

Histamine Intolerance

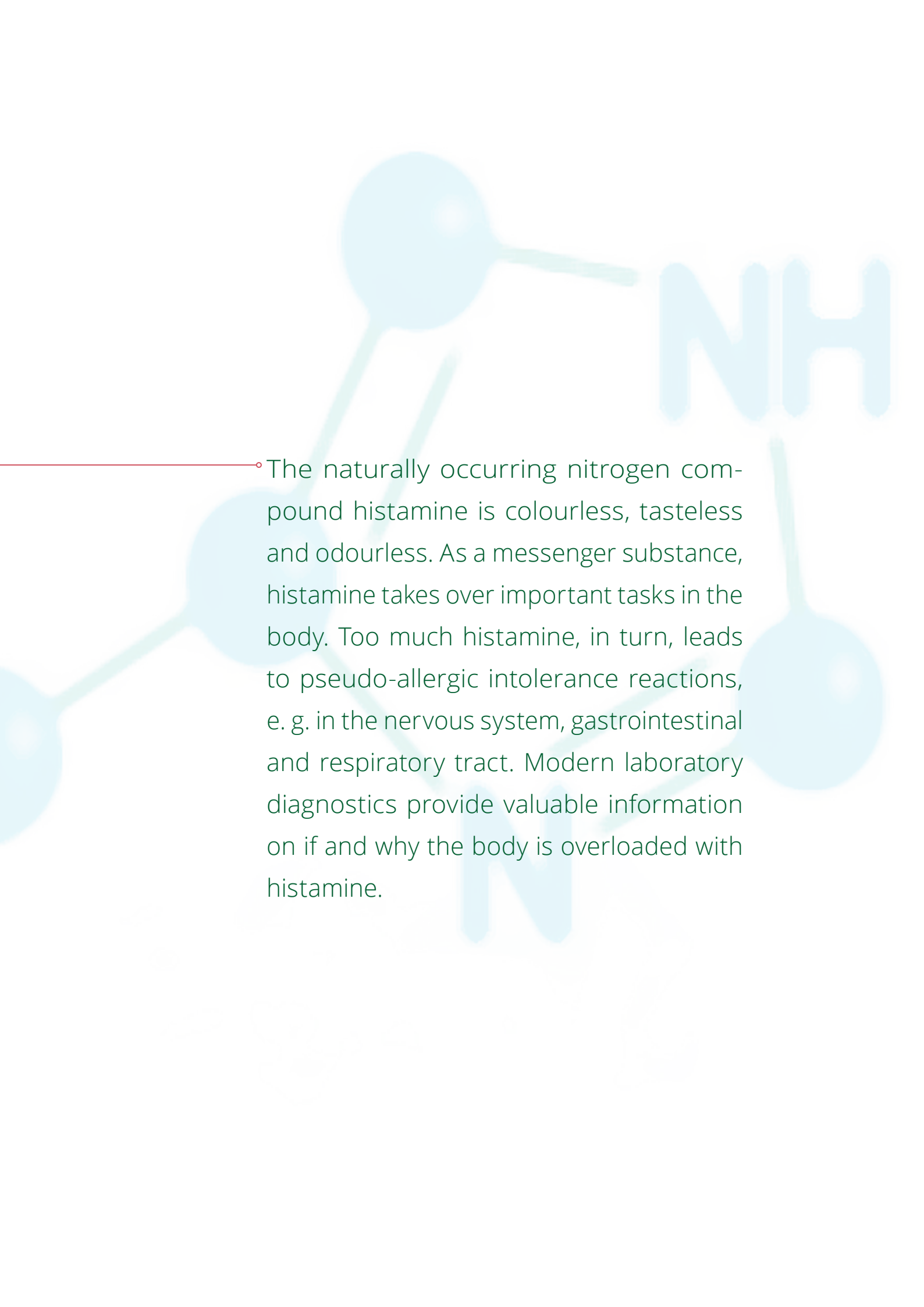


Tracking Histamine –
modern diagnostic clears the path

Histamine Intolerance

H₂N



- 
- The naturally occurring nitrogen compound histamine is colourless, tasteless and odourless. As a messenger substance, histamine takes over important tasks in the body. Too much histamine, in turn, leads to pseudo-allergic intolerance reactions, e. g. in the nervous system, gastrointestinal and respiratory tract. Modern laboratory diagnostics provide valuable information on if and why the body is overloaded with histamine.

