

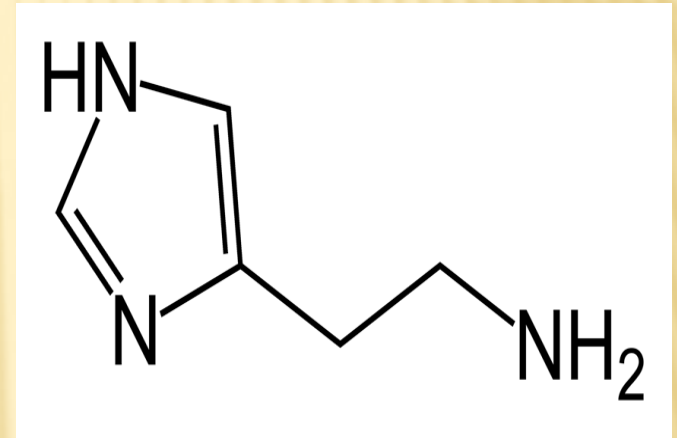
# HISTAMINE

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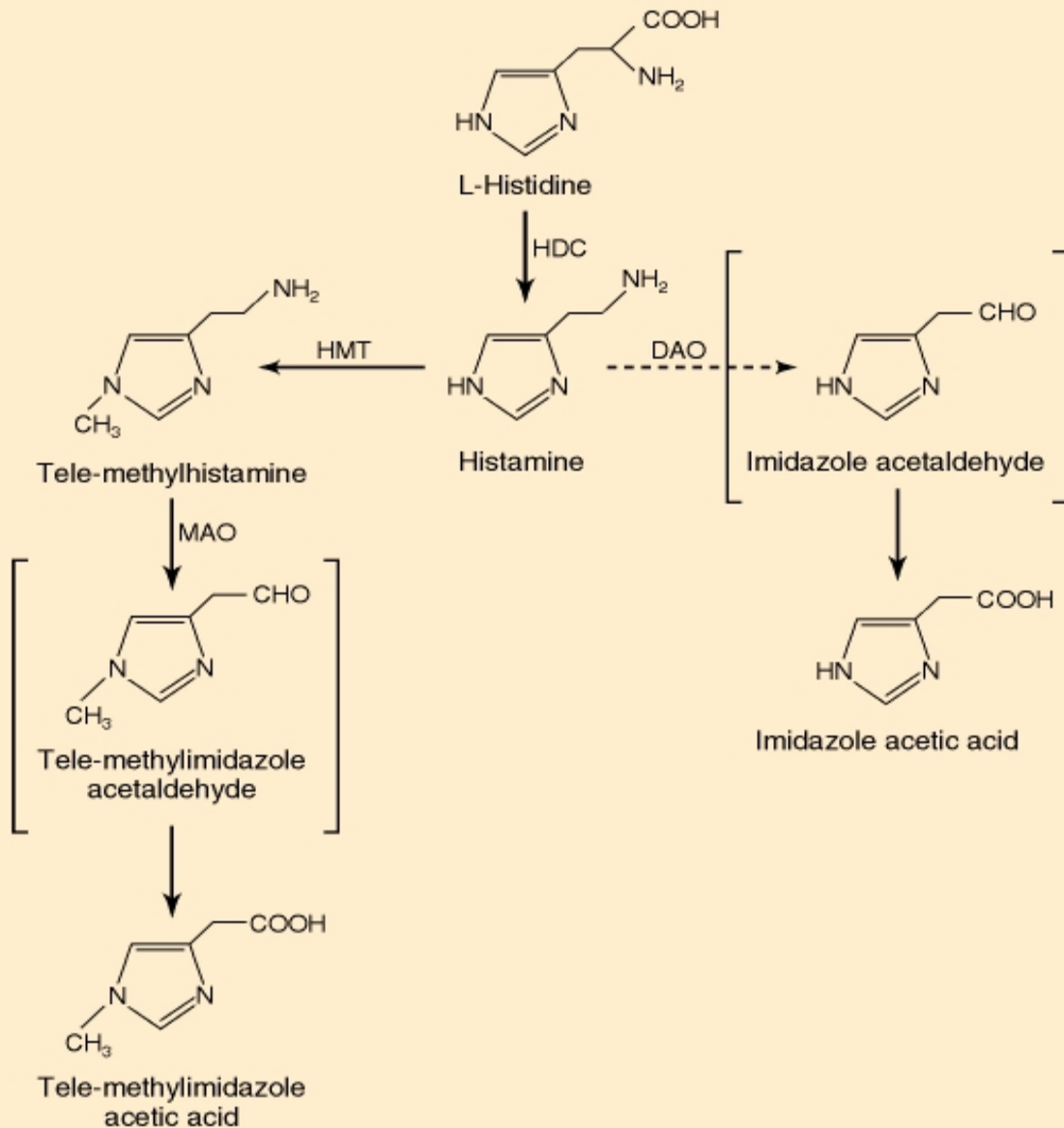
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# INTRODUCTION:

