

Histamine Intolerance

Information for Medical Professionals

Histamine intolerance (HIT) can mimic food allergy and should be considered when a patient complains of adverse reactions to foods where IgE-mediated allergy is not suspected or has been ruled out. HIT should also be considered in patients with chronic unexplained symptoms such as IBS-type symptoms, rashes / flushing, migraine-type headaches, sleep disorders, unexplained anxiety or palpitations and chronic urticaria (see full symptom list below)

A surprisingly large range of foods are naturally rich in histamine or develop high levels of histamine as they degrade during storage. Normally, a gut enzyme, diamine oxidase (DAO) destroys food-derived histamine which therefore does not cause any symptoms when histamine-rich foods are eaten. However in some people DAO activity is reduced and if a number of histamine-rich foods are consumed, some histamine is absorbed, causing local or systemic symptoms. DAO activity may be inherently reduced, or may be affected by medication; a number of commonly prescribed drugs affect DAO activity.

The lack of a single definitive test for HIT makes diagnosis less than straightforward but the following pathway is suggested.

EXCLUSION OF SIMILAR LOOKING ILLNESSES

- The patient should write a food diary for at least 2 – 4 weeks, and take this to the consultation. HIT should be considered if they regularly eat significant amounts of histamine-rich foods.
- Other food intolerances (e.g. lactose intolerance, coeliac disease, true food allergy) should be excluded or taken into account as part of the diagnosis. IgG tests are considered to be highly controversial and are NOT suitable for testing food intolerances such as histamine intolerance or lactose intolerance.
- Mastocytosis as a cause for symptoms should be checked for. Apart from allergic symptoms those of mastocytosis can also be very similar to those of histamine intolerance. More information can be found in the paper “Mastocytosis: state of the art”ⁱ.
- The patient should be referred to a gastroenterologist in order to establish or exclude any other gastroenterological diseases.

DETERMINATION OF HISTAMINE INTOLERANCE:

Indications:

- If the patient experiences two or more of the symptoms below
- If the patient starts to experience significant improvement of symptoms at the latest after 4 weeks of a low-histamine diet and relapses after dietary errors
- If the skin-prick test for allergies shows negative results for all substances except for an evidently strong reaction to the positive controlⁱⁱ

- If there is a significant improvement or even disappearance of symptoms after application of anti-histamines (see Figure 1 in Maintz & Novak paper)
- Low presence or activity of diamine oxidase
- High histamine levels in the blood serum (patient needs to have test done at the lab itself due to instability of histamine)
- High histamine levels in urine

CURRENT METHODS OF DIAGNOSIS:

Gold Standard is still an elimination diet under the supervision of a medical professional or/and a registered dietician with knowledge in the field and the continued usage of a diet diary to monitor improvement.

Another and possibly more conclusive option would be to test for DAO and histamine levels, put the patient on a two week low-histamine (also wrongly referred to as histamine-free) diet, and test for DAO and histamine levels again afterwards. If symptoms have improved, DAO levels have risen and histamine levels have gone down histamine intolerance is present. If DAO and histamine levels do not change and symptoms do not improve this means that the presence of histamine intolerance is unlikely.ⁱⁱⁱ

Some diagnoses of histamine intolerance have been acquired by only testing for DAO levels once before starting a diet regime. However, it has been pointed out that DAO levels can vary strongly and that a result of a normal DAO level does not exclude the likelihood of histamine intolerance.^{iv}

DAO tests from blood serum can be obtained privately via GP referral at the TDL:

Diamino Oxidase - {to detect histamine intolerance}

Sample requirement: Serum

Turn around time: 1 week appx.

All samples must be accompanied by a doctors request form or referral for them to run the tests.

Call 0207 307 7380 or e-mail to referrals2@tdlpathology.

SYMPTOMS:

The ingestion of histamine-rich food or of alcohol or drugs that release histamine or block DAO may provoke diarrhoea, headache, rhinoconjunctival symptoms, asthma, hypotension, arrhythmia, urticaria, pruritus, flushing, and other conditions in patients with histamine intolerance.^v

Symptoms involved can be two or more of the following:

Digestive tract

- Diarrhoea
- Diarrhoea alternating with normal motions (Irritable Bowel Syndrome – IBS)
- Chronic constipation
- Flatulence and feeling of fullness
- Stomach cramps
- Stomach ache
- Nausea
- Vomiting

