HISTAMINE

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REFERENCES
Histamine is a biogenic amine synthesized by the pyridoxal phosphate (vitamin B-6) – containing L-histidine decarboxylase (HDC) from the amino acid histidine. It is produced in mast cells, basophils, platelets and some neurons, where it is stored intracellularly in vesicles and released on stimulation.

Histamine is a potent mediator of a number of biological reactions. In addition to the well-known process of mast cell degranulation, which happens through cross linking of IgE antibody on the cell surface by binding of the specific allergen, histamine release also can happen independently of IgE. That kind of non IgE reaction can take place caused by several other non immunologic stimuli, such as neuropeptides, complement factors (i.e., C3a and C5a), cytokines, hyperosmolarity, lipoproteins, adenosine, superoxidases, hypoxia, chemical and physical factors (e.g., extreme temperatures, traumas), or alcohol and certain food and drugs, may activate mast cells.

Histamine is an important mediator of many biological processes including inflammation, gastric acid secretion, neuromodulation, and regulation of immune function. Because of the strong pharmacological activity of histamine even at very low concentrations, its synthesis, transport, storage, release and degradation has to be carefully regulated, in order to avoid unwanted reactions.

Histamine is also generated by microbiological action in the course of food processing and it is therefore present in substantial amounts in many fermented foodstuffs and beverages.
The biogenic amine - histamine (2-[4-imidazolyl] ethylamine) has an important role in many physiological and pathological processes. In the human organism, histamine fulfils various functions as tissue hormone, neurotransmitter and messenger substance (biochemical signal transduction).

Histamine causes contraction of smooth muscle cells, particularly the bronchi and intestine, dilation of vessels and their increased permeability, increases mucosal secretion, causes tachycardia and arrhythmias, influences blood pressure, stimulates secretion of gastric juices and irritates nociceptive nerve fibres. Other important processes in which histamine is involved include neurotransmission, immunomodulation (enhanced chemotaxis of eosinophils and neutrophils, production of prostaglandins and thromboxane B, suppressed synthesis of lymphokines, etc.), haematopoiesis, wound healing, intestinal ischemia, day-night rhythm, the regulation of histamine- and polyamine-induced cell proliferation and angiogenesis in tumour models.

At a molecular level, histamine exerts its actions through an activation of histamine receptors which are part of the family of G protein-coupled receptors [GPCR].

Presently, there are four subtypes of histamine receptors described: histamine receptor 1 (H1R), histamine receptor 2 (H2R), histamine receptor 3 (H3R) and histamine receptor 4 (H4R).

They are heptahelical transmembrane molecules, which act as transducers of extracellular signals via G-protein and intracellular system of second messengers. Histamine acts by binding to target receptors according to the lock and key model and modulating intracellular signal cascades (signal transduction chains).

**H1 RECEPTORS (H1R)**

An activation of H1 receptors is primarily responsible for the allergy symptoms triggered by histamine. These include itching and pain, contractions of smooth muscle tissue in the bronchial tubes and large blood
vessels (diameter of more than 80 µm) as well as dilation of smaller blood vessels with hives and flush.

In the central nervous system, histamine is involved in triggering vomiting and the regulation of the sleep-wake cycle via an activation of H1 receptors. H1 receptors also play a part in regulating the release of hormones such as adrenaline.

Histamine is a messenger substance active in inflammatory processes and burns, and furthermore boosts the release of additional inflammatory mediators. Besides, it seems to play a part in the regulation of body temperature, the central control of blood pressure and pain perception.

**H1R antagonists**

H1-antihistamines refer to compounds that inhibit the activity of the H1 receptor. Since the H1 receptor exhibits constitutive activity, H1-antihistamines can be either neutral receptor antagonists or inverse agonists.

Normally, histamine binds to the H1 receptor and increases the receptor’s activity; the receptor antagonists work by binding to the receptor and blocking the activation of the receptor by histamine; by comparison, the inverse agonists bind to the receptor and reduce its activity, an effect which is opposite to histamine’s.

