

Histamine Intolerance

Histamine Intolerance is an important consideration when seeing women in the context of a Menopause Clinic. The symptoms caused by Histamine Intolerance can be worse at the time of the menopause and can affect a woman's response to HRT.

This condition currently is under diagnosed and poorly recognised in the UK. Sometimes our patients have struggled with various symptoms caused by high histamine the whole of their lives, with no diagnosis or understanding of the condition.

Histamine is a *biological amine* synthesized from Histidine by the activity of L-Histidine decarboxylase enzyme. Vitamin B6 is the necessary cofactor.

Histamine is synthesised and stored in the following cells:

Mast cells, basophils, platelets and neurons and ECL cells in the gut.
(ECL – enterochromaffin – like cells.)

So what are the Biological Functions of Histamine?

It has 3 main functions:

1. Immune system-mast cells attract white blood cells to destroy pathogens in the tissues. This is the *inflammatory response*.
2. Regulation of physiological functions in the gut such as production of gastric acid, which aids the digestion of protein.
3. As a neurotransmitter it influences our wakefulness, the circadian rhythm and cognition.

Histamine, once synthesised, is stored or broken down by 2 enzymes:

- DAO (Diamine Oxidase) in the gut and
- HNMT (Histamine – n- methyltransferase) in the nervous system and lungs.

Histamine Intolerance (HIT)

This is where there is an imbalance between the production and the breakdown of the histamine. This causes a *toxic response* in the body.

The main cause seems to be impaired DAO activity. This is because of Gastro-intestinal disease or because of an inhibition of DAO enzyme due of the ingestion of DAO blockers such as green tea, black tea, alcohol and certain drugs. There is also a group of patients who have a genetic predisposition to low production of the relevant enzymes-DAO and HNMT.

Triggers-vary person-to-person and include:

1. Excessive histamine containing foods, or foods that block DAO (green and black tea, alcohol, and some medications)
2. Gut inflammation - leaky gut, SIBO, infections-H Pylori, Coeliac, Crohns Disease.
3. Chronic stress resulting in increased HPA activity. (Hypothalamic – pituitary – adrenal axis, which activates mast cells and increases histamine release.)
4. Genetic predisposition resulting in reduced levels of the DAO or HNMT enzyme production and thus reduced histamine breakdown.

Symptoms

These can be multiple and very varied. They can also be intermittent or continuous. They are caused by the histamine toxicity and can mimic allergic reactions:

- SKIN: itchiness, redness with flushing, rash/eczema, hives, urticaria, dermatographia, rosacea, psoriasis.
- GI TRACT: acid reflux, diarrhoea, constipation, wind, bloating, nausea, vomiting. Intolerance to certain foods (high histamine foods).
- RESPIRATORY: sinusitis, rhinitis, broncho-constriction, asthma, chronic cough, SOB.
- VASCULAR: vasodilatation-low BP, dizziness, fainting, tachycardia, oedema, migraine and headaches, fluid retention, easy bruising, poor clotting.

- **NEUROLOGICAL:** insomnia, anxiety, memory loss, brain fog, poor concentration, ADHD, panic attacks, Chronic fatigue.
- **HYPERSENSITIVITY:** to certain drugs-NSAIDs, Aspirin, Codeine, some General Anaesthetics.
- **GYNAECOLOGICAL:** painful periods, miscarriages, progestogen sensitivity, possible link with endometriosis.

The incidence of the genetic variant is about 2-3% of the population. However a recent German study found that 17% of their study population were susceptible to high histamine and suffered symptoms. Of the people with a genetic predisposition for the condition, 80% are women, 80% have hypermobility of their joints and 30% suffer from interstitial cystitis. Most will give a family history of some sort.

HIT is not an allergy and does not cause anaphylactic shock. This is where someone is exposed to or ingests something that they can have a very severe and sudden allergic reaction to causing all of the high histamine symptoms but all at once. This is life-threatening and extremely frightening. HIT is caused by a slow accumulation of excess histamine in the body and is not life-threatening but can be extremely difficult to live with and cause debilitating symptoms.

Sources of Histamine

Histamine is either made in the body by the mast cells, the basophils, platelets, neurons and gut cells, or it is ingested in our food and drink.

Some foods block DAO activity- green tea, black tea, alcohol especially. Some have high histamine content and others cause the body to release histamine.

Leftovers will be high in histamine because of bacterial growth after cooking and should never be eaten by HIT sufferers. However the same food eaten freshly cooked may be low in histamine.

Foods, which are fermented, should be avoided, such as kefir, yoghurt, and sauerkraut.

Breakdown of Histamine

Our histamine is broken down in the gut by the enzyme DAO, and by HNMT in the blood and tissues. There can be genetic variants that cause a reduction in the production of both of these enzymes. The activity of the enzymes can be affected by drugs, which are sometimes prescribed to help the symptoms of HIT and thus just make matters worse! These include antidepressants and NSAIDs. Certain general anaesthetics can also increase histamine levels and so make patients feel terrible when they wake up from an operation.

The Effect of Histamine on our hormones

Oestrogen and histamine are closely linked. Women have high levels of oestrogen production when they are teenagers and their periods first start, then at ovulation-mid cycle- and then during the perimenopause when, again, levels of oestrogen can fluctuate and can be very high.

