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Pharmacology II

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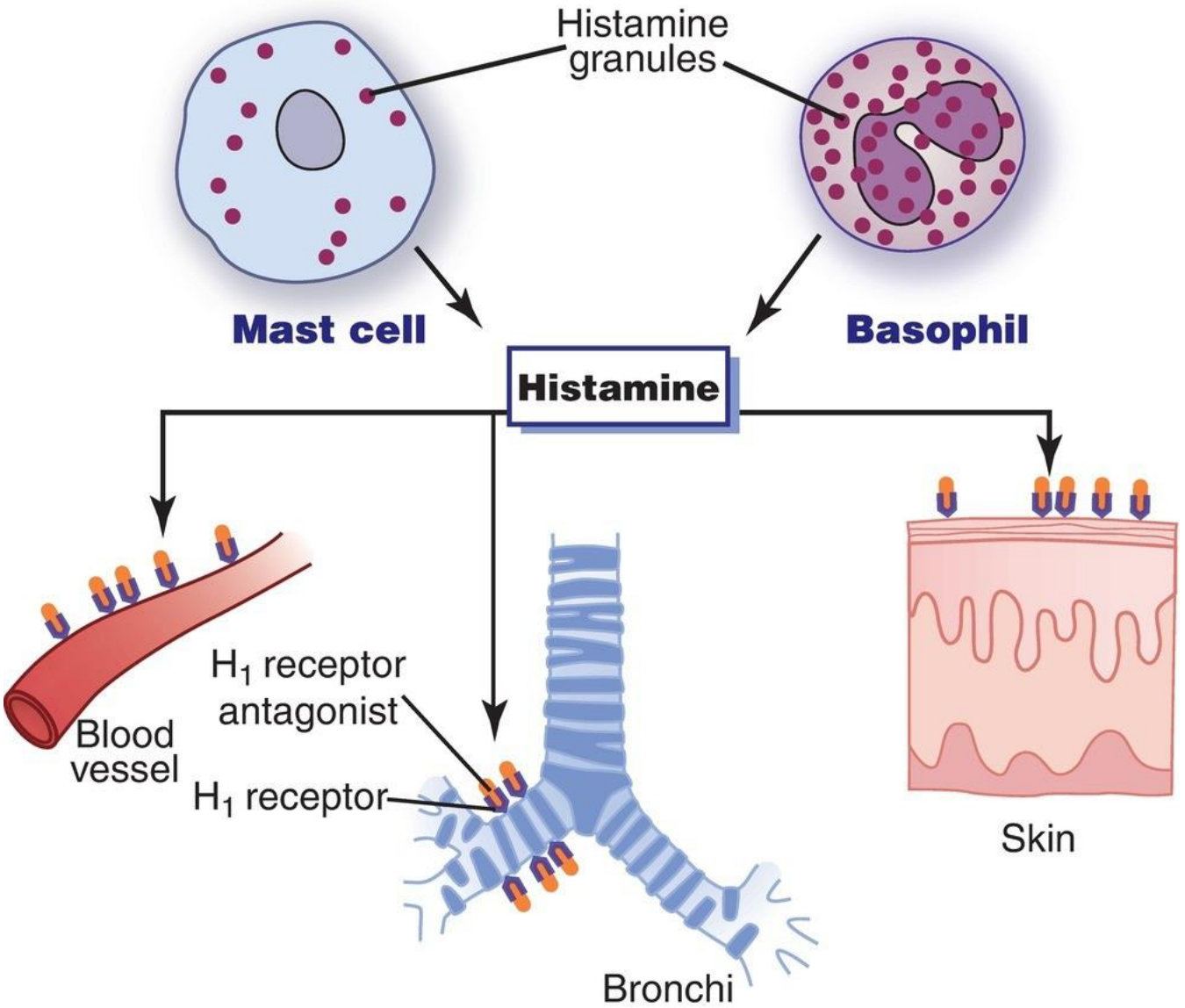
Drug Therapy to Decrease Histamine Effects and Allergic Response

Histamine is the first chemical mediator to be released in immune and inflammatory responses. It is synthesized and stored in most body tissues, with high concentrations in tissues exposed to environmental substances (e.g., the skin and mucosal surfaces of the eye, nose, lungs, and gastrointestinal [GI] tract). It is also found in the central nervous system (CNS). In these tissues, histamine is located mainly in secretory granules of mast cells (tissue cells surrounding capillaries) and basophils (circulating blood cells). Histamine is discharged from mast cells and basophils in response to certain stimuli (e.g., allergic reactions, cellular injury, extreme cold). After it is released, it diffuses rapidly into other tissues, where it interacts with H1 and H2 receptors on target organs.

Synthesis

Histamine is an amine formed by the decarboxylation of the amino acid histidine by the enzyme **histidine decarboxylase**, which is expressed in cells throughout the body, including neurons, gastric parietal cells, mast cells, and basophils .In mast cells, histamine is stored in granules. If histamine is not stored, it is rapidly inactivated by the enzyme **amine oxidase**

Histamine is just one of several chemical mediators released in response to stimuli. The stimuli for release of histamine from tissues may include destruction of cells as a result of **cold, toxins from organisms**, **venoms from insects and spiders**, and **trauma**. Allergies and anaphylaxis can also trigger significant release of histamine.