- Diphenhydramine
- Loratadine
- Cetirizine
- Fexofenadine
- Clemastine

**H2 RECEPTORS (H2R)**

H2 receptors are involved in the regulation of gastric acid production and bowel movements (motility, peristalsis). An increase of gastric acid production may be interpreted as a component of histamine-induced immune reaction. An accelerated onward transport of the intestinal contents leads to diarrhoea and may also be seen as an immune response.

A stimulation of H2 receptors also leads to an accelerated or stronger heart beat as well as dilation of smaller blood vessels.
H2R antagonists

H2-antihistamines, like H1-antihistamines, occur as inverse agonists and neutral antagonists. They act on H2 histamine receptors found mainly in the parietal cells of the gastric mucosa, which are part of the endogenous signalling pathway for gastric acid secretion.\(^8\)

Normally, histamine acts on H2 to stimulate acid secretion; drugs that inhibit H2 signalling thus reduce the secretion of gastric acid.\(^9\)

- Ranitidine
- Cimetidine
- Famotidine
- Nizatidine

H3 RECEPTORS (H3R)

In the human body the H3 receptors are primarily found presynaptically on cells of the central and peripheral nervous systems. As autoreceptors, they play a role when negative feedback prevents additional histamine release.

By the use of presynaptic receptors (in particular H2 receptors), histamine has a regulatory influence on noradrenergic, serotonergic, cholinergic, dopaminergic and glutaminergic neurons by blocking the release of neurotransmitters in the central and peripheral nervous systems.

As a result, it inhibits the release of the neurotransmitters acetylcholine, noradrenalin and serotonin as heteroreceptor. In this way, histamine influences indirectly the activity of these neurotransmitters.\(^4,10\)

Through these mechanisms, the H3 receptors play a role in the central regulation of hunger and thirst, the circadian rhythm, body temperature and blood pressure.

Furthermore, these receptors are said to be directly or indirectly implicated in the pathophysiology of neurological pain, schizophrenia, Parkinson’s disease and ADHS.\(^4\)
**H3R antagonists**

These are experimental agents and do not yet have a defined clinical use, although a number of drugs are currently in human trials. H3-antihistamines have a stimulant and nootropic effect.⁸

- ABT-239
- Ciproxifan
- Clobenpropit
- Thioperamide

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**H4 RECEPTORS (H4R)**

H4 receptors are involved in the targeted migration of immune cells such as eosinophil, granulocytes, T lymphocytes and monocytes. This is why it is assumed that these receptors play an important role in the recruitment of leukocytes during immune responses, in particular in allergic reactions.⁴

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**H4R antagonists**

These are experimental agents and do not yet have a defined clinical use, although a number of drugs are currently in human trials. H4-antihistamines appear to have an immunomodulatory role.⁸

- Thioperamide
- JNJ 7777120
SOURCES OF HISTAMINE
ENDOGENOUS SOURCES OF HISTAMINE IN ORGANISM

Histamine is a substance produced by the organism itself and stored in blood and tissue cells. Histamine originates in decarboxylation of amino acid histidine mediated by enzyme l-histidine decarboxylase, which contains pyridoxal phosphate (vitamin B6).

STORAGE

The storage takes place by binding to heparin in so-called vesicles. These are small organelles, separated by membranes, inside the cell. Enclosed in these vesicles, histamine is immobilized and cannot do any harm, but it is always able to be immediately released if required. Histamine is particularly synthesized and stored in the following cell types:

- Mast cells
- Basophil granulocytes
- Neurons and other nerve cells, such as cerebrovascular endothelial cells

Mast cells are found in tissue, in particular in epidermal cells of the skin, in histamine-storing cells of the mucous membranes, in bronchial tubes, the gastro-intestinal system (i.e. gastric mucosa) and the brain. The basophil granulocytes are blood cells. The highest histamine concentrations can be measured in the hypothalamus.

