

Treatment of Acute & Chronic Rhinitis and Cough

Learning objectives

At the end of the lecture, students should be able to:

- ▶ Define rhinitis and cough
- ▶ Classify drugs used in the treatment of **rhinitis**
- ▶ Expand on the pharmacology of different drug groups used in the treatment as; antihistamines, leukotriene antagonists, corticosteroids, decongestants and anticholinergics.
- ▶ Describe the pharmacology of different **expectorants** and mucolytics used in the treatment of productive cough
- ▶ Describe the pharmacology of **antitussives** (cough suppressants)

Rhinitis

- ▶ Rhinitis is the irritation and/or inflammation of the mucous membranes inside the nose
- ▶ **Types:**
 1. Allergic (seasonal ; hay fever and perennial)
 2. infectious (infection with bacteria, fungi and viruses)
- **Rhinitis may be:**
 - Acute (persist 7-14 days)
 - Chronic (persistent more than 6 weeks)

Signs and symptoms of rhinitis:

- ▶ Runny nose (rhinorrhea; excess nasal secretion & discharge)
- ▶ Sneezing
- ▶ Nasal congestion/stuffy blocked nose
- ▶ Post nasal drip
- ▶ Systemic effects may be (fever, body aches,....,....)

Treatment of Rhinitis

A. Preventive Therapy:

1. Environmental control (dust control, pets
2. Allergen immunotherapy

B. Pharmacotherapy:

1. Anti-histamines (H₁- receptor antagonists)
2. Anti-allergics
 - a) Cromolyn sodium (mast cell stabilizer)
 - b) Montelukast (Leukotriene receptor antagonists)
3. Corticosteroids
4. Decongestants (alpha- adrenergic agonists)
5. Anti-cholinergics
6. Antibiotics (if bacterial infection occur)

What is histamine?

- ▶ **Histamine** is a chemical messenger mostly generated in mast cell that mediates a wide range of cellular responses, Including;
 - Allergic and inflammatory reactions,
 - Gastric acid secretion
 - Neurotransmission in parts of the brain
- ▶ Histamine has no clinical application but antihistamines have important therapeutic applications

Antihistamines (H₁-receptor antagonists):

- ▶ The term antihistamine, without modifying objective, refers to the **classic H₁- receptor blockers**
- ▶ These drugs do not interfere with the formation or release of histamine
- ▶ **They block the receptor- mediated response of a target tissue**

1- ANTIHISTAMINES H_1 receptor blockers

CLASSIFICATION [Chemical / Functional] → USES *vs* ADVERSE EFFECTS

| | First GENERATION | Second GENERATION | Third GENERATION |
|---------------------|---|---|------------------------------------|
| 1) ALKYLAMINES | Chlorpheniramine | | |
| 2) ETHANOLAMINES | Dimenhydrinate Diphenhydramine | | |
| 3) ETHYLENEDIAMINES | Antazoline` | | |
| 4) PHENOTHIAZINES | Promethazine | | |
| 5) PIPERAZINE | Cyclizine | Cetirizine | → Levocetirizine |
| 6) PIPERIDINES | Azatidine | Loratadine | → Fexofenadine → Desoloratadine |
| 7) MISCELLANEOUS | Ketotifen Cyproheptadine | | |
| | Short duration | Longer duration = better control | |
| | Interactions; with enzyme inhibitors [macrolides, antifungals, calcium antagonists] + additive pharmacodynamic ADRs | No drug interactions & minimal ADRs | |

All are used systemic or topical

- ▶ The older **first generation** drugs still widely used because they are **effective and inexpensive**.
- ▶ These drugs **penetrate the blood brain barrier (BBB)** and cause **sedation**. Furthermore, they tend to interact with other receptors, producing a variety of **unwanted adverse effects**
- ▶ **Second generation (Non-sedating)** agents are specific for H₁ receptors and they carry **polar groups**, they **do not penetrate the BBB** causing less CNS depression

Actions:

- ▶ The action of all the H₁ receptor blocker is qualitatively similar
- ▶ **They are much more effective in preventing symptoms than reversing them once they have occurred**
- ▶ Most of these drugs have additional effects unrelated to their blocking H₁ receptors, which probably reflect binding of H₁ antagonists to:
 - Cholinergic,
 - Adrenergic or,
 - Serotonin receptors

