

## Histamine Intolerance Test

### Method for measuring the activity of the histamine-degrading enzyme diamine oxidase

#### SPECIAL FEATURE

Histamine is indispensable for the human body since it fulfils vital functions. It is both produced in the body and taken in with food in various quantities. Problems only occur in case of excessive quantities or not degraded histamine. In these cases, histamine will lead to allergic and pseudoallergic reactions.

Histamine intolerance is due to a (temporary) deficiency or an inhibition of the enzyme diamine oxidase (DAO). DAO is the enzyme responsible for the degradation of histamine. Although DAO is virtually found in the whole body, the bowels constitute its most important site of action. The enzymatic activity of DAO determines the rate of degradation of histamine. If a DAO deficiency and / or inhibition is present, the organism will not be able to degrade quickly enough the histamine taken in with food or released from body cells and the symptoms of histamine intolerance will occur.

#### SYMPTOMS

Millions of people suffer from considerable complaints after having eaten certain foodstuffs:

- migraine, headache
- dizziness
- gastrointestinal complaints, soft stools
- tachycardia, arrhythmia
- hypotension
- menstrual pain
- rhinitis
- dry nose
- asthma
- depressions
- itching of the skin, red skin

An excessive quantity of histamine in the body may be responsible for these complex complaints. Another cause of a reduced DAO function is the taking of substances inhibiting its activity such as alcohol or drugs.

Histamine-induced food intolerance is not mediated by IgE. Determining the DAO activity in the serum therefore is the suitable marker for diagnosing histamine intolerance and associated clinical pictures.

#### HISTAMINE INTOLERANCE TEST

Histamine intolerance, also called histamine incompatibility, can be detected beyond doubt by means of a blood test. The test

- measures the activity of the DAO contained in the blood
- determines the individual intensity of histamine intolerance
- makes possible further selective diagnostics and therapy recommendations

#### DESCRIPTION

##### In-vitro diagnostic procedure for quantitative determination of diamine oxidase activity in the serum

The test is based on a radio immuno assay (RIA) principle. The determination of the DAO activity is achieved by determining the concentration of a reaction product. Radiolabelled putrescine is used as substrate. The reaction product is radioactive 1-pyrroline that is transferred into an organic solvent by means of liquid phase extraction. After adding scintillator, radioactivity is determined by a beta counter. The quantity of radioactivity measured is directly proportional to the DAO activity of the sample.

A laboratory service of:

## Background information

### DEFICIENCY OF DAO

In case of histamine intolerance, the body cannot or can only partially degrade histamine. This is caused by a (temporary) deficiency or an inhibition of the diamine oxidase (DAO). According to the findings available up to now, in most instances, histamine intolerance is not a genetic, but an acquired disease that is manifest in approx. three per cent of the population. In up to 20%, symptoms occur in particular when foodstuffs rich in histamine are consumed together with DAO inhibitors such as alcohol. Approximately 80 per cent of the persons affected are women, most of them aged 40 and over. The risk of developing this intolerance is increased for persons who suffer from inflammatory intestinal diseases or cross sensitivities.

### WHAT IS HISTAMINE?

- decarboxylation product of histidine
- found in nearly all animals and plants
- main transmitter substance for nervous reactions
- present throughout all human tissues
- in high concentrations especially in lung, skin, colon

### DAO AS REGULATOR

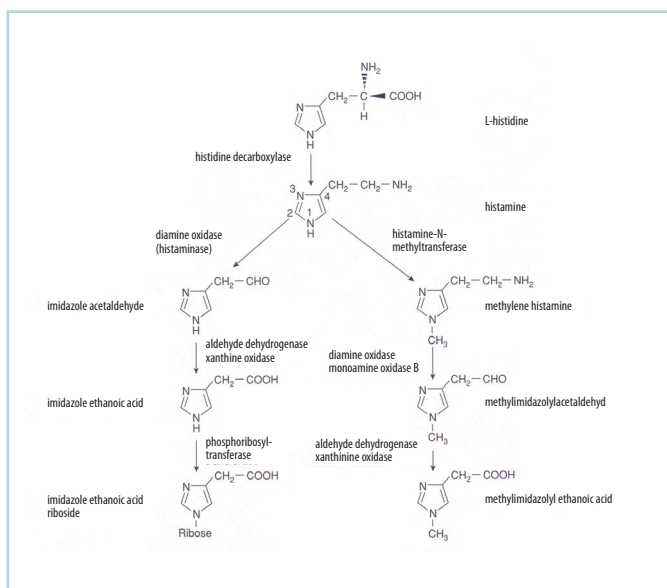
Histamine is a very active mediator for a large number of physical reactions and as such is regulated very well. DAO is the most important regulator for the histamine present in the tissue and in the blood circulation. Depending on the current requirements in the organism, the enzyme converts the histamine present in the tissue or in the blood circulation into imidazole acetaldehyde, a substance that does not trigger any action in the organism. This ensures a steady histamine level required for the balance of the countless chemical reactions taking place in the body.

### BIOGENOUS AMINES

Histamine is the most important representative of a class of substances combined under the name of biogenous amines. This is a large number of – in most cases aliphatic – polyamines (saturated organic compounds comprising several amino groups) that are found in nearly all living organisms as natural metabolic products. Polyamines have essential regulatory properties for cellular growth and cell division. Furthermore, they are highly reactive mediators of a large number of metabolic processes – in very small concentrations already. In nerve cells and other excitable cells, among other things, polyamines play an essential role as neurotransmitters for the regulation of the synaptic activity and the regeneration of cells.