Classical sources of histamine in the organism are gastric enterochromaffin cells, histaminergic neurons, mast cells and basophils, which store histamine in intracellular vesicles, from where it is released upon stimulation. Degranulation of mast cells and histamine release is a result of bonding of specific antigen to FcRI receptor, which can be inhibited by luteolin (flavonoid with antioxidant properties).

Activation of mast cells can also occur in non-immune stimuli, such as neuropeptides (substance P), parts of the complement system (e.g. C3a and C5a), cytokines (IL-1, IL-3, IL-8, and GM-CSF), platelet activating factor (PAF), hyperosmolarity, lipoproteins, adenosine, superoxidases and hypoxia.

Many chemical and physical factors can be responsible for histamine release as well, for example extreme temperatures, trauma, vibrations or alcohol and some certain types of food and medication.

Mast cell activation plays a crucial role in the pathogenesis of many diseases - not only allergic,
but autoimmune as well, such as rheumatoid arthritis. de novo synthesis of histamine is also present in other cell types, e.g. platelets, monocytes/macrophages, dendritic cells, neutrophils and lymphocytes.

RELEASE OF HISTAMINE

Histamine is released from the vesicles during IgE-induced immediate-type (type I) allergic reactions or through complement factors such as an endotoxin-induced shock. In addition to tissue hormones, medications such as opiates, muscle relaxants, plasma expanders and radiopaque agents, may trigger the release of histamine.

Other important storage sites of histamine are the ECL cells of the gastric mucosa, which can release histamine induced by hormones and tissue hormones such as gastrin, acetylcholine and pituitary adenylate cyclase activating polypeptide (PACAP). A release of histamine in the synaptic cleft of histaminergic neurons is inhibited by acetylcholine, noradrenalin, and histamine via the presynaptic receptors.

EXOGENOUS SOURCES OF HISTAMINE

Apart from endogenous production, histamine is introduced in the organism from exogenous sources by ingestion of some types of food, where histamine is naturally present in a high concentration. Histamine is a component that can be found in most foods in varying concentrations. It occurs when food perishes, particularly products that are fermented, matured or have been stored over a long period of time. An additional, but less important source of exogenous histamine is the gut flora. Many kinds of microorganisms found in the intestines are able to produce histamine. Histamine ingested with food or produced in the gut must not get into the body, because an increased histamine level (referred to as histamine poisoning) may disrupt the body’s own histamine degradation, leading to numerous histamine-induced symptoms. Healthy people have two effective enzymatic barriers.

Histamine in exogenous sources can be synthesized by microbial decarboxylation of histidine by different fermenting bacteria, including natural human flora in the gut. Some bacteria are able to decarboxylate histidine in temperatures around +4 °C. To prevent histamine contamination of food the cooling is insufficient, freezing and early liquidation of viable bacteria is necessary.

Due to thermostability, histamine which is present in food is almost irremovable. Some types of food contain naturally high amount of histamine (cocoa, spinach, tomatoes, etc.). A high content of histamine is present in foods which originate by fermentation, either spontaneous or targeted (fermentation of alcoholic beverages - beer, wine, fermented vegetables, cheeses, meat, soy, yoghurt,
etc.). It is also important not to forget bacterial contamination of food when stored improperly.

The ability to produce histamine is present in Gram-positive, as well as Gram-negative bacteria. Many Gram-negative bacteria with this ability are common contaminants of food. In fish, there may be histamine intoxication from the following strains:

- Hafnia alvei
- Morganella morganii
- Klebsiella pneumonia
- Morganella psychrotolerans
- Photobacterium phosphoreum
- Photobacterium psychrotolerans

In fermented foods, histamine production is responsible for the strains of:

- Oenococcus oeni
- Pediococcus parvalus
- Pediococcus damnosus
- Tetracenomococcus species
- Leuconostoc species
- Lactobacillus saerimneri 30a
- Lactobacillus hilgardii
- Lactobacillus buchnerii
- Lactobacillus curvatus

It was discovered during the wine manufacturing process that histamine was produced and was responsible for the strains of:\(^{13}\)

- Lactobacillus parabuchneri
- Lactobacillus rossiae

Enzymatic activity of histidine decarboxylase can last even after bacterial autolysis.