GOOD CONTROL of Rhinitis, Conjunctivitis, Urticaria, Flu (cough & sneezing)
POOR CONTROL of Asthma, Otitis, Anaphylaxis, Sinusitis, Atopic dermatitis

INDICATIONS linked to H1 block

INDICATIONS not linked to H1 block

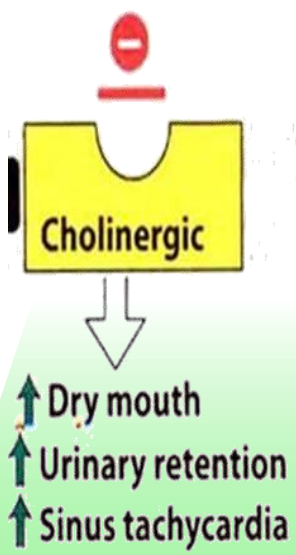
ANTI HISTAMINES

ALLERGIES

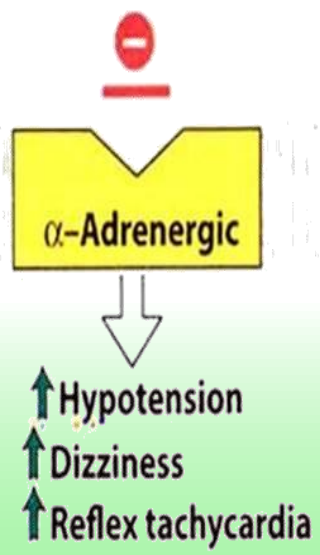
ITCHING
Even if non-allergic

Others

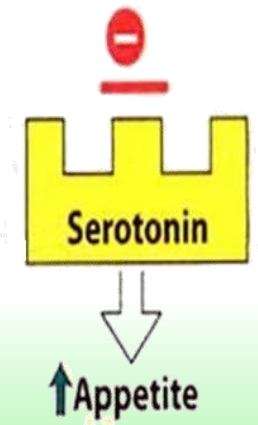
Insomnia
Sleep aid
Vertigo
Anxiety
Cough



Side Effects
Interactions



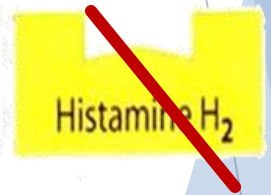
Side Effects
Interactions



Side Effects
Interactions



↓ Allergic inflammation, itching, sneezing, and rhinorrhea
 ↓ Neurotransmission in the CNS
 ↑ Sedation
 ↓ Cognitive and psychomotor performance
 ↑ Appetite



Therapeutic uses:

1. **Allergic rhinitis**, relieves rhinorrhea, sneezing, and itching of eyes and nasal mucosa
2. **Common cold**: dries out the nasal mucosa. Often combined with nasal decongestant and analgesics
3. **Motion sickness**
4. **Allergic dermatoses**: can control itching associated with insect bites.
5. **Nausea and vomiting** (Promethazine)

Pharmacokinetics:

- ▶ H₁ receptor blockers are well **absorbed after oral** administration
- ▶ Maximum serum levels occurring at **1-2** hours
- ▶ Average plasma half life is **4 to 6** hours
- ▶ H₁- receptor blockers have **high bioavailability** and distributed to all tissues including CNS
- ▶ Metabolized by the **hepatic cytochrome P450** system
- ▶ Excretion occur via kidney except **fexofenadine** excreted in feces unchanged

Adverse effects:

- ▶ Sedation, tinnitus, fatigue, dizziness, blurred vision, dry mouth

Drug interaction:

- ▶ CNS depressants & cholinesterase inhibitors

Overdose:

- ▶ The most common and dangerous effects of acute poisoning are those on **CNS**; including hallucinations, excitement, ataxia and convulsions

CROMOLYN & NEDOCROMYL

↓ Histamine release [mast cell stabilizer by inhibiting Cl channels]
i.e. can act only **prophylactic**; it does not antagonize the released histamine

Used more **in children** for prophylaxis of **perennial allergic rhinitis**

Should be given on daily base and never stop abruptly.