- **Histamine** is a biogenic amine, with a imidazole ring and act as a neurotransmitter.
- It is involved in local immune responses as well as regulating physiological function in the gut.
- Histamine triggers the inflammatory response.
- Histamine is found in basophils and by mast cells found in nearby connective tissues.
- Histamine increases the permeability of the capillaries to white blood cells and other proteins, in order to allow them to engage foreign invaders in the affected tissues.
- It is found in virtually all animal body cells.



# SYNTHESIS AND METABOLISM OF HISTAMINE:



— pathways for histamine formation in brain.

----- pathways that can occur outside of the nervous system.

HDC - histidine decarboxylase;

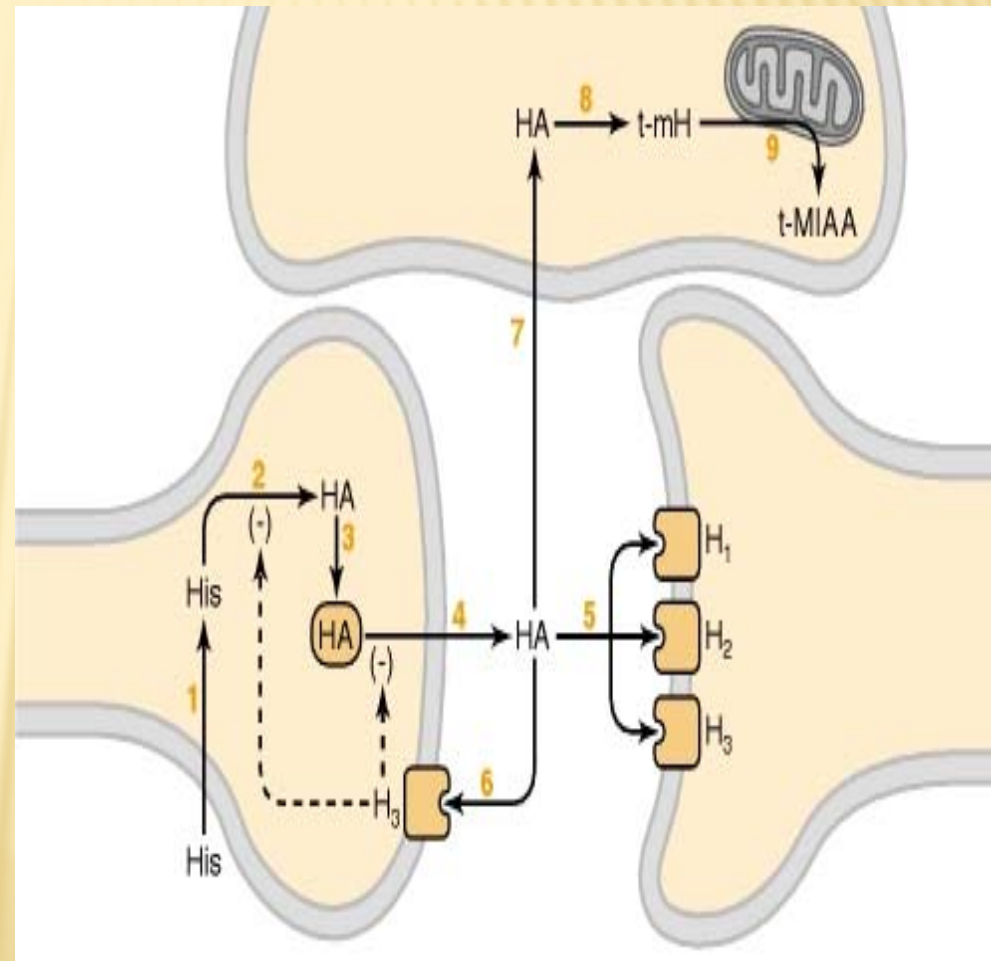
HMT - histamine methyltransferase;