**METABOLISM**

Histamine is formed by decarboxylation of the amino acid L-histidine in a reaction catalyzed by the enzyme histidine decarboxylase. The major routes of histamine inactivation in mammals are methylation of the imidazole ring, catalysed by histamine N - methyltransferase, and oxidative deamination of the primary amino group, catalysed by diamine oxidase.\(^{14}\)
Histamine may be metabolized through four mechanisms, whereby the first two mentioned constitute the primary degradation pathways:

- Oxidative deamination through diamine oxidase (DAO, histaminase).
- Cyclical methylation through histamine N-methyltransferase (HNMT).
- Acetylation into acetyl histamine. (This degradation pathway is primarily important in microbial degradation)
- Hydroxylase into hydantoin propionic acid.

(Vitamin C could be a cofactor in hydroxylase reactions, which convert histamine into hydantoin propionic acid - analogous to histidine degradation into hydantoin propionate. Presumably, this degradation mechanism is less significant in terms of quantity)

Research indicates that histamine from exogenous sources tends to be catabolised differently from endogenous histamine. The former is metabolised principally via oxidative deamination by diamine oxidase; the latter by ring N-methylation by histamine N-methyltransferase. The two systems produce different end-products.

This provides a means whereby the fate of histamine from the diet may be studied independently from that of the histamine arising within the body that is designed for participation in many essential body functions. The contribution of each of the enzymes systems (DAO and HNMT) to histamine breakdown seems to vary between tissues. Diamine oxidase activity seems to predominate in the intestine, whereas, N-methyltransferase activity predominates in the brain.

However, there is evidence inhibition of one pathway may switch the degradation to the other, even within the same organ. Recent research indicates in tissues where both enzymes occur together (in this case the porcine kidney), DAO tends to exhibit a histamine-degrading capacity ten times higher than that of HNMT.
D A O
NORMAL FUNCTION

The DAO gene is a protein coding gene. Diamine oxidase, also known as histaminase, is an enzyme encoded by the DAO gene. It is involved in the metabolism, oxidation, and inactivation of histamine in animals.

The enzyme is located mainly in the digestive tract (intestinal mucosa), therefore it acts during the digestion of food. High content is observed in the placenta as well. It is also secreted by eosinophils. This enzyme catalyses the degradation of compounds involved in allergic and immune responses, cell proliferation, tissue differentiation, tumour formation, and possibly apoptosis. That includes substances such as putrescine, histamine, spermine, and spermidine.

It is also involved in several metabolic pathways, including histidine and tryptophan metabolism. The histamine molecule is derived from an essential amino acid, histidine, which has many physiological and patho-physiological functions that are of a vital meaning for the body.

When there is an alteration in the metabolism of histamine, the imbalance between ingested histamine and histamine released from the storage cells may occur. Furthermore, insufficient DAO activity leads to histamine accumulation in plasma and the occurrence of it’s adverse effects on health.

Usually, the cause of this enzymatic dysfunction or functional lack of the main digestive enzyme responsible for the histamine elimination has a genetic origin. DAO as a hereditary factor is the main reason that some people have or produce few diamine oxidase (have a deficiency) of the enzyme.

CHROMOSOMAL LOCATION

The location of the human DAO gene is on chromosome 7, which contains more than 1,000 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

The chromosome spans about 159 million DNA building blocks (base pairs) and represents more than 5 percent of the total DNA in cells.