Histamine granules
Mast cell
Basophil
Histamine
Blood vessel
H1 receptor antagonist
H1 receptor
Bronchi
Skin

When histamine binds with these receptors and stimulates them, effects include the following

- Contraction of smooth muscle in the bronchi and bronchioles (producing bronchoconstriction and respiratory distress).
- Stimulation of vagus nerve endings to produce reflex bronchoconstriction and cough.
- Increased permeability of veins and capillaries, which allows fluid to flow into subcutaneous tissues and form edema.
- Increased secretion of mucous glands. Mucosal edema and increased nasal mucus produce the nasal congestion characteristic of allergic rhinitis and the common cold.
- Stimulation of sensory peripheral nerve endings to cause pain and pruritus . Pruritus is especially prominent with allergic skin disorders.
- Dilation of capillaries in the skin, to cause flushing

- **Hypersensitivity** involves allergic reactions—exaggerated responses by the immune system that produce tissue injury and may cause serious disease.
- **Allergic Rhinitis** Allergic rhinitis is inflammation of nasal mucosa caused by a type I hypersensitivity reaction to inhaled allergens.
- **Allergic Contact Dermatitis** Affected areas of the skin are usually inflamed, warm, edematous, intensely pruritic, and tender to touch.
- **Allergic Food Reactions**

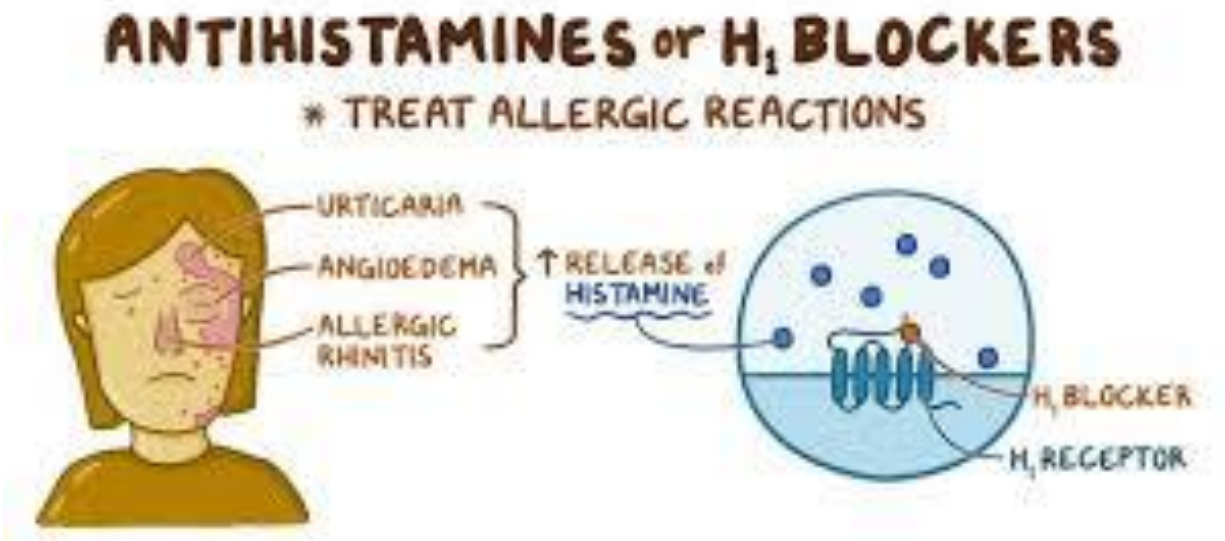
food allergies are an immune response to the ingestion of a protein. Some food allergens such as shellfish, fish, corn, seeds, bananas, egg, milk, soy, peanut, and tree nuts have a higher inherent risk of triggering anaphylaxis than others.

- **Allergic Drug Reactions** Allergic drug reactions are complex and diverse and may include any of the types of hypersensitivity

