

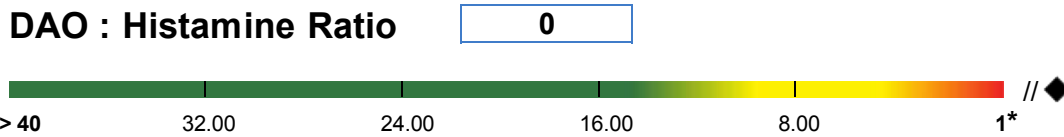
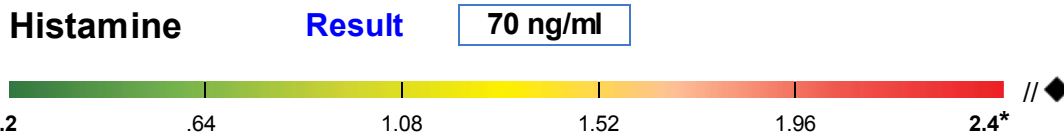
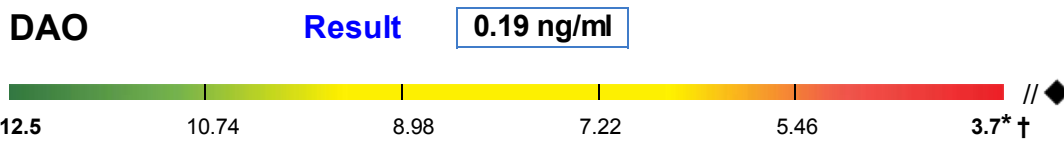
RESULTS: DRIED BLOOD SPOT TEST

Accession #: 100039465 • Patient: Jane Smith

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Patient: Jane Smith
Sex: Female **Age:** 37 yr **Date of Birth:** 1982-09-25
Health Care Professional: John Smith

Accession #: 100039465
Sample received: 2020-07-01
Report issued: 2020-07-08
Sample collection: 2020-06-25

DIAMINE OXIDASE (DAO) / HISTAMINE


*Reference range derived from a normal distribution of results, encompassing 95% of a randomly selected population

† DAO values are shown in ng/ml, where the conversion factor is 1U/ml = 1.25 ng/ml

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[Convert to pdf, Save or PRINT >>](#)**GENERAL COMMENTARY Diamine Oxidase (DAO) / Histamine**

The comments provided here are for educational purposes only. The results in this report should not be interpreted as diagnostic, nor should they be viewed as treatment recommendations. Those decisions are the responsibility of the health care professional. Moreover, the reference range shown in this report is derived from a normal distribution of results, that encompass 95% of randomly selected individuals in a population (see below).

Histamine and Diamine Oxidase

Histamine is a nitrogenous compound known to be involved in twenty three different physiological functions which include local immune responses, neurotransmission, as well as regulation of physiological function in the gastrointestinal tract.

Histamine is either stored or rapidly metabolized and inactivated by either of two degradative enzymes, histamine-N-methyltransferase or diamine oxidase (DAO); the latter being the principal enzyme observed in the digestive tract.

The testing of histamine, together with DAO levels, provides important information that is not revealed with standard food sensitivity tests. The latter is often thought to be the underlying cause of gut inflammation and dysfunction, when in fact the reason may actually be an imbalance of accumulated histamine and the capacity for its degradation by enzymes such as DAO. This imbalance may result in a condition known as Histamine Intolerance (HIT).¹¹ HIT is an acquired problem and is seen in approximately 3% of the population. Symptoms may occur in up to 20% when histamine-rich food is consumed together with DAO inhibitors, such as alcohol. Women represent about 80% of those affected, with most of them aged 40 or over. It is important to note that the risk of developing this intolerance is increased in those individuals who suffer from inflammatory intestinal diseases or cross-sensitivities.¹¹

Why Test for Histamine?

Histamine is involved in many inflammatory and allergic processes, including both immediate and delayed hypersensitivity reactions. Histamine excess can be triggered by its release in the body as a result of a variety of environmental triggers, from the ingestion of foods with high histamine content, a deficiency in DAO, or both.

The Histamine reference range is from 0.2 to 2.4 ng/ml:

- Below the reference range levels, < 0.2 ng/ml, indicate a low probability of HIT.
- Above the reference range levels, > 2.4 ng/ml, indicate a high probability of HIT.
- Levels between 0.2 to 2.4 ng/ml indicate an increasing probability of HIT as the value approaches the upper limit of the reference range.¹⁰

High levels of histamine:

- Runny nose, sneezing, congestion
- Itching, hives, skin flushing
- Dizziness or vertigo
- Headache, migraine
- Nausea, vomiting
- Intestinal cramps, gas
- Diarrhea

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- Abnormal menstrual cycle
- Shortness of breath
- Abnormal heart rate
- High blood pressure
- Severe allergic reactions (anaphylaxis)
- Abnormalities may also arise in the following:
 - Memory
 - Body temperature
 - Circadian rhythm
 - Locomotion
 - Learning

What causes high histamine levels?