The cytogenetic location of the gene is 7q36.1, which is the long (q) arm of chromosome 7 at position 36.1.
OTHER NAMES FOR THIS GENE

• AOC1 (amine oxidase, copper containing 1)
• ABP1

SNPS IN THE DAO GENE

• rs1049742 - ABP1/DAO S332P
• rs1049793- AOC1/DAO H664A
• rs10156191 - ABP1/DAO T16M
• rs2052129– DAO G691T

HEALTH CONDITIONS RELATED TO GENETIC CHANGES

• Central Nervous System: Migraine, headaches and/or dizziness.
• Digestive System: Irritable Bowel Syndrome (diarrhoea, constipation), Crohn disease, stomach pain, nausea and/or vomiting.
• Cardiovascular System: hypotension, hypertension and/or arrhythmia.
• Epithelium: hives, oedema, atopic skin, eczema and/or rash.
• Respiratory System: nose congestion, rhinitis, asthma and/or sneezing.
• Muscular System: muscle pain, fibromyalgia and/or fatigue.
• Bone System: bone pain

NORMAL FUNCTION

Histamine N-methyltransferase (HMT, HNMT) is an enzyme that in humans is encoded by the HNMT gene.18

HNMT is a key enzyme concentrated in the liver which is responsible for degrading histamines generated as a result of the functions of the body and in particular mast-cells. The liver filters the blood to remove fat-soluble toxins, then disassembles those toxins into water soluble toxins, ready for excretion, disassembles all inflammatory material including histamine released from mast-cells, along with a long list of chemicals manufactured by the body and those ingested.

In mammals, histamine is metabolized by two major pathways: N (tau)-methylation via histamine N-methyltransferase and oxidative deamination via diamine oxidase. This gene encodes the first enzyme which is found in the cytosol and uses S-adenosyl-L-methionine as the methyl donor. In the mammalian brain, the neurotransmitter activity of histamine is controlled by N (tau)-methylation as diamine oxidase is not found in the central nervous system. A common genetic polymorphism affects
the activity levels of this gene product in red blood cells.\textsuperscript{19}

Histamine acts as a neurotransmitter in the brain which participates in the regulation of many biological processes including inflammation, gastric acid secretion, and neuromodulation. The enzyme histamine N-methyltransferase (HNMT) inactivates histamine by transferring a methyl group from S-adenosyl-L-methionine to histamine, and is the only well-known pathway for termination of neurotransmission actions of histamine in mammalian CNS.

**CHROMOSOMAL LOCATION**

The HNMT gene location is on chromosome 2. Chromosome 2 is the second largest human chromosome, spanning about 243 million building blocks of DNA (base pairs) and representing almost 8 percent of the total DNA in cells.

Chromosome 2 likely contains 1,300 to 1,400 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

The cytogenetic location of HNMT gene is 2q22.1, which is the long (q) arm of chromosome 2 at position 22.1, and the molecular location is from 137,964,068 to 138,016,364 base pairs on chromosome 2.

Chromosomal Location of HNMT gene
https://ghr.nlm.nih.gov/gene/HNMT#resources

**OTHER NAMES FOR THIS GENE**

- HMT
- HNMT-S1
- HNMT-S2
- MRT51
SNPS IN THE HNMT GENE

According SNPedia, the HNMT gene has the following SNPs

- rs1378321 – HNMT A47507G
- rs1050891 - HNMT T939C
- rs17583889 - HNMT C29232A
- rs1801105 merged into rs11558538 - HNMT Thr105Ile - ASSOCIATED WITH A 50% DROP IN HNMT ACTIVITY
- rs745756308 - HNMT Leu208Pro
- rs758252808 - HNMT Gly60Asp

HEALTH CONDITIONS RELATED TO GENETIC CHANGES

There are health conditions relating to the genetic changes of the HNMT gene. Most of them are as consequence of the SNPs (single nucleotide polymorphisms) that can be found in this gene.