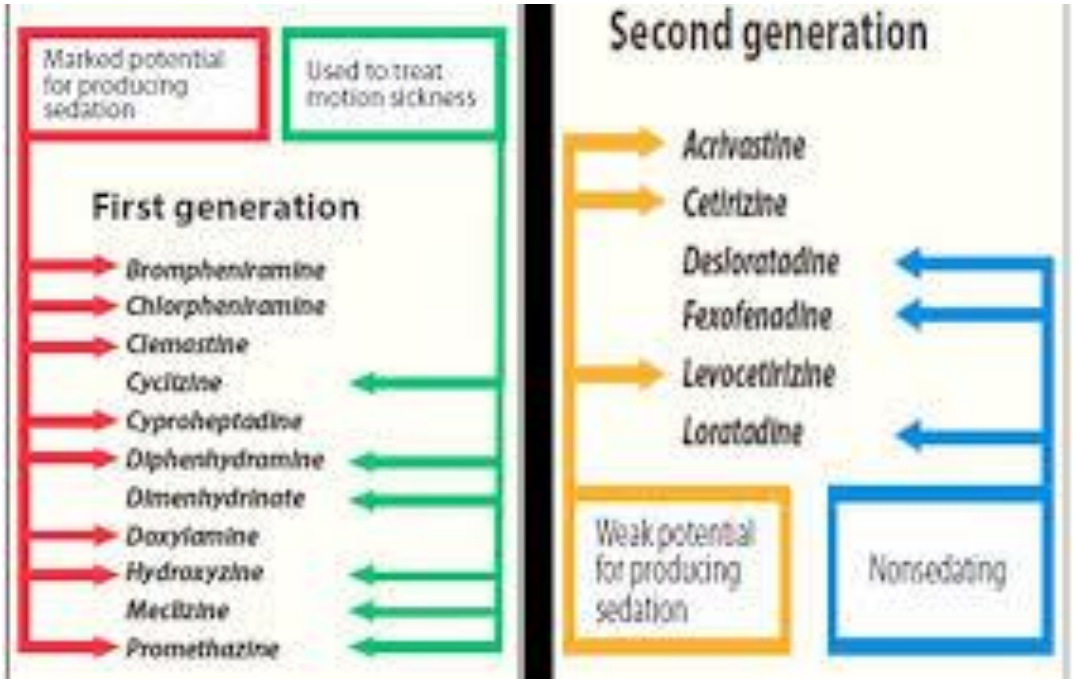
H1 Antihistamines

The term antihistamine refers primarily to the classic H1-receptor blockers. The H1-receptor blockers can be divided into **first- and second-generation drugs** .

The older first-generation drugs are still widely used because they are effective and inexpensive. However, most of these drugs penetrate the central nervous system (CNS) and cause sedation. Furthermore, they tend to interact with other receptors, producing a variety of unwanted adverse effects.

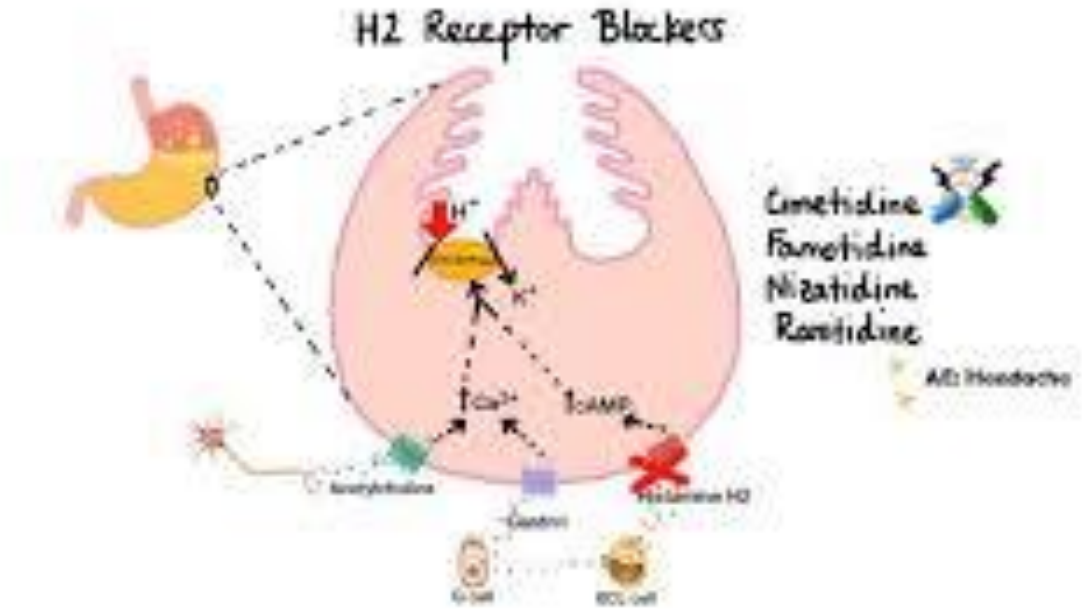


By contrast, **the second-generation agents** are specific for peripheral H1 receptors. The second-generation antihistamines are made polar, mainly by adding carboxyl groups (for example, **cetirizine** is the carboxylated derivative of **hydroxyzine**), and, therefore, these agents do not penetrate the blood–brain barrier and cause less CNS depression than do the first-generation drugs. Among the second-generation agents, **desloratadine** ,**fexofenadine** ,and **loratadine** ,show the least sedation . ***Cetirizine*** and **levocetirizine** are partially sedating second generation agents.



Histamine H2-Receptor Blockers

Histamine H2-receptor blockers have little, if any, affinity for H1 receptors, their chief clinical use is as inhibitors of gastric acid secretion in the treatment of ulcers and heartburn. The H2-receptor blockers **cimetidine**, **ranitidine**, **famotidine**, and **nizatidine**




Thank You!