- Allergies (IgE reactions)
- Gluten Intolerance
- Small Intestinal Bacterial Overgrowth (SIBO)
- Intestinal Permeability (“Leaky Gut”)
- Gastrointestinal bleeding
- Histamine-rich foods
- DAO deficiency or DAO-blocking foods: alcohol, energy drinks, and tea
- Genetic mutations (common in people of Asian descent)
- Inflammatory bowel diseases: Crohn’s, ulcerative colitis
- Medications:
 - Non-steroidal anti-inflammatory drugs (eg: Ibuprofen-Motrin, ASA-Aspirin)
 - Antidepressants (eg: Effexor, Zoloft, Prozac, Cymbalta)
 - Immune modulators (eg: Enbrel, Humira)
 - Anti-arrhythmics (eg: Propanolol, Norvasc, Cardizem)
 - Antihistamines (eg: Benadryl, Allegra)
 - H2 blockers (eg: Zantac, Pepcid, Tagamet)

Low levels of histamine (Histapenia):

- Fatigue
- Sleep-wake disorders
- Depression and anxiety in older adults; paranoia in younger people
- Convulsions

What causes low histamine levels?

Excess copper can create low levels by decreasing histamine in the brain. In turn, the lowered levels of histamine allow more copper to accumulate. High copper in the brain may lead to a state of restlessness, insomnia, violence, depression, irritability, paranoia, and high blood pressure.

Why Test for DAO?

The ingestion of histamine rich food, alcohol or drugs that release histamine or block DAO, may provoke an imbalance of accumulated histamine and the capacity for its degradation, already referred to above as Histamine Intolerance (HIT).

An impaired histamine degradation, based on reduced DAO activity and the resulting histamine excess, may cause numerous symptoms mimicking an allergic reaction.¹¹

DAO activity does not depend on the DAO alone, but also on cofactors such as vitamin C, vitamin B6, copper or manganese ions. Copper is a central component of DAO. A deficiency in copper can result in insufficient DAO being produced. Vitamin B6 is a cofactor of DAO. If vitamin B6 is missing, DAO is unable to degrade histamine.

Therefore, in assessing HIT via the DAO activity test one should also consider determining the levels of these cofactors. The symptoms of HIT can be caused by low DAO activity because the above-mentioned cofactors are not sufficiently available.

If the DAO levels are in the normal range but the histamine levels are high, it may indicate that the issue is not insufficient DAO, but rather an overproduction of histamine, due to factors such as gut dysbiosis.

However, if the histamine levels are normal, but the DAO levels are very low, it suggests a possible genetic deficiency of diamine oxidase.

The DAO reference range is from 12.5 to 3.75 ng/ml (10-3 U/ml), with no significant daily variations or gender differences:

- Below the reference range levels, < 3.75 ng/ml, indicate a high probability of HIT.
- Above the reference range levels, > 12.5 ng/ml, indicate a low probability of HIT.
- Levels from 12.5 to 3.75 ng/ml indicate an increasing probability of HIT.¹¹

Low levels of DAO:

- Skin rash and pruritis (itching), urticaria (hives), eczema, psoriasis
- Nasal congestion, asthma
- Headache, migraine
- Chronic fatigue
- Anxiety, depression
- Inflammation, irritable bowel syndrome (IBS)
- Estrogen dominance, dysmenorrhea, Premenstrual Syndrome (PMS)
- Muscular pain, fibromyalgia
- Rheumatoid arthritis
- Hypertension, hypotension, arrhythmia,

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- Multiple sclerosis and other neurological conditions

Determination of DAO activity, together with a detailed history, helps to differentiate food allergy and histamine intolerance. It should be performed in suspected patients who have headaches, urticaria, pruritus, diarrhea and hypotension, where food allergy has been excluded.¹²

Individuals who are unable to metabolize histamine will often improve with a variety of antihistamines. Because DAO formation occurs in the gastrointestinal system, lower than normal levels are suggestive of poor digestive dysfunction, as well as problems in the intestinal barrier.¹³

The Importance of the DAO : Histamine Ratio

The DAO : Histamine Ratio is helpful in highlighting the imbalances in DAO and histamine levels.

High Ratio: There is enough DAO enzyme available for histamine degradation, or that there is a relatively low level of free histamine in the system.

Low Ratio: There is insufficient DAO enzyme available to degrade the relative amount of free histamine. It should be noted that even if DAO levels are normal, symptoms may still occur if the histamine levels are very high.

References

1. Vanuytsel T et al. *Tissue Barriers* 2013; 1: 1-9;
2. Fasano A et al. *Lancet* 2000; 355: 1518-19;
3. Fasano A. *Ann N Y Acad Sci* 2012; 1258: 25–33;
4. Sapone A et al. *Diabetes* 2006; 55: 1443-1449;
5. Pacifico, L et al. *World J of Gastroenterol* 2014; 20: 17107-17114;
6. Skardelly M, et al. *Transl Oncol* 2009; 2: 117–120;
7. Rittirsch D, et al. *Am J Physiol Lung Cell Mol Physiol* 2013; 304: L863–L872;
8. Turner JR. *Am J Pathol* 2006; 169: 1901-1909;
9. Lee SH. *Intest Res* 2015; 13: 11-18;
10. Jean Dyer BS et al. *Measurement of plasma histamine: description of an improved method and normal values.* *J Allergy Clin Immunol* 1982; 70 (2): 82-87.;
11. Maintz L, Novak N. *Histamine and histamine intolerance.* *Am J Clin Nutr.* 2007; ; 85:1185-1196;
12. Music E, et al. *Serum diamine oxidase (DAO) activity as a diagnostic test for histamine intolerance.* *Food Allergy and Anaphylaxis Meeting 2011,;* Venice, Italy. 17-19 February, 2011;
13. Farhadi A, et al. *Intestinal barrier: An interface between health and disease.* *J Gastroenterol and Hepatol* 2003; 18: 479–497.