Histamine Intolerance

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Histamine is a chemical that is released by white blood cells into the bloodstream when the immune system is defending against a potential allergen. This release can result in an allergic reaction from triggers such as pollen, mold, and certain foods.

Histamine has many important and diverse biological functions: it protects against infection, regulates physiological functions in the gut, and acts as a neurotransmitter.

Once formed, histamine is either stored or rapidly inactivated by its primary degradative enzymes - diamine oxidase (DAO) in the gut, and histamine-n-methyltransferase (HNMT) in the nervous system and lungs. Histamine degradation is altered by genetics and environmental factors. Impaired histamine degradation can result in histamine toxicity and numerous symptoms that mimic an allergic reaction:

- **Skin:** itchiness, redness, rash, eczema, hives
- **Gastro-intestinal tract:** stomach acid reflux, diarrhoea, nausea, vomiting
- **Respiratory:** runny nose, broncho-constriction, asthma, chronic cough, nasal congestion
- **Vascular:** vasodilation, low blood pressure, dizziness, fainting, rapid heart beat, oedema, migraine/headaches
- **Neurological:** insomnia, anxiety, memory and concentration problems, ADHD

Because of its multifaceted symptoms, histamine intolerance is frequently underestimated, or its symptoms misinterpreted as they are often mistaken for a food allergy or a gastrointestinal disorder.

This report describes the genes, nutrients, and lifestyle and environmental factors that can impact histamine degradation. It provides a personalised summary pathway and detailed results, followed by a generic histamine intolerance guide.

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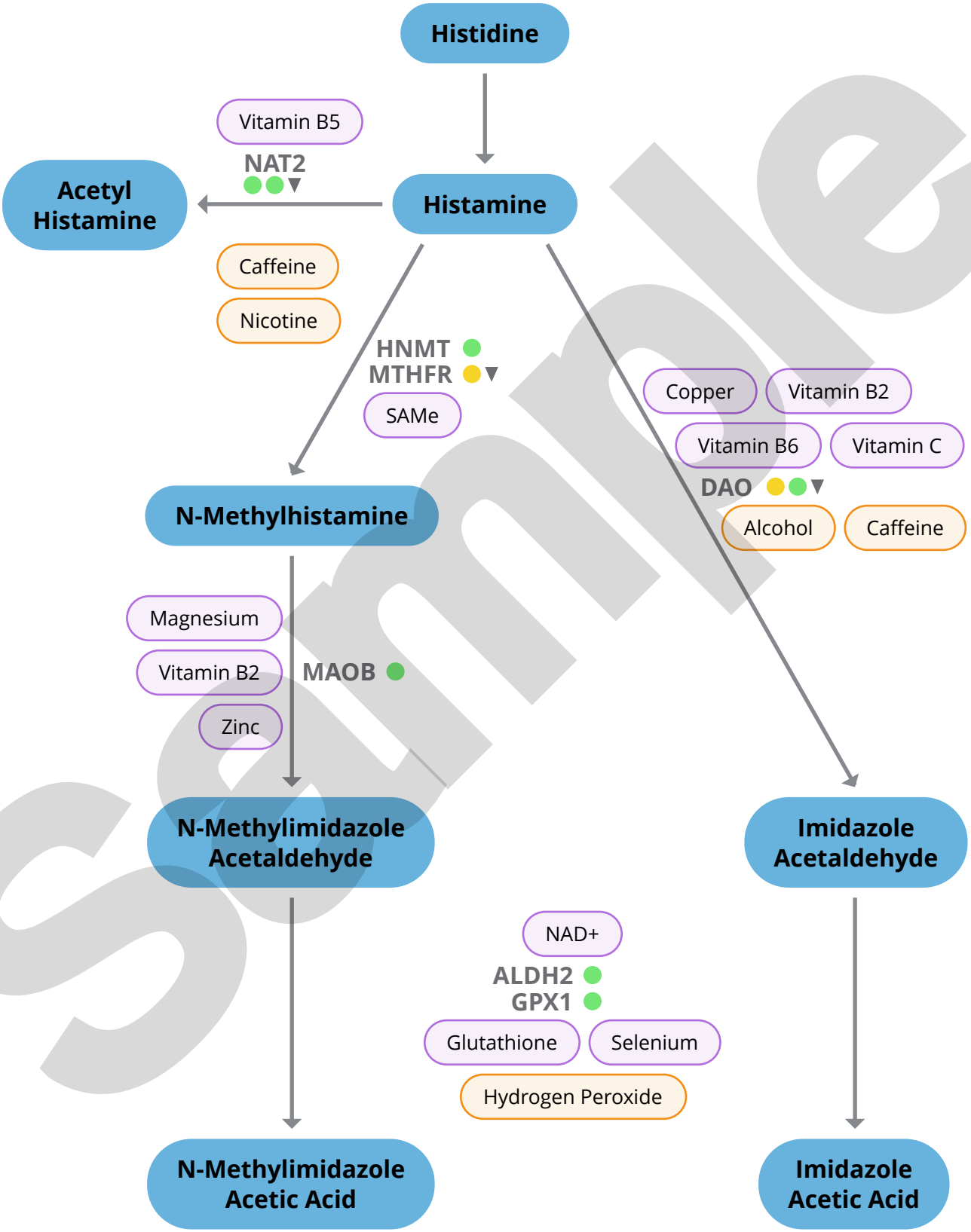
Histamine Intolerance