Histamine – an important substance

Histamine is Latin for a nitrogenous compound in tissue.

Primarily, histamine is a biogenic amine, formed from amino acid histidine and occurs in human, animal and plant organisms. It is mainly stored in mast cells and is known as a defense and inflammation mediator against harmful substances or predators. Anyone who has ever come into contact with the burning hairs of a stinging nettle knows about its defensive potential. The skin area turns red, itches, hurts and swells.

Allergy sufferers also know this kind of reactions. The body releases histamine to protect against supposedly harmful foreign substances, leading to reactions on the skin, mucous membranes and in the gastrointestinal tract.

In addition to the protective defense and inflammatory reactions, histamine serves as a neurotransmitter, tissue hormone and messenger substance. Thus it is responsible for stimulating the production of gastric acid, lowering blood pressure, regulating the sleep-wake rhythm and appetite, among other things. ⁽¹⁾

A certain dose of histamine is important. Yet, if this dose is exceeded, disorders occur - „The dose makes the poison!“

How does histamine enter the body and how do we get rid of it?

Basically, there are two ways how histamine is obtained by the body. On one hand, the body can produce histamine itself (endogenous synthesis), on the other hand, histamine can be attained from the outside (exogenous supply). Besides the physiological endogenous synthesis, there is a pathological synthesis causing an overproduction of histamine (mast cell disease). The exogenous supply takes place either via histamine-forming bacteria, which normally do not occur in the intestine and if so, only in small quantities (malcolonization of the intestine) or via food ⁽²⁾.

By means of histamine-degrading enzymes, a healthy person is usually able to keep the balance between histamine production and degradation. The situation is different when this ratio gets out of balance. Reasons may either be an overloaded degradation capacity due to a too high histamine concentration (e.g. by eating spoiled fish = poisoning) ⁽²⁾ or a reduced histamine degradation ⁽³⁾.

In histamine degradation (see Fig. 1) two enzymes are of central importance: Diaminooxidase (DAO) and histamine N-methyltransferase (HNMT). DAO is predominantly extracellular (in the intestine) and HNMT is intracellularly (in liver, lung, kidney, bronchi etc.) active ^(3,4). The reason for reduced enzymatic degradation may be that the amount of enzymes and/or the enzymatic performance is too low. The latter could be based on a lack of so-called cofactors. Cofactors of DAO are vitamin B6, vitamin C, copper and zinc ⁽²⁾. For HNMT, S-adenosylmethionine (SAM) is considered to be the decisive factor ⁽⁵⁾ and thus, due to the superior methionine/homocysteine and folate cycle, B12, magnesium, B9 ⁽⁶⁾ and B2 are the cofactors of SAM or rather the indirect cofactors of HNMT ⁽⁷⁾. If the amount or performance of DAO or HNMT is reduced, histamine is insufficiently degraded and therefore accumulates in the body. The excess histamine binds to its specific receptors (H1R, H2R, H3R and H4R) triggering certain mechanisms which can result in a variety of symptoms.