DAO - diamine oxidase;

MAO - monoamine oxidase.

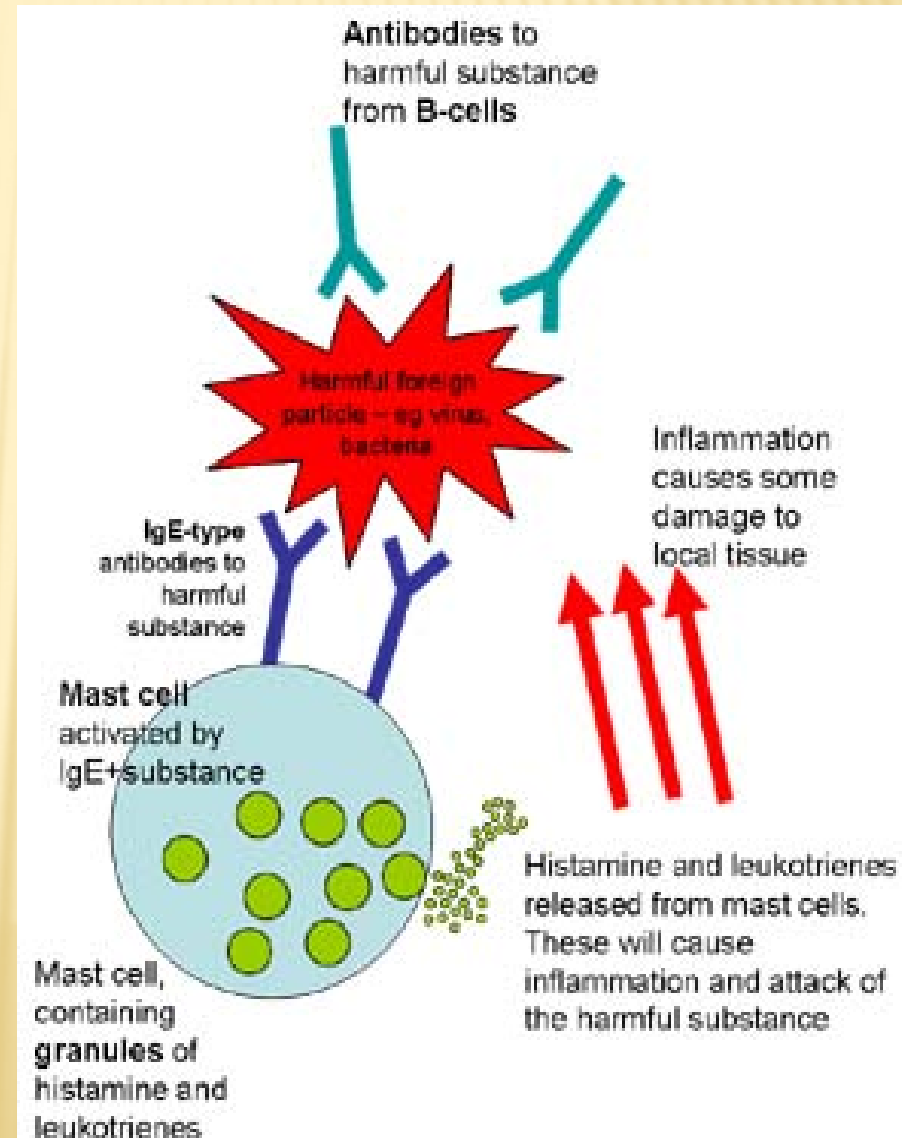
# DYNAMICS OF NEURONAL HISTAMINE

- 1) l-histidine (*His*) transport into nerve terminal.
- 2) Histamine (*HA*) synthesis by histidine decarboxylase.
- 3) Formation of histamine containing vesicles.
- 4) Histamine release by exocytosis.
- 5) Activation of post-synaptic receptors.
- 6) Feedback inhibition of histamine synthesis and release by  $H_3$  autoreceptors.
- 7) Histamine transport by astrocytes (re-uptake by nerve terminals has not been found).
- 8) Metabolism by histamine-*N*-methyltransferase (HMT).
- 9) Oxidation of t-MH by monoamine oxidase-B.



## STORAGE AND RELEASE OF HISTAMINE:

- Histamine is mostly present in storage granules of mast cells.
- Tissues rich in histamine are skin, gastric and intestinal mucosa, lungs, liver and placenta.
- Non mast cell histamine present in brain, epidermis.



# MECHANISM OF ACTION:

Histamine exerts its actions by combining with specific cellular histamine receptors.

Type	Location	Function
H <sub>1</sub> histamine receptor	Found on smooth muscle, endothelium, and central nervous system tissue	Causes vasodilation, bronchoconstriction, bronchial smooth muscle contraction, the primary receptors involved in allergic rhinitis symptoms and motion sickness.
H <sub>2</sub> histamine receptor	Located on parietal cells	Primarily stimulate gastric acid secretion
H <sub>3</sub> histamine receptor	Found on central nervous system and to a lesser extent peripheral nervous system tissue	Decreased neurotransmitter release: histamine, acetylcholine, norepinephrine, serotonin
H <sub>4</sub> histamine receptor	Found primarily in the basophils and in the bone marrow. It is also found on thymus, small intestine, spleen, and colon.	Plays a role in chemotaxis.