Symptoms affecting head and face

- Flushing of face and/or chest (very common symptom)
- Headaches, similar to migraine
- Runny nose and weepy eyes, although there is no clinical sign of allergies
- Fits of dizziness
- Extreme tiredness, feeling knocked out
- Quinke Oedema (swellings mostly appearing around eyes and lips, sometimes in the area of the throat)

Skin problems

- Skin rashes, itchiness
- Eczema,
- Urticaria
- Acne (pimples)

Chest area

- Asthma
- Cardiac arrhythmia, such as a fast beating or irregular heart beat

Women

- Dysmenorrhoea (severe period pains)
- HIT symptoms go away during pregnancy and return after birth of child

Other symptoms

- Chills and shivers
- Low blood pressure
- Circulatory collapse
- Sudden psychological changes (e.g. aggressiveness, inattentiveness, lack of concentration)
- Sleep disorder^{vi}

A summary of histamine-mediated symptoms and their interlinked connection with histamine receptors (H1, H2, H3, H4) which determines the application of appropriate antihistamine medication for the patient can be found here:

Histamine and histamine intolerance.

Laura Maintz, Natalija Novak (2007)

The American Journal of Clinical Nutrition 85 (5) p. 1186, FIGURE 1

<http://www.ncbi.nlm.nih.gov/pubmed/17490952>

TRIGGERS AND CAUSES

HIT symptoms can be triggered by one or a combination of several causes:

- Medication that suppresses the enzyme Diamine oxidase or N-Methyltransferase.

Foods that have lower histamine levels and are thus to be preferred:

- Fresh meat (cooled, frozen or fresh)
- Freshly caught fish
- Chicken (skinned and fresh)
- Egg yolk
- Fresh fruits – with the exception of strawberries, most fresh fruits are considered to have a low histamine level (also see histamine liberators below)
- Fresh vegetables – with the exception of tomatoes
- Grains – rice noodles, yeast free rye bread, rice crisp bread, oats, puffed rice crackers, millet flour, pasta (spelt and corn based)
- Fresh pasteurised milk and milk products
- Milk substitutes – coconut milk, rice milk
- Cream cheese, butter (without the histamine generating rancidity)
- Most cooking oils – check suitability before use
- Most leafy herbs – check suitability before use
- Most non-citric fruit juices
- Herbal teas – with the exception of those listed below

Foods that have higher levels of histamine:

- Alcohol
- Pickled or canned foods – sauerkrauts
- Matured cheeses
- Smoked meat products – salami, ham, sausages...
- Shellfish
- Beans and pulses – chickpeas, soy beans, peanuts
- Nuts – walnuts, cashew nuts
- Chocolates and other cocoa based products
- Most citric fruits
- Wheat based products
- Vinegar
- Ready meals
- Salty snacks, sweets with preservatives and artificial colourings

Foods that release histamine (histamine liberators)

- Most citric fruits – kiwi, lemon, lime, pineapple, plums...
- Cocoa and chocolate
- Nuts
- Papaya
- Beans and pulses
- Tomatoes
- Wheat germ
- Additives – benzoate, sulphites, nitrites, glutamate, food dyes

Foods that block the diamine oxidase (DAO) enzyme:

- Alcohol

- Black tea
- Energy drinks
- Green tea
- Mate tea

Debatable:

- Yoghurt – depends on the bacteria culture used
- Egg white – it is a histamine liberator only when in its raw state

Other:

- Yeast – even though it does not contain histamine as such, yeast serves as a catalyst for histamine generation during manufacture. There is no yeast in the end product.

TREATMENT

There is currently no cure for histamine intolerance.

The key to success is for the patient to learn to adjust to a low-histamine diet and manage the condition(s) until it either goes away, or for life.

The patient needs to avoid stress.

Symptoms can be alleviated (but this is not the overall solution!) with the help of the following options:

ANTIHISTAMINES:

H1, H2, H3, H4,... receptor blockers according to the symptoms of the patient.

DAO ENZYME SUPPLEMENTS:

The same product under different commercial names is available, but in the UK at the time of writing this document is only available via the internet. Success rates are variable depending on the usage and personal threshold of the individual patient. However, there have been reports of successful therapy with the help of this DAO supplement, independently of those reports given for PR purposes by the producer of the product.