Oestrogen and histamine also increase each other. Therefore high levels of histamine will stimulate oestrogen production, which in turn increases oestrogen. This can become a vicious cycle.

This relationship can lead to various high histamine symptoms when women start their periods, mid cycle and at the perimenopause. (headaches or diarrhoea midcycle). High histamine can also be associated with painful heavy periods, endometriosis, miscarriages and difficulty finding a hormonal contraceptive that suits them. Most women with this condition are progesterone sensitive and therefore usually react to all the progesterone-only or progesterone-containing methods.

During pregnancy, when the levels of oestrogen are very high, women with HIT often feel at their best because the placenta makes large quantities of Diamine oxidase thus increasing production 500 fold! This is to protect the fetus from high histamine. Thus the histamine levels are reduced to normal and the symptoms resolve in pregnancy.

Women who are perimenopausal will often experience symptoms, many of which are similar to those caused by high histamine. Most non HIT sufferers will respond well to HRT, relatively quickly, especially the body-identical HRT we use as the gold-standard. However, women with HIT may not respond so well as they may be progesterone sensitive and the oestrogen will increase their histamine levels and therefore their symptoms.

Diagnosis

Two or more symptoms, plus improvement when eating a low-histamine diet for 4 weeks and when taking antihistamines.

1. Keeping a food diary may be very helpful.

You can download this one to try and record which foods seem to be the best or worst for you: <https://www.histamineintolerance.org.uk/about/the-food-diary/>

2. It is best to avoid alcohol, tea, green tea, coffee, fermented foods and sauces, processed food, avocados, spinach, aubergines, tomatoes, gluten, dairy, hard cheeses, strawberries and tropical fruits, and chocolate.

3. Consult a nutritionist or dietician who is familiar with the condition and can help you with the diet-it can be quite tricky and some support initially may be helpful.

We recommend Nigel Denby : www.nigeldenbydietitian.co.uk

4. Buy food regularly so it's as fresh as possible for you to eat. Take cold bags with you so that meat can be kept cold in transit and then cook it straight from the fridge. Avoid minced meat, as this is high in histamine because it contains a lot of bacteria. Avoid aged meats.

Treatment

1. The most important thing is to reduce the histamine in your diet.

For patients with normal production of DAO and HNMT this may be all that is necessary, and it may be that they just need to avoid certain very high histamine triggers (such as alcohol that also blocks DAO) to feel well and keep their histamine in balance. For women with low DAO production this avoidance may be necessary longterm.

2. Women with low production of the enzymes may also need antihistamines, both type 1 and type 2 (H1 and H2 blockers). These do not lower the histamine levels but block the receptors and so reduce the symptoms.

3. Type 1 non-sedating antihistamines, that can be bought over the counter, include Cetirizine and Loratidine. These need to be taken twice a day as their effect does not last long enough. However more often than not, women

require stronger antihistamines such as Fexofenadine, which is only available on prescription.

The type 2 antihistamines block the receptors in the stomach. Currently these are unavailable unfortunately, both over the counter and on prescription.

4. Vitamin C is a natural antihistamine but needs to be taken in small doses 3-4 x a day. It is metabolised quickly and therefore once a day, unless it is a slow release preparation, is insufficient. It can cause diarrhoea if we have too much, but because of its fast metabolism it is not toxic in high doses.

5. L Glutamine 500mg daily is also a natural antihistamine. This can be bought over the counter.

6. Quercetin 500mg x 2 can be taken with a meal, as it is a natural mast cell stabiliser.

7. DAO can be bought online. This is expensive but useful. One or two tablets can be taken 30-60 minutes before a meal-especially if eating out or if you are going to eat something that has histamine in it.

8. Saunas and steam rooms may help to sweat out some of the histamine. Doing this twice a week is recommended.

9. A group of HIT sufferers will benefit from a Mast Cell Stabiliser if there is an element of mast cell activation syndrome caused by the high levels of histamine or by leaky gut syndrome.

10. Toxoprevent, a clinoptilolite, can also lower histamine in the gut, when taken with meals. Use the code NOU-172 for a 10% discount and free shipping.

www.toxaprevent.co.uk

11. It may be useful in some cases to have some genetic testing performed, mapping certain relevant pathways such as the oestrogen, thyroid, methylation and histamine pathways.

An excellent company we recommend is LifecodeGX- see the link below. This may help identify the vitamins and minerals needed to support your pathways which have some genetic variant that may cause problems.

Some patients will be able to manage their symptoms with dietary and lifestyle changes and will be able to just take the supplements regularly, taking the antihistamines intermittently when necessary.

Lifestyle

Avoid stress if at all possible. Meditation and yoga may help. Some patients find that exercise can increase their histamine levels and so you will have to experiment and see what type of exercise works best for you.

HRT

HRT gives symptom control and future health benefits by reducing the risk of osteoporosis and cardiovascular disease to all women who decide to take it. However, many HIT sufferers are progestogen sensitive and so it is important that they consult a specialist to help them with the management of their HRT.

At The Menopause Consultancy the doctors are all familiar with HIT and can help you if you think you may have this condition.

Helpful links

<https://thecommunality.com/hit-mcas-treatment>

www.histaminintoleranz.ch

www.histamineintolerance.co.uk

www.drTinapeers.com

<https://youtube.be/em-BxplmE6A>

www.toxoprevent.co.uk

www.LifecodeGX.com