LEUKOTRIENE RECEPTOR ANTAGONISTS **Montelukast**

Block leukotriene actions

For **prophylaxis** of lower respiratory [i.e perennial allergen, exercise or aspirin-induced asthma] > upper respiratory allergies [chronic rhinosinusitis]

ADRs; as in asthma

3-CORTICOSTEROIDS

Anti-inflammatory → blocks phospholipase A₂ →
↓ arachidonic a. synthesis → ↓ prostaglandins & leukotrienes

Topical (inhaled); steroid **spray**; **beclomethasone**, & **fluticasone**

Given if severe intermittent or moderate persistent symptoms

ADRs; Nasal irritation, fungal infection, hoarseness of voice

4. DECONGESTANTS

SYSTEMIC

+ PSEUDOEPHEDRINE

- Can cause nervousness, insomnia, tremors, palpitations, hypertension
- Better avoided in hypertension, heart failure, angina pectoris, hyperthyroidism, glaucoma

α -Adrenergic agonists → For treatment of nasal stuffiness

TOPICAL

PHENYLETHYLAMINES

- + Phenylephrine
- + Methoxamine

IMIDAZOLINE

- + Naphazoline
- + Oxymetazoline HCl
- + Xylometazoline HCl

can cause **Rebound nasal stuffiness** (repeated administration (10 days -2 weeks))

5. ANTICHOLINERGICS

Ipratropium

Given as nasal drops to **control rhinorrhea**

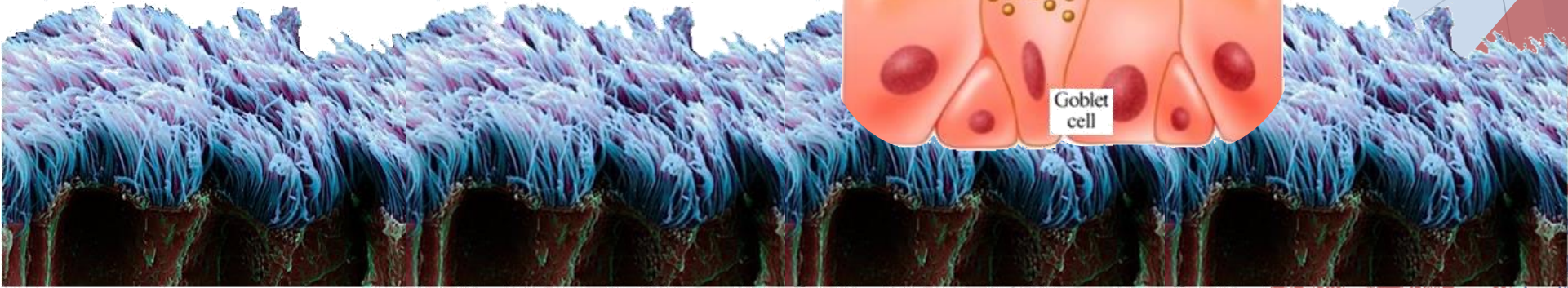
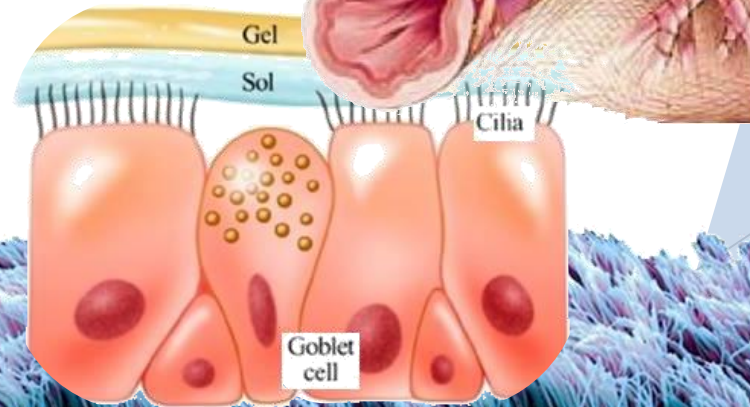
So very effective **in vasomotor rhinitis** (watery hyper-secretion).