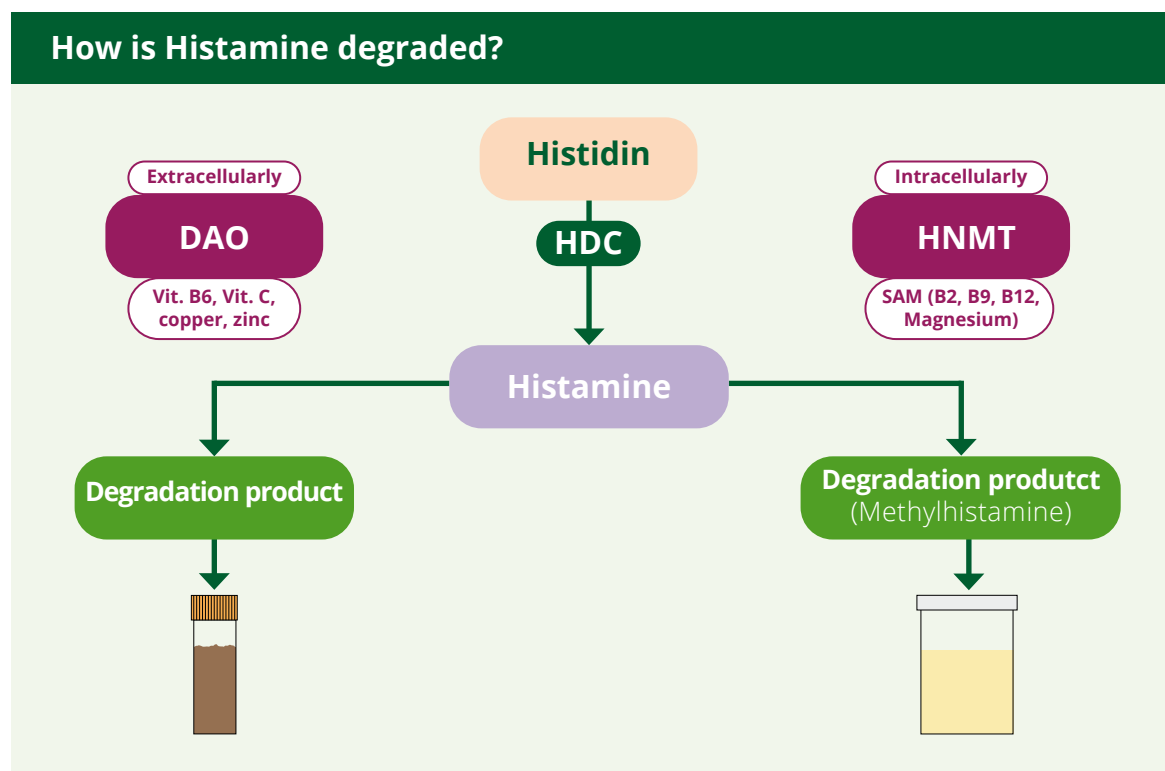


Figure 1
Enzymatic degradation of histamine (Mod. after 4, 7)
HDC - Histidin-Decarboxylase

Histaminosis, histamine sensitivity or histamine intolerance?

Regarding this topic, there are several terms in circulation that are used as synonyms. However, this is not quite correct. "Histaminosis" is the generic term and describes the present condition "There is too much histamine in the body". The term does not indicate why histamine is increased. Instead, "histamine sensitivity" is a subordinate term to histaminosis and indicates that the increased histamine level is due to a histamine release disorder, degradation disorder or poisoning. Food intolerance is defined as an enzyme defect or -deficiency ⁽⁸⁾. In the case of "histamine intolerance" the enzymes required for histamine degradation are not, or only insufficiently functional or only available in reduced concentration, thus the histamine cannot be degraded fast enough.

Histamine intolerance is therefore always based on an enzymatic degradation disorder and can be one of the reasons for histamine sensitivity ⁽⁸⁾.

Typical symptoms of histamine intolerance

Whether histaminosis, histamine sensitivity or histamine intolerance, the result is always the same.

There are increased histamine levels in blood or stool, caused by an imbalance between histamine accumulation and enzymatic histamine breakdown.

