Histamine Intolerance Protocol‡

DEVELOPED IN COLLABORATION WITH OUR MEDICAL ADVISORS

Histamine intolerance (HIT) is a practical label clinicians use to describe the accumulation of histamine at a rate that exceeds the body's ability to eliminate it.[1] As a result, patients with a histamine intolerance may report a repeatable group of symptoms after eating histamine-rich foods.[1] This protocol provides clinicians with structured guidance to support patients with histamine intolerance.‡

FOUNDATIONAL SUPPORT

In addition to a nutrient-dense, diverse diet focused on lower-histamine foods, consider the following foundational support to help meet daily nutrient needs:‡

PRODUCT RECOMMENDATIONS	FEATURES‡	SUGGESTED USE
O.N.E.™ Multivitamin (Order Code: ONE1 / ONE6 / ONE3)	Foundational support for essential nutrients, including vitamin D, B-vitamins, zinc, chromium and more.	1 capsule daily, with a meal
Vitamin D_3 25 mcg (Order Codes: VD1 / VD12 / VD16)	Vitamin D's role in immune health has long been established; vitamin D receptors are found in a number of immune cells, including lymphocytes and macrophages, maintaining healthy immune cell activation.[3‡]	Dosage determined by 25-hydroxyvitamin D assessment
DAO Enzyme (Order Code: DAE6)	Promotes the breakdown of dietary histamine and reduces gastrointestinal discomfort associated with sensitivity to histamine-rich foods‡	1 capsules, 2-3 times daily, with meals

TARGETED SUPPORT

The products in this category support common clinical objectives related to histamine intolerance. Choose from the options listed below, as applicable, based on your clinical objectives:‡

CLINICAL OBJECTIVE‡	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Modulate Mast Cell and Immune Mediator Activation	**Hist Reset** (Order Code: HRT1) Supports healthy mast cell stabilization and histamine metabolism‡	2 capsules daily, between meals
Support Healthy Immune Response	**Liposomal Vitamin C** (Order Code: LVC1) Easy to absorb, enhanced-retention form of vitamin C that is formulated with clinically studied PureWay-C® to promote healthy immune function‡	2 capsules, 1-2 times daily, with or between meals
	Aller-Essentials (Order Code: ALE21 / ALE26) Supports healthy immune response to environmental factors and supports both innate and adaptive immune response‡	2 capsules, 1-2 times daily, with or between meals

TARGETED SUPPORT *CONTINUED*

The products in this category support common clinical objectives related to histamine intolerance. Choose from the options listed below, as applicable, based on your clinical objectives:‡

CLINICAL OBJECTIVE‡	PRODUCT RECOMMENDATIONS	SUGGESTED USE
Th2 Immune Response	**Th2 Modulator** (Order Code: TH2A1) Supports healthy mast cell stabilization and histamine metabolism‡	2 capsules, 1-2 times daily, with or between meals
Cytokine Balance	**A.I. Formula®** (Order Code: AI1) Supports healthy cytokine balance‡	1 capsule, 1-2 times daily, between meals

NUTRITION AND LIFESTYLE RECOMMENDATIONS

Suspected histamine intolerance is best approached as a clinical pattern recognition problem. When you guide patients to track timing, preparation methods, food storage habits, alcohol intake, stress and sleep, you often uncover that the issue is not simply the food itself but rather the combination of histamine load and the rate of histamine clearance, which varies day to day. You may also discover that the histamine response is not food-driven.‡

Step 1: Discovery

The first action step is to ask patients to track the onset of their symptoms in relation to food intake and timing for approximately 7 days. If symptoms occur within 20-30 minutes and resolve within a few hours, a histamine-related mechanism becomes more plausible.[4]

Ask your patients to track:

- Their symptoms, rating scale and frequency as accurately as possible.
- The time from first bite to the onset of the symptoms, as well as the time to resolution.
- Co-factors that may worsen symptoms, such as alcohol, exercise, heat, poor sleep and stress. Alcohol can interfere with histamine degradation.[5]
- Cooking methods (e.g., raw, broiled, baked, fried), age of food and storage time (e.g., leftovers).

Bring awareness to the age, storage and preparation of food.

Age of food

Due to naturally occurring bacterial activity, the histamine levels in foods increase as they ripen, including foods that are lower in histamine.[6,7] For example, a green or yellow banana has less histamine compared to a ripened yellow banana. Ask your patients to pay attention to the ripeness of the food they are consuming.

Preperation of food

Cooking methods can also alter histamine content in food. For example, grilled and fried foods tend to have higher histamine levels than raw or boiled foods. Boiling has been reported to decrease histamine levels in some foods. Reheating foods can also increase histamine levels.[8]

Ask your patients to note the cooking method(s) used in meal preparation to help differentiate between the food and the preparation.