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Detailed Results

ALDH2 rs671	GG	No impact on acetaldehyde metabolism. ALDH2 is the second enzyme of the major oxidative pathway of alcohol metabolism and is also needed to breakdown the amine neurotransmitters. Support ALDH2 by limiting alcohol consumption, and increasing cofactors - vitamins B2 and B3, magnesium, molybdenum and zinc.
DAO	CC	Normal DAO activity, normal degradation of histamine. Support DAO with vitamin B2, as it uses FAD as a cofactor.
DAO	GC ▼	Slower DAO activity. Associated with slower degradation of histamine, which may cause symptoms mimicking an allergic reaction. Support DAO with vitamin B2, as it uses FAD as a cofactor.
GPX1	GG	Normal GPX1 activity and ability to break down the toxin hydrogen peroxide resulting from histamine metabolism. Ensure adequate intake of antioxidants glutathione and selenium.
HNMT	CC	No variance. No reported impact on HNMT activity or effect on histamine metabolism. Support HNMT with B vitamins, zinc and magnesium.
MAOB	TT	Normal MAOB activity, normal breakdown of histamine metabolites in the HNMT pathway. Support MAOB with vitamin B2, magnesium and zinc.
MTHFR	AG ▼	Reduced gene function impacting levels of 5-MTHF (methyl-folate) and subsequently SAMe, which is needed to support HNMT degradation of histamine. Methylation and histamine status are often inversely correlated. Methylation (and HNMT activity) can be supported by increasing intake of folate (green leafy vegetables) and other methylation promoting nutrients - B vitamins, vitamin C, zinc, copper and methionine (found in meats, fish, eggs, nuts and beans).

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A Guide to Histamine Intolerance

This guide contains detailed explanations of the genes involved in Histamine Intolerance.

Histamine is a biological amine that is synthesised from the amino acid histidine by L-histidine decarboxylase (HDC) and requires vitamin B6 as a cofactor.

Histamine is synthesised by and stored predominantly in mast cells - in tissue, but also in basophils and platelets in the blood, neurons - in the nervous system and enterochromaffin-like (ECL) cells in the gut.

Once formed, histamine is either stored or rapidly inactivated by its primary degradative enzymes - diamine oxidase (DAO) in the gut and histamine-n-methyltransferase (HNMT) in the nervous system and lungs.

Histamine intolerance is a toxic response by the body resulting from an imbalance between accumulated histamine and the capacity to break it down. It seems to occur mainly as a result of impaired DAO activity either due to gastro-intestinal disease or through inhibition of DAO, by 'blockers' such as alcohol, black tea, green tea and medications. There is also evidence for a genetic predisposition in a subgroup of people with histamine intolerance.

Triggers are heterogeneous and differ greatly between individuals. The most common ones are:

- Ingestion of histamine-rich food, or of alcohol or drugs which release histamine or inhibit DAO
- Gastro-intestinal injury due to 'leaky gut', SIBO (small intestinal bacterial overgrowth), Crohn's or other IBDs, coeliac disease or infections such as H. Pylori
- Chronic stress and increased HPA (hypothalamic-pituitary-adrenal axis) activity which activates mast cells and increases histamine release
- Genetic predisposition due to variants on the DAO and/ or HNMT genes which reduce activity of the enzymes that break down histamine.

Histamine is primarily metabolised by two major pathways - DAO, and HNMT. The main DAO metabolite, acetaldehyde, is then oxidised to acetic acid by ALDH2, whilst the N-methyl-histamine product of the HNMT pathway is broken down by MAOB, which is then oxidised by ALDH2 too. NAT2 is an alternative pathway that converts histamine into acetylhistamine, which is then excreted in the urine.

Histamine Intolerance Genetics

The DAO gene - which is also known as AOC1 or ABP1 - produces the main enzyme for the metabolism of ingested putrescine, histamine and related compounds. The enzyme uses Flavin Adenine Dinucleotide (FAD) produced from Vitamin B2 as a cofactor. Variants on DAO may down-regulate enzyme activity, resulting in excess histamine and causing symptoms mimicking an allergic reaction. Alcohol is one of the most harmful products for people with DAO deficiency. It simultaneously releases endogenous histamine and blocks DAO activity, even in people not predisposed to low DAO levels.

HNMT controls the neurotransmitter activity of histamine in the brain and plays an important role in regulating the airway response to histamine. Variants have been reported to increase susceptibility to asthma. HNMT inactivates histamine via methylation - using SAMe as the methyl donor - therefore genetic variants that impact methylation (such as MTHFR) may also affect HNMT activity. The resultant N-Methylhistamine is then oxidatively deaminated to N-methyl-imidazole acetaldehyde by MAOB.

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How to Read the Report

Genes

Results are listed in order of the gene short name. The 'rs' number is the reference sequence number that identifies a specific location on the genome. It is also known as a SNP (Single Nucleotide Polymorphism) pronounced 'snip', polymorphism or mutation.

Personalised Result

Your genotype result is shown as two letters (A,G,T or C) which represent the DNA bases present at that location.

GPX1 rs1050450	AG ▼	Less efficient removal of hydrogen peroxide, which can increase risk of accumulation and oxidative damage, TPO antibodies and Hashimoto's. Ensure good intake of antioxidants, particularly glutathione and selenium.

Arrow Direction

The direction of the arrow indicates the potential effect of the SNP on gene expression, where applicable - it can increase or decrease activity, or neither.

▲ up-regulates or increases the activity and effect on the gene

▼ down-regulates or decreases the activity and effect on the gene

No arrow - no effect on the activity of the gene

Highlight Colour

The genotype result highlight indicates the potential effect of the SNP on gene function in a particular context.

RED the effect of the variant is negative

AMBER the effect of the variant is somewhat negative

GREEN no variation, or the effect of the variant is positive

Pathway Diagram Key

Cofactor Inhibitor

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MAOB Monoamine Oxidase B

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MTHFR Methylenetetrahydrofolate Reductase (NAD(P)H)

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