The following diagram shows possible symptoms of histaminosis:

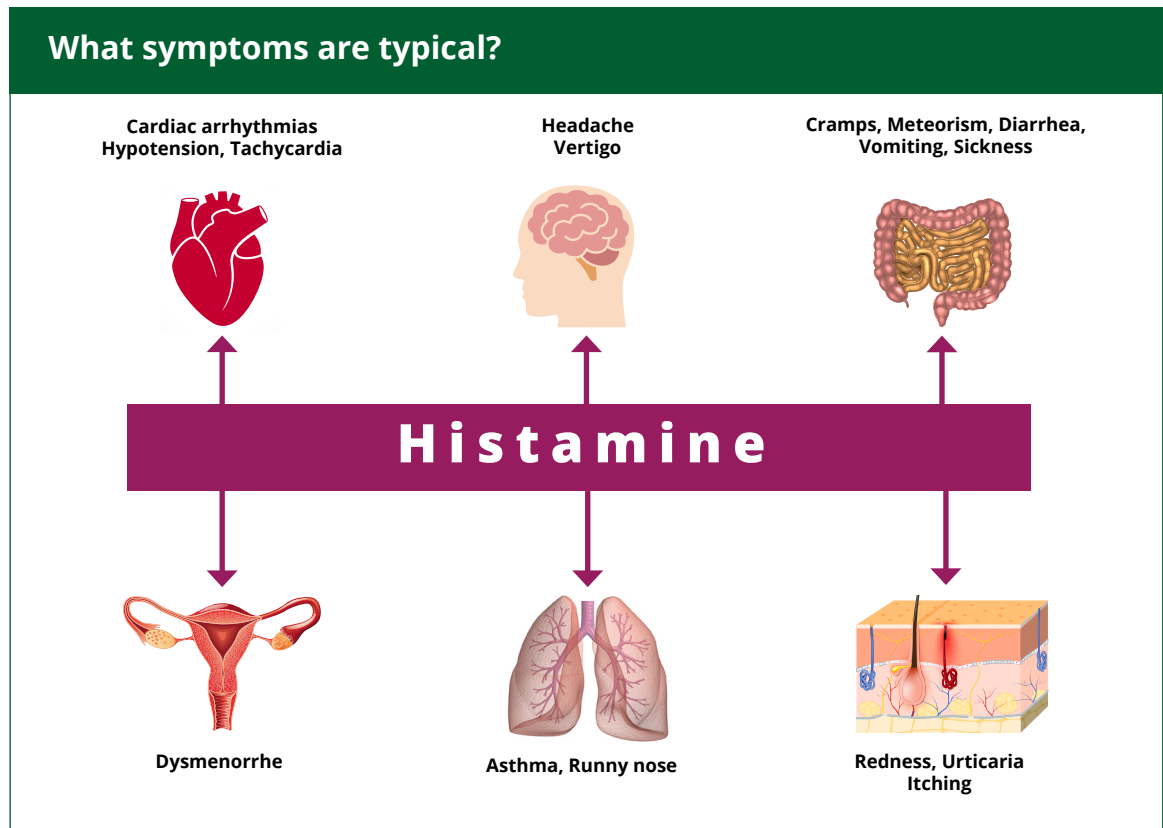


Figure 2
Possible symptoms of Histamine Intolerance (Mod after 4, 9)

The path to diagnosis „Histamine Intolerance“

In patients suffering from the above mentioned symptoms (at least two) and who have been tested negative for allergies, autoimmune diseases and intestinal diseases, a histamine intolerance must be considered. The best diagnostic options are the following:

Proof of increased histamine concentration in stool

Material: Test Set 909

Histamine that has accumulated in the intestine and couldn't be degraded, is eliminated via stool. The cause of increased faecal histamine levels can be related to the consumption of histamine-rich food, but also to a food allergy, increased stress or an impaired degradation. In case of a positive test result, further diagnostics should follow in order to find the exact cause.

Proof of increased histamine concentration in urine

Material: Test Set 908

An increased histamine concentration in urine may be due to a reduced histamine degradation by HNMT. However, an allergy, a parasitic infection or an endocrine tumor are further possible causes.