- Respiratory sensitivity ie: COUGH
- Mental retardation, autosomal recessive
- Hypersensitivity drug reactions (Non-steroidal anti-inflammatory drugs (NSAIDs))
- Nonsynonymous polymorphism
- Parkinson disease (PD) development and Essential tremor (ET) development
- Non-syndromic autosomal recessive intellectual disability (mental retardation)
- ADHD and food dye sensitivity
- Anthracycline cardiotoxicity (ACT)
- Allergic versus Non-Allergic Asthma
- Asthma
H I T
Histamine intolerance (HIT) is a pathological process, where there is a disproportion between intake of histamine and the ability of the organism to eliminate it, so excessive accumulation of histamine occurs.

HIT has typically presented more often in people who are middle-aged and prevalence of it is estimated to be 1% of the population, although this diagnosis can be unrecognized and underestimated, because it manifests via the multi-faced clinical symptoms, which are often misinterpreted by the patient as well as by the physician.

Under normal circumstances, there is an enzymatic barrier formed by DAO and HMNT in cells of intestinal epithelium in otherwise healthy individuals, which sufficiently protects from resorption of histamine from ingested food into the bloodstream. Histamine intolerance, therefore increased histamine concentration in blood, can be caused when the amount of these protective enzymes is insufficient or these enzymes are inhibited.

In such cases, development of symptoms resulting from increased concentration of histamine occurs even in ingestion of a small amount of histamine in food, which is usually well tolerated in healthy individuals. Insufficient activity of DAO can occur based on genetic predisposition, in diseases of gastrointestinal tract, which decrease production of DAO by damaged enterocytes (inflammatory bowel diseases, infections, parasitic infestations, dysmicrobia, metabolic malabsorption), or in inhibition of DAO by other biogenic amines, alcohol or medications.

DAO gene polymorphisms significantly influence expression and activity of DAO, but they are not sufficient for the development of HIT on their own. Concurrence of environmental cofactors is of high importance, such as potential modifications of alternative histamine N-methyltransferase pathway, vesicular shift of both enzymes and amines or ability of enterocytes to reuptake histamine. Therefore, on the development of HIT there is a contribution of genetic, as well as environmental factors.

Reduced DAO activity can be found in patients with chronic renal failure, viral hepatitis, advanced hepatic cirrhosis, and chronic urticaria - a typically histamine related illness with a reduced tolerance for endogenous histamine. Decreased degradation capacity of DAO can be caused by lack of its cofactors, vitamin B6, vitamin C, copper and zinc. Some substances (histamine liberators) have the ability to release histamine from endogenous reserves in the organism.

Histamine can be synthesized from l-carnosine, which is released in the organism in physical activity and in stress in general. Dipeptide carnosine is present in tissues and is hydrolysed in stress, thus providing histamine.

Histamine concentration in the organism is also influenced by psychological stress. Hormones, which are released during stress reaction directly activate mast cells, which leads to the release of
histamine and other inflammatory factors. Apart from that, stress has negative effects on the epithelium of the small intestine with proven influence on activity of membrane processes and increased permeability of this important barrier. This potentiates an increase of histamine from the intestine and its liberation from mast cells by CRH-dependent mechanisms.

Because the fact that histamine is an important mediator responsible for symptoms of classical allergy reaction type I - [IgE-mediated] hypersensitivity reactions, it is difficult to differentiate this reaction from histamine intolerance, which has basically the same clinical manifestations.

Unlike IgE-mediated food allergy, when even a small amount of ingested antigen leads to development of symptoms, in histamine intolerance the cumulative amount of ingested histamine plays the key role.¹

**SYMPTOMS OF HIT**

Most symptoms of HIT develop primarily due to an increase in concentration of histamine in the organism. Secondary symptoms result from the fact that increased concentration of histamine stimulates synthesis and release of catecholamines, which can cause paradoxical increase of blood pressure (even though histamine itself causes its decrease), tachycardia, dysrhythmias, nervousness, sensation of inner tremor and sleep disturbances.

