

HISTAMINE & ANTIHISTAMINE

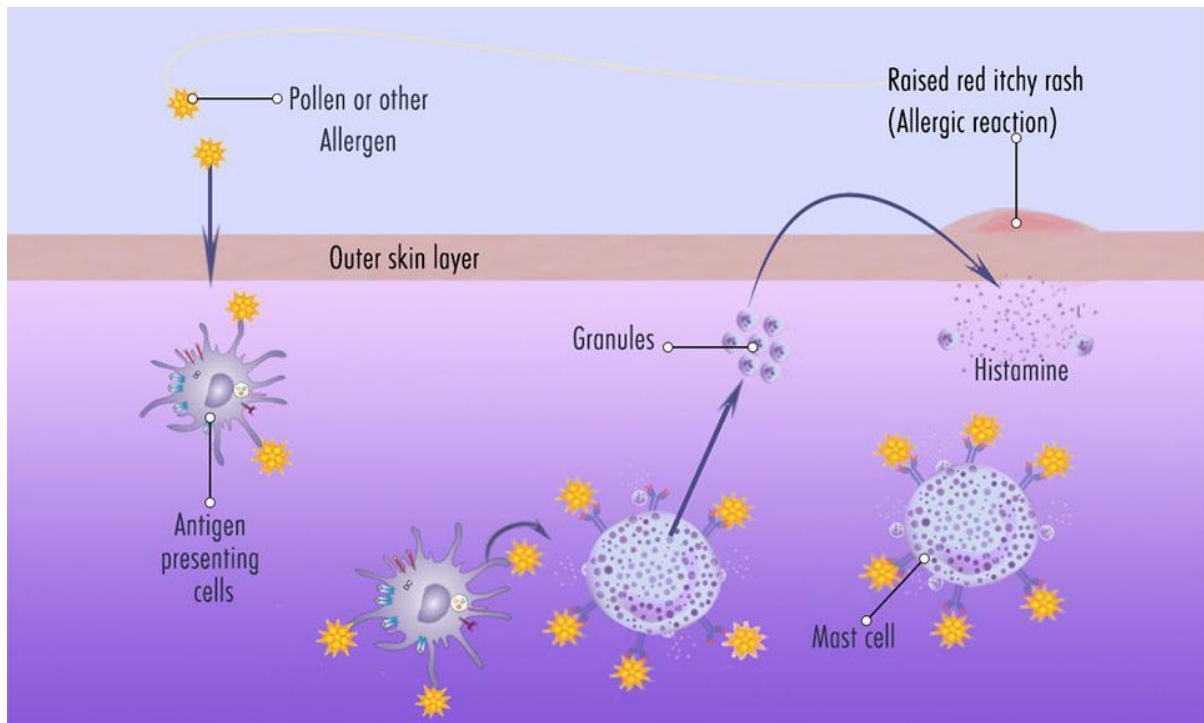
Point Wise Important Facts

Autacoids- Autacoids are the biochemical substance released by the local cells and then response locally to any influencing signals. It was synthesized in 1907 and latter isolated from mammalian cell.

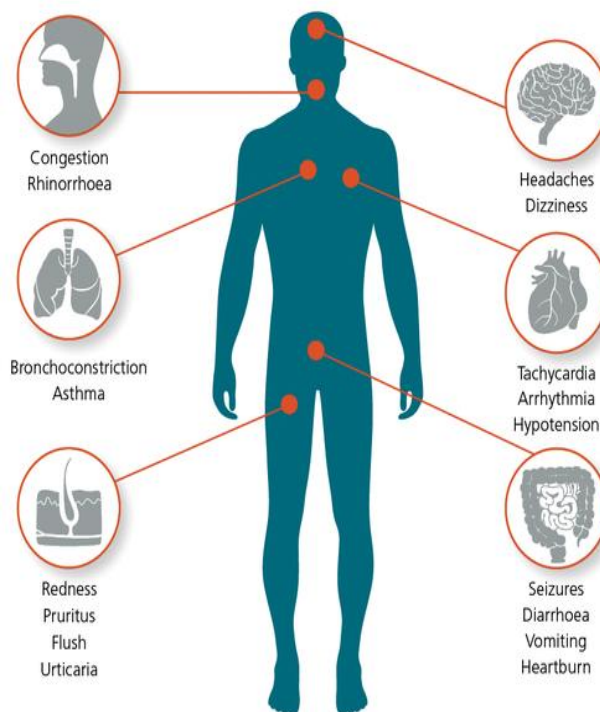
Solution

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1. **Histamine was first autacoids discovered.**
2. Histamine stored in a complex with Heparin, Chondroitin Sulfate, Eosinophilic Chemotactic factor, and Neutrophilic Chemotactic factor.
3. **According to their chemical nature they are classified into three main categories-**
 - A- **Amine-** Histamine and Serotonin
 - B- **Peptide-** Bradykinin, Angiotensin and Kallidin
 - C- **Lipids-** Prostaglandins, Leukotrienes and Platelet activating components
4. Histamines are released by mast cell granules from its precursor **Histidine** by decarboxylation, which are stored in local tissue like, lungs, skin, GIT, blood vessels. According to their action on different sites they have separated specifically as- **H₁, H₂, and H₃.**



5. Non mast cell histamine are found in various tissue including brain, where it acts as a neurotransmitter,
6. Drugs and other foreign compounds like- Morphine, Dextran, Antimalarial drugs, Dyes, Antibiotic base, Alkaloids, Amides, Quaternary Ammonium compounds, Peniciline, Tetracycline, Toxins, Venoms, Proteolytic enzyme also release the histamine from mast cell.
7. Even histamines work specifically at H₁, H₂, and H₃ though they give mild action to other histamine receptor too.