### DEVELOPMENT OF HISTAMINE INTOLERANCE

Complaints basically develop due to an excessive quantity of histamine in the organism. The activity of DAO is limited; histamine taken in through food and produced in the body cannot be degraded at all or only to a limited extent.



Biosynthesis and degradation of histamine

## CAUSES OF INTOLERANCE

There are various reasons that can lead to the development of histamine intolerance:

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### Consumption of foodstuffs rich in histamine

- fish: e.g. tuna fish, sardine
- cheese: e.g. Emmental, Gouda
- vegetables: e.g. sauerkraut, spinach
- smoked meat: e.g. salami
- alcohol: e.g. red wine, sparkling wine
- vinegar: e.g. balsamic vinegar

After the consumption, the histamine concentration in the blood will increase. In particular foodstuffs that ripen for a very (too) long time or that are stored for a very (too) long time, have a high content of histamine that may cause problems depending on DAO activity.



### Consumption of biogenous amines & histamine liberators

- chocolate and cocoa
- citrus fruits
- nuts
- pulses
- wheat germs
- black and green tea
- tomatoes
- strawberries, bananas, pineapples, kiwifruits, papaya, raspberries, pears

In case of a high consumption of biogenous amines, DAO is no longer available in sufficient quantities for the degradation of histamine. Other foodstuffs, so-called histamine liberators, can release the body's histamine and thus have a negative influence on the histamine level in the body.

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### Inhibition of the enzyme

- alcohol
- drugs like e.g.: acetylcysteine, ambroxole, aminophylline, amitriptyline, chloroquine, clavulanic acid, isoniazid, metamizole, metoclopramide, propafenone, verapamil

The inhibition of the DAO enzyme results in histamine intolerance. Possible potent inhibitors of DAO are in particular alcohol, but also some common drugs.

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### Affected intestinal flora

An affected intestinal flora produces considerable quantities of histamine and other biogenous amines that lead to an additional inhibition of DAO.

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### Vitamin B6 and copper deficiency

Copper is a central component of DAO. A deficiency of copper results in not enough DAO being produced. Vitamin B6 is a co-factor of DAO. Without vitamin B6, the enzyme is not able to degrade histamine.

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### Congenital deficiency of DAO

This very rare type of histamine intolerance is based on a congenital enzyme defect due to which the enzyme is not produced in sufficient quantities.

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### BLOOD TEST AND FURTHER DIAGNOSTICS

The histamine intolerance test measures the activity of the DAO contained in the blood, since the DAO circulates through the body in the blood. The blood is mixed with a substance similar to histamine and the degradation of this substance is measured. The larger the quantity of DAO in the blood, the larger is the portion of the substance that is degraded.

In the next step - as a basis for therapy - two possible causes of histamine intolerance can be determined by means of further diagnostics. Copper is a central component in the DAO. If not enough copper is present, DAO cannot be produced in sufficient quantities. Vitamin B6 is a co-factor that means that the DAO cannot convert any histamine without this factor. If a reduced DAO activity is found, the determination of vitamin B6 and copper in the serum can be made in a second step.

### THERAPY

- sticking to a diet poor in histamine (elimination diet)
- avoiding foodstuffs rich in histamine, histamine liberators, alcoholic drinks and drugs that inhibit DAO
- taking the enzyme DAO as dietary supplement
- as the case may be, taking antihistaminic agents
- as the case may be, administration of vitamin preparation e.g. vitamin B6

### PREANALYTICS AND PERFORMANCE

- withdrawal of blood at the surgery of the attending physician into a serum monovette (1 ml)
- serum is stable for 48 hours at room temperature, for an unlimited period of time at -20°C
- sending in to: InVitaLab-laboratory, also together with blood sample for type III food allergy test (ImuPro)
- processing time approx. one week



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### REFERENCES

- **Food induced histaminosis as an epidemiological problem: plasma histamine elevation and haemodynamic alterations after oral histamine administration and blockade of diamine oxidase (DAO).**

Sattler J et al. Agents and Actions 23:361-65 (1988)

- **Determination of DAO-activity in normal human blood serum.**

Tufvesson G et al. Scand J Clin Lab Invest 24:163-68. (1969)

- **The red wine maximization test: drinking histamine rich wine induces a transient increase of plasma diamine oxidase activity in healthy volunteers.**

Wantke F et al. Inflammation Research 48:169-70. (1999)

- **The red wine provocation test: intolerance to histamine as a model für food intolerance.**

Wantke F et al. Allergy Proceedings 15:27-32. (1994)

- **Daily variations of serum diamine oxidase and the influence of H1 and H2 blockers: a critical approach to routine diamine oxidase assessment.**

Wantke F et al. Inflammation Research 47:396-400. (1998)

- **Role of food allergy and food intolerance in recurrent urticaria.**

Jarisch R et al. In: Wüthrich B (Hrsg): The Atopy Syndrome in the Third Millennium. Curr Probl Dermatol, Basel, Karger, 28:64-73. (1999)

- **Histamine free diet: treatment of choice for histamine induced food intolerance and supporting treatment for chronic headaches**

Wantke F et al. Clin Exp Allergy 23: 982-85. (1993)

- **Histamin-Intoleranz und Diaminooxidaseangel**

Götz M et al. Allergologie 9: 426-30. (1996)

- **Histamin Intoleranz.**

Jarisch R Stuttgart, Thieme 21 (1999)