

# Histamine intolerance and the influence of bowel microbiome: an Editorial

## Editorial

The medical community is becoming increasingly aware of the increase in Histamine Intolerance (HIT) among the general population. A groundbreaking article was published in 2007.<sup>1</sup> Printed in USA. © 2007 American Society for Nutrition – that explains the cause and effect of histamine dysregulation in the small bowel. Histamine can be metabolized in 2 ways: by oxidative deamination by diamine oxidase (DAO) or by ring methylation by histamine-*N*-methyltransferase (HNMT). Histamine intolerance is described as the absence or inability of diamine oxidase DAO or HNMT to break down histamine. Since histamine is a degradation product of digestion, bowel microbial flora plays a role in both the breakdown of histamine to lower levels and in the production of histamine creating higher levels.

Since the publication of this article in 2007, although some research has been forthcoming, no defined clinical diagnostic procedures exist, there is not an available list of pharmaceuticals that prompt the illness, genetic studies that solidify the predispositions to this condition are incomplete, and there are no physician-aware approaches for advising patients.

The purpose of this editorial is to emphasize the opportunities for microbiological research in this area due to the damaging systemic effects of high histamine. As microbiology researchers, the opportunities center around bodily histamine load as a product of digestion and how it may be influenced by the microbial composition in the bowel microbiome. Because gut bacterial composition can influence the metabolism of histamine, changes in microbial composition can alter these metabolic pathways, affecting histamine levels.

Excess histamine levels can cause a host of symptoms throughout the body. Histamine intolerance presents in patients with allergy-like symptoms who have no diagnosable allergies or internal complications. Symptoms may include osteoarthritis, urticaria, hives, asthma, depression, reaction to cefuroxime, arrhythmia and/or hypotension. Because of these varied symptoms, the recognition of histamine intolerance has been and continues to be underestimated. Further double-blind, placebo-controlled studies are needed in patients where histamine intolerance is considered the underlying cause.

**A short list of some pharmaceutical compounds** associated with histamine intolerance include:

Contrast media

Muscle relaxants: Pancuronium, alcuronium, D-tubocurarine

Narcotics: Thiopental

Analgesics: Morphine, pethidine, nonsteroidal anti-inflammatory drugs, acetylsalicylic acid, metamizole

Local anesthetics: Prilocaine

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Antiprotonic: Dobutamine

Antihypertensive drugs: Verapamil, oxprenolol, Di hydralazine

Antiarrhythmics: Propafenone

Diuretics: Amiloride

Drugs influencing gut motility: Metoclopramide

Antibiotics: Cefuroxime, cefotiam, isoniazid, pentamidine, clavulanic acid, chloroquine

Mucolytics: Acetylcysteine, ambroxol

Broncho lytic: Aminophylline

H2-receptor antagonists: Cimetidine

Cytostatic: Cyclophosphamide

Antidepressants: Amitriptyline

All SSRI's and SNRI's

Alcohol

Foods high in histamine content

**Patients who are suspected of having histamine intolerance** should have a designation. Their condition should be noted with a warning that the administration of contrast or drugs that release histamine should be avoided. If such drugs must be used, pre-medication of an antihistamine nature is indicated.

**Certain bacterial populations in the gut microbiome** can aid in reducing symptoms of histamine intolerance by promoting the degradation of histamine and supporting gut health. Key beneficial bacteria include:

***Lactobacillus* species:** These bacteria are known for their probiotic properties and can help degrade histamine. Strains like ***Lactobacillus rhamnosus*** and ***Lactobacillus plantarum*** are particularly beneficial.

***Bifidobacterium* species:** These bacteria can also assist in reducing histamine levels and improving gut health. ***Bifidobacterium longum***

is one example that has been associated with better histamine metabolism.

**Faecalibacterium prausnitzii:** This bacterium is known for its anti-inflammatory properties and contributes to gut barrier health, which can indirectly help manage histamine intolerance.

**Akkermansia muciniphila:** This species is linked to improved gut barrier function and may help regulate intestinal permeability, potentially reducing histamine absorption.

Incorporating the use of probiotics, can help promote the growth of these beneficial bacteria and alleviate symptoms of histamine intolerance.

#### Available resources for people who have histamine intolerance

Individuals with histamine intolerance, rely on available books and cookbooks, websites that inform on symptoms and foods to avoid, support groups, and the rare healthcare provider. Online forums and social media groups can provide community support and shared experiences.<sup>2-7</sup>

#### What to expect

Histamine intolerance is a condition that affects many organ systems in the body. It has roots in a genetic predisposition (MTHFR genes) and an exposure to offending pharmaceutical compounds. Although the scientific literature has been talking about this condition for several years, the mystery around a clear diagnosis remains. The number of physicians who know about it is staggeringly low, and the scientific research around it has yet to produce reliable diagnostic capabilities or inroads into management. Directed efforts are needed to improve information and management of this condition. As microbiologists, opportunities for research in this area are plentiful.

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#### Conflict of interests

Authors declare no conflict of interest.

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