Food storage

Histamine content in a meal increases as it is stored or reheated (e.g., leftovers), even with proper storage.[8]

Some tips for leftovers:

1. Set the refrigerator to 40°F or cooler.
2. Cool food rapidly to reach safe refrigerator storage. To do this, place food in shallow bowls, though hot foods can also be placed directly in the refrigerator for quick cooling.
3. Seal the food tightly to prevent bacteria and retain moisture.
4. Use the "3-to-4" guideline. Most leftovers are safe for 3 to 4 days when stored at or below 40°F, though histamine levels will increase.[9] If leftovers will not be eaten within this timeframe, freezing them is a safer option. Frozen leftovers can generally maintain quality for 3 to 4 months, though texture may change for some foods.[9]

Step 2: Structured Dietary Trial and Re-Challenge

Next, help patients reduce exposure to foods that contribute to the accumulation of histamine or reduce the breakdown of histamine.

FOODS THAT ARE HIGH IN HISTAMINE, LIBERATE HISTAMINE OR INHIBIT DAO PRODUCTION [7,10,11]	
Proteins	Fermented, cured or smoked meats (e.g., sausage); canned and preserved fish (e.g., herring, canned sardines, tuna, anchovy); egg white; cow's milk; seafood; and ripe cheeses (e.g., gouda, cheddar, Danish bleu, Swiss, goat, gorgonzola, parmesan, mascarpone)
Vegetables and Fruits	Eggplant, spinach, fermented vegetables (e.g., sauerkraut), tomatoes, lemons, limes, pineapples, kiwis, papayas, bananas, citrus and strawberries
Beverages	Alcohol, coffee, tea and energy drinks
Other	Vinegars, ketchup, fermented soy products (i.e., miso, natto), cocoa, chocolate, peanuts and walnuts

A dietary approach can include a phased process[5,10]

1 Baseling Phase

For approximately 7 days, have the patient follow their usual diet while keeping a diary of food, timing, symptoms, stress, sleep and alcohol.

2 Avoidance Phase

Have the patient restrict foods that trigger histamine reactions or symptoms for up to 4 weeks while optimizing nutrient intake.

3 Test Phase
(to determine individual histamine tolerance)

- Slowly reintroduce smaller portions of the higher-histamine foods over 1-2 weeks, keeping the patient's food preferences in mind.
- If a smaller portion is tolerated, increase to larger portions of the higher-histamine foods over 1-2 weeks, or longer, as determined by the patient's reaction.
- If there is no meaningful change, revisit what may be contributing to the histamine intolerance-like response rather than tightening the diet indefinitely.
- If symptoms improve and recur with the test phase, shift from restriction to tolerance building and address amplifiers (e.g., food storage habits, alcohol, sleep, stress).

4 Long-Term Intake

Continue with the tolerated foods and nutrient dense dietary intake.

LIFESTYLE STRATEGIES AND OTHER FACTORS

While some patients experience histamine intolerance due to the dietary intake of histamine-rich foods exceeding breakdown by DAO enzymatic activity, it is important to assess and account for personal and lifestyle factors that may contribute to or cause the histamine-related response.

- **Stress**: Acute stress can alter immune function, increase cytokine production, and promote mast cell activation.[12]
- **Medications**: Some prescribed and over-the-counter medications inhibit DAO enzyme function.[1,5]
- **Genetics**: Testing for genetic polymorphisms that encode DAO enzyme has the potential to uncover the genetic etiology of histamine intolerance.[4]
- **Exercise**: Histamine is released from mast cells during aerobic activity, helping to promote vasodilation, deliver glucose for energy and maintain healthy blood pressure response.[13]
- **Microbiome imbalance**: Certain strains of bacteria, molds and yeast can contribute to the formation of histamine. An overabundance of these microbes may cause increase sensitivity to histamine-rich foods.[14]
- **Body temperature or heat**: Histamine plays a role in thermoregulation, therefore patients who run warmer likely produce more histamine from their mast cells.[15]

For some patients, a combination of dietary and lifestyle factors contributes to histamine intolerance, making it important not to focus solely on food when assessing symptoms.

RESOURCES

For additional information refer to the resources below:

- How to Evaluate a Patient with Suspected Histamine Intolerance [Blog]
- Drug-Nutrient Interactions Checker: Provides valuable information on potential interactions between your patients' prescriptions, over-the-counter medications and nutritional supplements.
- You can also explore Pure Encapsulations® to find On Demand Learning, Clinical Protocols and other resources developed with our medical and scientific advisors.

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