<b>TYPE</b>	<b>RECEPTOR TYPE</b>	<b>AGONISTS</b>	<b>ANTAGONIST</b>
<b>H1</b>	<b>Gq</b>	<b>2 – methyl histamine, 2 – pyridylethyl amine</b>	<b>Mepyramine, Chlorpheniramine</b>
<b>H2</b>	<b>Gs</b>	<b>4 – methyl histamine, Dimaprit</b>	<b>Cimetidine, ranitidine</b>
<b>H3</b>	<b>G Protein coupled</b>	<b><math>\alpha</math> – methyl histamine</b>	<b>Thioperamide, Impromidine</b>

# **PHARMACOLOGICAL ACTIONS OF HISTAMINE:**

## **➤ BLOOD VESSELS:**

Dilatation of small blood vessels, larger arteries and veins are contracted mediated by H<sub>1</sub>.

## **➤ HEART:**

Heart rate and force of contraction are increased (H<sub>2</sub>) and negative dromotropic (slowing of A-V conduction) (H<sub>1</sub>)

## **➤ VISCERAL SMOOTH MUSCLE:**

H<sub>1</sub> mediated contraction & H<sub>2</sub> mediated relaxation is also seen.



➤ **GLANDS:**

Increased in gastric secretion mediated by increased cAMP generation through H<sub>2</sub> receptors.

➤ **SENSORY NERVE ENDINGS:**

Itching when injected via i.v. Higher concentrations cause pain.

➤ **AUTONOMIC GANGLIA AND ADRENAL MEDULLA :**

Stimulated and release adrenaline and cause rise in B.P.

➤ **CNS:**

Cannot penetrate BBB. Intracerebroventricular administration cause rise in B.P., cardiac stimulation, hypothermia, ADH release. These effects are both by H<sub>1</sub> & H<sub>2</sub> receptors.

## **USES OF HISTAMINE:**

- **Sleep regulation**
- **Suppressive effects**
- **Schizophrenia**
- **Betahistine is used to control vertigo in patients of Meniere's disease, acts by causing vasodilatation in internal ear.**
- **As diagnostic aid to**
  - ✓ **test of acid secreting capacity of stomach**
  - ✓ **test bronchial hyperactivity in asthmatics**

## REFERENCES:

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