* 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 Leukotrines
* 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
* Wakefullness
* Increased acidity (Gastric acid secretion)
* Antihistamines: H1 receptor blocker
* First generation
* Second generation
* **H1-Antinistaminics /First generation**
* **H1-Antinistaminics /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.