Proof of reduced total histamine degradation capacity (THDC)

Material: Serum

Some patients are symptom-free under a histamine-free diet, even though they do not suffer from a decreased DAO amount or concentration. It is therefore assumed that yet unknown degradation and neutralization reactions take place. The total histamine degradation capacity test is not limited to a specific enzyme but all possible degradation mechanisms are considered. A special diet or a histamine provocation is not required for this test.

Proof of reduced DAO concentration

Material: Serum

High histamine levels in stool may indicate reduced DAO concentration. If this is confirmed, it needs to be kept in mind that the intestine is the main site of DAO formation. Thus, a DAO deficiency could indicate a damaged gut mucosa.

Further impairment of the intestinal health e.g. an inflammation or a Leaky gut syndrome should be ruled out before starting treatment with a DAO substitution ⁽¹⁰⁾.

Proof of reduced concentration of cofactors of DAO

Material: EDTA, Heparin

An increased histamine concentration in stool may be due to a reduced enzymatic DAO activity. A deficit of cofactors, can lead to such reduced enzymatic activity. For this reason DAO is not able to work at its maximum speed. Corresponding deficiencies should be compensated.

Proof of increased concentration of histamine forming bacteria

Material: Stool

Histamine-forming bacteria are able to convert histidine into histamine. An increased concentration of histamine-producing bacteria in the intestine ⁽¹¹⁾, such as *Morganella morganii*, *Klebsiella pneumoniae* and *Hafnia alvei*, can cause this increase in stool histamine levels. Therapy needs to focus on the development of an intact intestinal flora.

What to avoid in case of histamine intolerance?

1. Food containing histamine

Histamine is naturally present in some plant-based foods. Some products, however, only become rich in histamine through processing, preservation or maturation processes. Responsible are microorganisms that have the ability to convert amino acid histidine into histamine ⁽¹⁾. The microorganisms are either already contained in the product itself or are added for processing. Therefore, the fresher and more natural the food is, the better it is tolerated.

2. Biogenic Amines

Biogenic amines are formed by enzymatic conversion of various amino acids. Responsible for these enzymatic conversion are bacteria. Biogenic amines are mainly found in protein-rich fermented foods, but also in, for example, cereal sprouts, walnuts, pineapples and bananas. Besides the biogenic amine histamine, there are many other biogenic amines, such as tyramine, phenyl ethylamine and serotonin. All biogenic amines are degraded by the same metabolic pathway as histamine, creating a competitive situation. Since histamine has a lower affinity to DAO than other biogenic amines, its degradation rate is lower ⁽¹²⁾.



3. Histamine Liberators

Substances with the property of releasing histamine from the body's own storage cells are called histamine liberators. They do not possess any histamine of their own, but considerably raise the body's histamine level by activating storage cells to release histamine. This can potentially overload the capacity of the histamine degradation system. Examples for some of these substances are alcohol, certain foodstuffs such as strawberries, nuts, chocolate and citrus fruits, but also some active ingredients in medicine ^(2, 9).



4. Diaminooxidase Blocker

DAO blockers block DAO, thus inhibiting the degradation of histamine/biogenic amines. Potential DAO blockers are alcohol, nicotine and certain medical substances ^(9,13).

Nutritional recommendations for histamine intolerance

In the case of histamine intolerance the diet strongly depends on the individual tolerance limit. Some patients develop symptoms at the slightest histamine intake, while other patients tolerate some histamine-containing foods well. In general, the consumption of histamine-containing foods, biogenic amines and histamine liberators should be limited as far as necessary and possible.





Alcohol plays a crucial role as it acts not only as a histamine liberator but also as a DAO blocker. This means that alcohol releases large amounts of histamine and prevents its degradation. Alcohol should therefore be avoided completely. If medication containing active ingredients with histamine-releasing or DAO-blocking properties is taken, a change in medication should be discussed with the doctor.

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