Its indication as bronchodilator in asthma and ADRs → see asthma

DRUGS USED IN

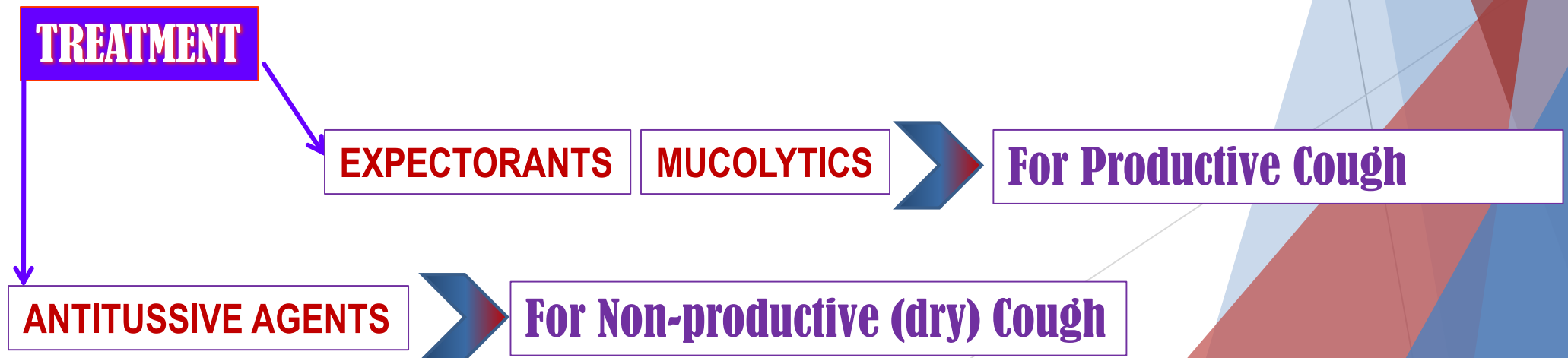
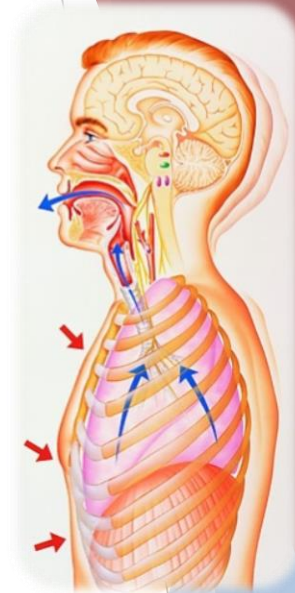


TREATMENT OF COUGH



- Coughing is sudden expulsion of air from the lungs through the epiglottis at an amazingly fast speed (~100 miles/ hr) to get of unwanted irritants.
- Abdominal & intercostal muscles contract, against the closed epiglottis → pressure ↑ → air is forcefully expelled to dislodge the triggering irritant.

Cough may be → *“wet or productive”* or
 → *“dry or irritant”*
 2ndry to irritant vapors, gases, infections, cancer→



EXPECTORANTS

Act by removal of mucus through



↓ **Reflex stimulation** Irritate GIT → stimulate gastropulmonary vagal reflex → loosening & thinning of secretions → **Guaiifenesin**

ADRs ; Dry mouth, chapped lips, risk of kidney stones (↑ uric a. excretion) ↓

↓ **Direct stimulation** Stimulate secretory glands → ↑ respiratory fluids production → **Iodinated glycerol, Na or K iodide / acetate, Ammonium chloride, Ipecacuahna**

↓ ADRs of iodide preparations ; Unpleasant metallic taste, hypersensitivity, hypothyroidism, swollen salivary glands (overstimulation of salivary secretion), & flare of old TB.

INDICATIONS ← Final outcome is that cough is indirectly diminished

- + Common cold
- + Bronchitis
- + Pharyngitis
- + Chronic paranasal sinusitis



MUCOLYTICS

Mucolytic agents are used to dissolve or breakdown mucus in the respiratory tract. They make the mucus less viscous so that it can be coughed up with more ease.

MECHANISM OF ACTIONS

Mucolysis occurs by one or more of the following;

- ✦ ↑ water content; **Hypertonic Saline & NaHCO₃**
- ✦ ↓ Adhesiveness; **Steam inhalation**
- ✦ Breakdown S-S bonds in glycoproteins → less viscid mucous; **N-Acetyl Cysteine**
- ✦ Synthesize serous mucus + activate ciliary clearance **Bromohexine & Ambroxol**
- ✦ Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of infection; **rhDNAase** = recombinant human deoxyribonuclease (**Pulmozyme**)

INDICATIONS

- ✦ Most mucolytics → effective as adjuvant therapy in COPD, asthma, bronchitis, ...etc. (when there is excessive, thick mucus....)