**MEDICATION INDUCED SNP**

Medication induced SNP can happen in the absence of an actual gene SNP. Certain medications can act as “drug muggers” on a pathway, stealing the actual nutrients that the pathway needs to run properly. If your body runs out of a nutrient that a specific pathway needs, then the pathway stops working. It’s kind of like a double homozygous SNP that is expressing, but it occurs from medicines you take (that rob the necessary nutrients). This phenomenon is known as a “Medication-Induced SNP” by some specialists.

**CONTROLLING HISTAMINE**

Some individuals with high histamine are considered to be “under methylated”. This suggests they have few methyl groups needed to break down histamine.

The four key nutrients that support a lack of methylation activity include:

- Vitamin B-6
- SAMe and the amino acid L-methionine
- Zinc
Betaine hydrochloride

Additionally, there are natural enzyme formulations that are employed to increase histamine breakdown in the gut. These are commercially available today. Additional herbs and nutrients have been reported as effective for modulating histamine release during allergy flare-ups. This include:

- Quercetin
- Skullcap
- Eyebright
- Platycodon
- Silk tree
- White mulberry
- Bromelain
- Vitamin C
- Calcium
- MSM
- DAO enzyme
- Stinging nettles

**DIET**

Despite everything, no matter the intake of different supplements, medications or drugs, the most important thing is our diet. Many foods are high in histamine so monitoring those and keeping levels low are often the key for many people.

Rather than only focusing mainly on what you should not be eating, it is much better to turn your attention and effort to what you can eat to support your healing, health and wellness.

DAO and HNMT, the same as all other genes, enzymes, proteins and other important compounds in our body, have their cofactors that contribute to either speed up or inhibition of the genes function.

When you have a SNP in your histamine genes (DAO or HNMT), the best prevention for accumulation of histamine, is regulation of the diet. Some foods naturally have more histamine, while others accumulate histamines while they age. So, a low histamine diet must be focused around getting foods at their top level of freshness.

This list gives you an indication of some of the foods that affect those who have a histamine intolerance (high in histamine, releasing histamine, DAO blocking foods, low histamine) that will really help devise a diet for your patients.

**FOODS HIGH IN HISTAMINES**

- Fermented alcoholic beverages, especially wine, champagne and beer
• Fermented foods: sauerkraut, vinegar, soy sauce, kefir, yogurt, kombucha, etc.
• Vinegar-containing foods: pickles, mayonnaise, olives
• Cured meats: bacon, salami, pepperoni, luncheon meats and hot dogs
• Soured foods: sour cream, sour milk, buttermilk, soured bread, etc.
• Dried fruit: apricots, prunes, dates, figs, raisins
• Most citrus fruits
• Aged cheese including goat cheese
• Nuts: walnuts, cashews, and peanuts
• Vegetables: avocados, eggplant, spinach, and tomatoes
• Smoked fish and certain species of fish: mackerel, mahi-mahi, tuna, anchovies, sardines
• Processed foods of all types – Preservatives are high in histamines

HISTAMINE-RELEASING FOODS

• Alcohol
• Bananas
• Chocolate
• Cow’s Milk
• Nuts
• Papaya
• Pineapple
• Shellfish
• Strawberries
• Tomatoes
• Wheat Germ
• Many artificial preservatives and dyes

DAO-BLOCKING FOODS

• Alcohol
• Energy drinks
• Black tea
• Mate tea
• Green tea

LOW HISTAMINE FOODS

• Freshly Cooked Meat & Poultry (frozen or fresh)
• Freshly Caught Fish
• Extra Virgin Olive Oil
• Pasture-Raised Eggs
• Gluten-Free Grains: brown rice & quinoa
• Fresh Fruits: Other than citrus, avocado, tomato, pineapple, bananas and strawberries
• Fresh Vegetables (except spinach and eggplant)
• Coconut milk, Rice milk, Hemp milk,
• Coconut oil & Grass-fed Butter/Ghee
• Leafy herbs
• Herbal teas
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