

- **Case study**
- A 24 year old male patient John , suffers from allergic rhinitis. Every winter, he develops a runny nose, itchy eyes, and sneezing.
- To relieve his symptoms, he takes an over-the-counter antihistamine, diphenhydramine.
- John is annoyed by the unpleasant effects that accompany his allergy medication. Every time he takes his antihistamine, he feels drowsy and his mouth feels dry.
- He makes an appointment with his doctor who, advises him to take loratadine. Upon taking new allergy medication, his symptoms are relieved and he experiences no drowsiness or other adverse effects.
- **Questions**

- **Why does John develop seasonal rhinitis?**
- **Why does diphenhydramine relieve John`s symptoms?**
- **Why does diphenhydramine cause drowsiness?**
- **Why doesn't loratadine cause drowsiness?**

- Autacoids (Histamine & Antihistamine)
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- Objectives

- Describe the pharmacology of histamine & enumerate its related drugs.
- Classify the generation and sub-group of Histamine-1(H1) antagonists.
- Discuss the pharmacology of H1 Antihistaminics with emphasis on clinical uses, adverse drug reactions & interactions
- Autacoids
- Autos = self; Akos = remedy (*Greek*).

- Secreted locally to increase or decrease the activity of nearby cells.
- Includes
 - Histamine, Serotonin
 - Prostaglandins and Leukotrienes
 - Cytokines
- Synthesis of histamine
- Mechanism of action
- Four types of receptors-
 - H₁ , H₂, H₃ and H₄.
- All are seven transmembrane G-protein coupled receptors.
- Some wide actions are mediated by both (H₁ and H₂) receptors.

- Mechanism of Action of Histamine
- Histamine receptor subtypes
- Actions of histamine
- Actions of histamine (contd.)
- Drugs that cause release of histamine
- D-tubocurarine
- Morphine
- Adverse effects of histamine release
- Itching, Urticaria
- Flushing
- Hypotension
- Tachycardia

- Bronchospasm
- Angioedema
- Wakefulness
- Increased acidity (Gastric acid secretion)
- Antihistamines: H1 receptor blocker
- First generation
- Second generation
- **H1-Antihistaminics /First generation**
- **H1-Antihistaminics /second generation**
- Therapeutic uses
- Allergic diseases
 - Rhinitis, urticaria, conjunctivitis.
 - Bronchial asthma

- Anaphylaxis
- Topical preparations-
 - Levocabastine
 - Azelastine
 - Ketotifen
 - Olopatadine

- uses: First Generation Antihistamines

- Insomnia
- Anxiety
- Motion sickness
- Nausea and vomiting
- Morning sickness
- Vertigo

- Uses: second Generation Antihistamines
- Allergies
- Reduce symptoms of itching, sneezing
- Rhinorrhea
- Allergic conjunctivitis
- Common Adverse Effects
Anticholinergic (Atropine-like)
 - Blurred vision
 - Dry mouth
 - Tachycardia
 - Urinary retention
 - Dizziness

- Drowsiness
- Paradoxical excitement in infants and children
- Overdose of Astemizole and Terfenadine may cause arrhythmias

- Contraindications
 - Acute angle-closure glaucoma
 - Hypersensitivity
 - Urinary obstruction

- Drug interactions
 - Terfenadine and astemizole
 - Ketoconazole
 - Macrolide antibiotics

Lethal ventricular arrhythmias.

Torsades de pointes

Withdrawn from market

- Grapefruit juice also inhibits CYP3A4.
 - Increased levels of antihistamines.
- **Answers**
- The IgE-mediated hypersensitivity reaction is responsible for initiation of certain inflammatory disorders, like **allergic rhinitis** .
- John suffered from allergic rhinitis, with a runny nose, itchy eyes, and sneezing.
- An environmental allergen, such as pollen, crosses the nasal epithelium and enters the underlying tissue. There, the allergen encounters previously sensitized

mast cells and crosslinks IgE/Fc receptor complexes on the mast cell surface.

- The mast cell degranulates and releases histamine, which binds to H1 receptors in the nasal mucosa and local tissues.
- **Answers**
- Stimulation of H1 receptors causes blood vessel dilation and ↑es vascular permeability, leading to edema. This swelling in the nasal mucosa is responsible for the nasal congestion experienced in allergic rhinitis.
- The accompanying itching, sneezing, runny nose, etc result from the combined

action of histamine and other inflammatory mediators, including kinins, prostaglandins etc.

- These molecules initiate the hypersecretion and irritation characteristic of allergic rhinitis.