VITAMIN AND MINERAL SUPPLEMENTS:

Following supplements have been suggested. It is however advisable to try to ingest these elements by eating foods that contain them and only to resort to taking supplements when absolutely necessary and in accordance with the doctor's advice or that of a dietician:

- Vitamin C: lowers the histamine level in the blood
- Vitamin B6: is an important co-factor of the enzyme diamine oxidase and its activity
- Calcium: reduces the development of wheals and flushing of the skin
- Zinc: has anti-allergic and anti-inflammatory properties and constrains histamine release

- Copper: is able to elevate the plasma level of DAO slightly
- Magnesium: a Magnesium deficit lowers the allergic reaction threshold
- Manganese: elevates diamine oxidase activity^{vii}
- Vitamin B1
- Vitamin B12
- Folic Acid^{viii}

DRUGS THAT IMPAIR DIAMINE OXIDASE (DAO) ACTIVITY

Some drugs interfere with the DAO enzyme, reducing its activity:

<u>ACTIVE INGREDIENT</u>	<u>NAME</u>
➤ Aminophylline	Phyllocontin, Uniphyllin, Nuelin, Slo-Phyllin
➤ Amitriptyline	Triptafen
➤ Chloroquine	Avloclor, Malarivon, Nivaquine, Paludrine/Avloclor
➤ Clavulanic Acid	Augmentin, Co-amoxiclav
➤ Isoniazid	
➤ Metoclopramide	Maxalon, Paramax
➤ Propafenone	Arythmol
➤ Verapamil	Cordilox, Securon

Anti-inflammatory/painkilling drugs can increase histamine release in allergy sufferers

<u>ACTIVE INGREDIENT</u>	<u>NAME</u>
➤ Mefenamic acid	Ponstan,
➤ Diclofenac	Voltarol, Dicloflex, Diclomag, Motifene, Arthrotec
➤ Indometacin	Indacid, Rimacid
➤ Flurbiprofen	Froben
➤ Naproxen	Naprosyn, Synflex, Napratec, Arthroten
➤ Ketoprofen	Orudis, Oruvail
➤ Acetylsalicylic acid	Aspirin, Caprin, Anadin and many others

ⁱ Mastocytosis: state of the art. Hans-Peter Horny, Karl Sotlar, Peter Valent (2007), Pathobiology : journal of immunopathology, molecular and cellular biology 74 (2) p. 121-32, <http://www.ncbi.nlm.nih.gov/pubmed/17587883>

ⁱⁱ Wegweiser Nahrungsmittel-Intoleranzen, Ledochowski, pg.114

ⁱⁱⁱ [NMI Portal](#) Platform for Food Intolerances providing a bridge between doctor and patient, offering information to both sides so that doctors can reach a swifter diagnosis and patients can achieve a symptom-free life (in German). Supported by several medical professionals on a voluntary basis without vested interest. Histamine and histamine intolerance. Laura Maintz, Natalija Novak (2007) The American Journal of Clinical Nutrition 85 (5) p. 1191

^{iv} Wegweiser Nahrungsmittel-Intoleranzen: Wie Sie Ihre Unverträglichkeiten erkennen und gut damit leben , Univ.Do. Dr. Maximilian Ledochowski, Trias, pg. 114

^v Histamine and histamine intolerance. Laura Maintz, Natalija Novak (2007), The American Journal of Clinical Nutrition 85 (5) p. 1185-96, <http://www.ncbi.nlm.nih.gov/pubmed/17490952>

^{vi} **Food-induced histaminosis as an epidemiological problem: Plasma histamine elevation and haemodynamic alterations after oral histamine administration and blockade of diamine oxidase (DAO);** J. Sattler, D. Häfner, H. -J. Klotter, W. Lorenz, P. K. Wagner (1988); Agents and Actions 23 (3-4) p. 361-365
Histamine and histamine intolerance. Laura Maintz, Natalija Novak (2007), The American Journal of Clinical Nutrition 85 (5) p. 1185-96

Jarisch, R. "**Histamin-Intoleranz, Histamin und Seekrankheit**, Thieme Verlag, 2nd Edition

^{vii} Patienteninformation, Histaminunverträglichkeit, Histaminintoleranz, Facharztpraxis Labor Doz. Schön, pg. 11

^{viii} Jarisch pg 90: „Um eine ausreichende Aktivität der histaminabbauenden Enzyme (Diamineoxidase) zu erreichen, sollte neben den üblichen Aspekten für eine gesunde Ernährung auf eine ausreichende Zufuhr von Vitamin B1, Vitamin B12, Folsäure, Kupfer und Vitamin C geachtet werden.“