INTRODUCTION:

- **Histamine** is a biogenic amine, with an imidazoline 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 H₃ 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.

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>Function</th>
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<tbody>
<tr>
<td>H₁ histamine receptor</td>
<td>Found on smooth muscle, endothelium, and central nervous system tissue</td>
<td>Causes vasodilation, bronchoconstriction, bronchial smooth muscle contraction, the primary receptors involved in allergic rhinitis symptoms and motion sickness.</td>
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<tr>
<td>H₂ histamine receptor</td>
<td>Located on parietal cells</td>
<td>Primarily stimulate gastric acid secretion</td>
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<tr>
<td>H₃ histamine receptor</td>
<td>Found on central nervous system and to a lesser extent peripheral nervous system tissue</td>
<td>Decreased neurotransmitter release: histamine, acetylcholine, norepinephrine, serotonin</td>
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<tr>
<td>H₄ histamine receptor</td>
<td>Found primarily in the basophils and in the bone marrow. It is also found on thymus, small intestine, spleen, and colon.</td>
<td>Plays a role in chemotaxis.</td>
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<tr>
<td>TYPE</td>
<td>RECEPTOR TYPE</td>
<td>AGONISTS</td>
</tr>
<tr>
<td>--------</td>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>H1</td>
<td>Gq</td>
<td>2 – methyl histamine, 2 – pyridylethylamine</td>
</tr>
<tr>
<td>H2</td>
<td>Gs</td>
<td>4 – methyl histamine, Dimaprit</td>
</tr>
<tr>
<td>H3</td>
<td>G Protein coupled</td>
<td>α – methyl histamine</td>
</tr>
</tbody>
</table>
PHARMACOLOGICAL ACTIONS OF HISTAMINE:

- **BLOOD VESSELS:**
  
  Dilatation of small blood vessels, larger arteries and veins are contracted mediated by H1.

- **HEART:**
  
  Heart rate and force of contraction are increased (H2) and negative dromotropism (slowing of A-V conduction) (H1)

- **VISCERAL SMOOTH MUSCLE:**
  
  H1 mediated contraction & H2 mediated relaxation is also seen.
GLANDS:
Increased in gastric secretion mediated by increased cAMP generation through H2 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 H1 & H2 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:


- www.bio.davidson.edu/courses/immunology/.../mfirp.htm