms that occur with ovulation or right before menses)
- Exercise
- Stress
- Mold exposure

If any of these dynamics are at play, consider alternatives to NSAIDs and antihistamines, address estrogen dominance, exercise earlier in the day (to avoid insomnia), help minimize and manage stress, and reduce exposure to allergens such as mold, dust, pollen, etc.

If you're passionate about this topic and want to do a deeper dive, here are some great articles:

- https://www.seekinghealth.com/blogs/education/histamine-intolerance
- https://chriskresser.com/headaches-hives-and-heartburn-could-histamine-be-the-cause/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7463562/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8467868/
- https://drbeckycampbell.com/the-thyroid-histamine-connection/
- https://draxe.com/health/histamine-intolerance/




©2022 B Better Membership