1. N-Acetylcysteine → Breakdown S-S bonds in glycoproteins

→ It is also a free radical scavenger → used in acetaminophen overdose

2. Bromhexine & its metabolite **Ambroxol** → Synthesize serous mucus

They also ↑ immuno defence so ↓ antibiotics usage

They also ↓ pain in acute sore throat

3. Pulmozyme (Dornase Alpha)

→ A recombinant human deoxyribo-nuclease-1 enzyme that is neubilized

→ Full benefit appears within 3-7 days

ANTITUSSIVE AGENTS

Stop or reduce cough by acting either peripherally or centrally

1. PERIPHERALLY ACTING ANTITUSSIVES

A. Inhibitors of airway stretch receptors

In Pharynx → Use Demulcents → form a protective coating

Lozenges & Gargles

In Larynx → Use Emollients → form a protective coating

menthol & eucalyptus.

In Tracheobronchial Airway → Use aerosols or inhalational of hot steam

tincture benzoic compound & eucalyptos

During bronchoscopy or bronchography → Use local anaesthetic aerosols, as **lidocaine, benzocaine, and tetracaine**

B. Inhibitors of pulmonary stretch receptors in alveoli

Benzonatate → ↓ sensitivity (numbing) of receptors by local anesthetic action.

ANTITUSSIVE AGENTS



2. CENTRALLY ACTING ANTITUSSIVES

A. OPIOIDS activating μ opioid receptors
e.g. Codeine & Pholcodine

B. NON-OPIOIDS  Antihistaminics (>sedating)

Dextromethorphan

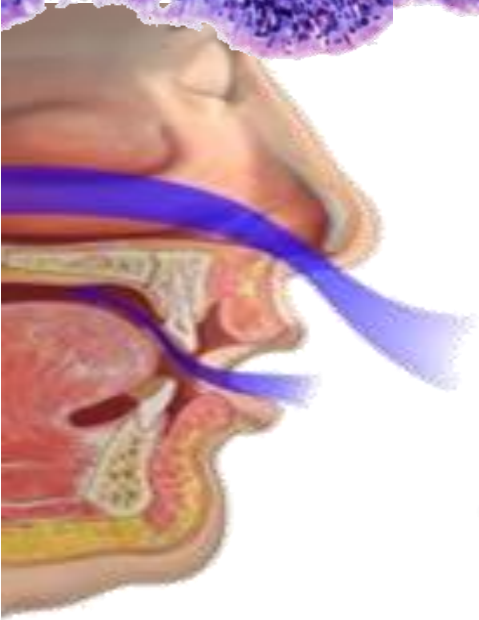
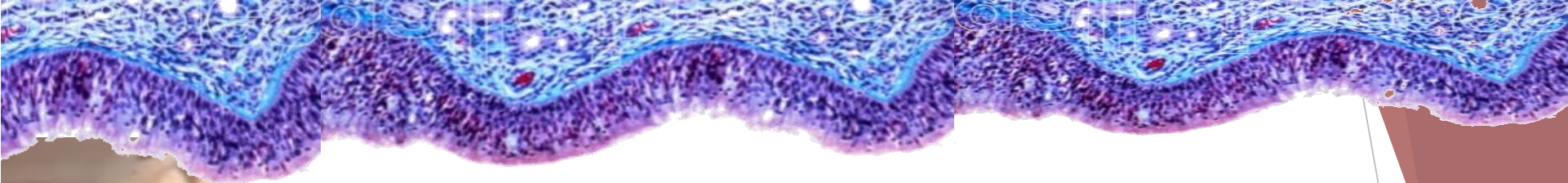
It \uparrow threshold at cough center. It has benefits over opioids in being \rightarrow

1. As potent as codeine
- 2- Less constipating
- 3- No respiratory depression.
- 4- No inhibition of mucociliary clearance
- 5- No addiction.

ADRs

In normal doses , nausea, vomiting, dizziness, rash & pruritus

In high doses, hallucinations + opiate like side effects on respiration & GIT



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