8. Function of Histamine receptor on their preferred sites-

S.N.	Type	Action
1	H₁	Responsible for allergic reaction due to invasion of antigen in the body.
		Initiation for constriction of bronchial smooth muscle, which will lead to difficulty in breathing and triggering the asthmatic attack.
		Create mental alertness by generating reticular cells in brain.
2	H₂	It is locally found in GIT and thus responsible for secretion of gastric juice (Hydrochloric Acid) which will further reduced the action of ranitidine and ultimately cause lack of pepsin (Dyspepsia)
3	H₃	Found in pre synaptic vesicles
		Inhibit release of histamine Solution www.facebook.com/pharmavideo/
4	H₄	Located at eosinophiles, basophiles and other mast cells which also promote chemotaxis

9. One of the most important functions of histamine is to contract the visceral smooth muscle, bronchoconstriction, and abdominal cramp.
10. Histamine is powerful stimulant of sensory nerve ending, especially those mediating pain and itching.

11. In human injection of histamine cause a decrease in systolic and diastolic blood pressure and increase in heart rate. This is due to direct vasodilator effect of histamine.
12. Contraction of guinea pig ileum is a slandered bioassay of histamine. Human ileum is not as sensitive as guinea pig. Intradermal injection of histamine cause triple response as like inflammation- red spot, edema, and pain.
13. It also plays an important role in nociception.
14. Adverse effect of histamine- flushing, hypotension, tachycardia, headache, wheals, bronchoconstriction, GIT upset,
15. **Contraindicated to asthmatic and ulcerative patient.**

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ANTI HISTAMINE

These are the drugs act against the action of histamine either competitively or non competitively.

16. H₁ antagonists are competitive antagonist at H₁ site. They are classified as 1st generation and 2nd generation compound based on their **penetration capability** at central nervous system.
17. First generation antihistaminic drugs can **cross the blood brain barrier** and result in sedation and psychomotor impairments. As these drugs are sedative in nature these are were not suitable for those patients who require concentration. Due to this reason 1st generation, antihistaminic drugs are contraindicated in drivers and mechanical employee.
18. **Example of 1st generation Antihistamines-** (1) Alkylamines (2) Ethanolamines (3) Ethylenediamines (4) Piperazines (5) Phenothiazines (6) Piperadines
19. Highly sedative drugs- Diphenhydramine, Dimethydrinate, Promethazine, Hydroxyzine and Doxepin.
20. Moderately Sedating- Pheniramine, Cycloheptadine, Meclizine, Buclizine and Cinnarzine
21. Mildly Sedative- Chlorpheniramine, Mepyramine, Cyclizine, Clemastine
22. Mechanism of H₁ antihistamine is displacement of histamine from its receptor, which is G-Protein coupled receptor.

23. Histamine leads to formation of IP₃ (Inositol Tri Phosphate) and release of stored calcium ion.
24. Use of anti histamine drugs- as name indicates they act against the histamine so they will oppose the effect of histamine. They provide relief from allergic response due to allergens of any kind, prevent itching, common cold, migraine, urticaria, hay fever. Insect bite, also have antiparkinsons effect due to anticholinergic effects.
25. Drug Interaction of H₁ blocker- **potentiate CNS depressants (barbiturate, opiates, general anesthetics and alcohol)**
26. Adverse effects of 1st generation anticholinergic drugs are- sedation, psychomotor impairments, and anticholinergic effects like- dry mouth, blurred vision, urinary retention, and constipation.
27. Second generation anti histaminic drugs- these drugs have advantage over 1st generation antihistaminic drugs as they don't cross the blood brain barrier and they don't cause sedation and psychomotor impairment effect. Example include- cetirizine and azelastine

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Drugs	Important Points
Terfenadine	It is the faster acting anticholinergic drug, in overdose it may block the K channel and may cause polymorphic ventricular tachycardia. Use of these drugs with microsomal enzyme inhibitor like ketoconazole, erythromycin, clarithromycin increase the risk of arrhythmia
Astemizole	It is slowest and longest acting agent having arrhythmogenic property.
Cetirizine	It is active metabolites of first generation antihistaminic drug hydroxyzine. All second generation antihistaminics are metabolized to active products except cetirizine and mizolastine.
Azelastine	It possesses maximum topical activity and can be given by nasal spray for allergic rhinitis.
Olopatadine	It is recently approved second-generation antihistaminic drugs for seasonal allergic reaction.
Alcaftadine	It is approved as ophthalmic solution for allergic conjunctivitis.

28. All H₁ receptor blocker are well absorbed after oral administration with maximum serum level occurring at 1- 2 hours. Average plasma half-life is- 4-6 hours. They have high bioavailability and are distributed in all tissue including CNS.
29. Use of H₂ antagonist are- in peptic ulcer, gastric ulcer, **Zolinger-Ellison Syndrome** (A pathological hypersecretory state resulting in excessive gastric pepsin and HCl)

gastroesophageal reflux disease, used prior to surgery in patient with GI obstruction to elevate gastric pH, reflux esophagitis, as antacid.

30. Most common side effects of H₂ antagonist are- Diarrhea, Dizziness, Somnolence, Headache, Rash, Constipation, and vomiting.

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(2) Basic and Clinical Pharmacology- Katzung

(3) Essential of Medical Pharmacology- K.D. Tripathi

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