

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) Leukotriene receptor antagonists (montelukast)
3. Corticosteroids
4. Decongestants (alpha- adrenergic agonists)
5. Anticholinergics
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 and 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

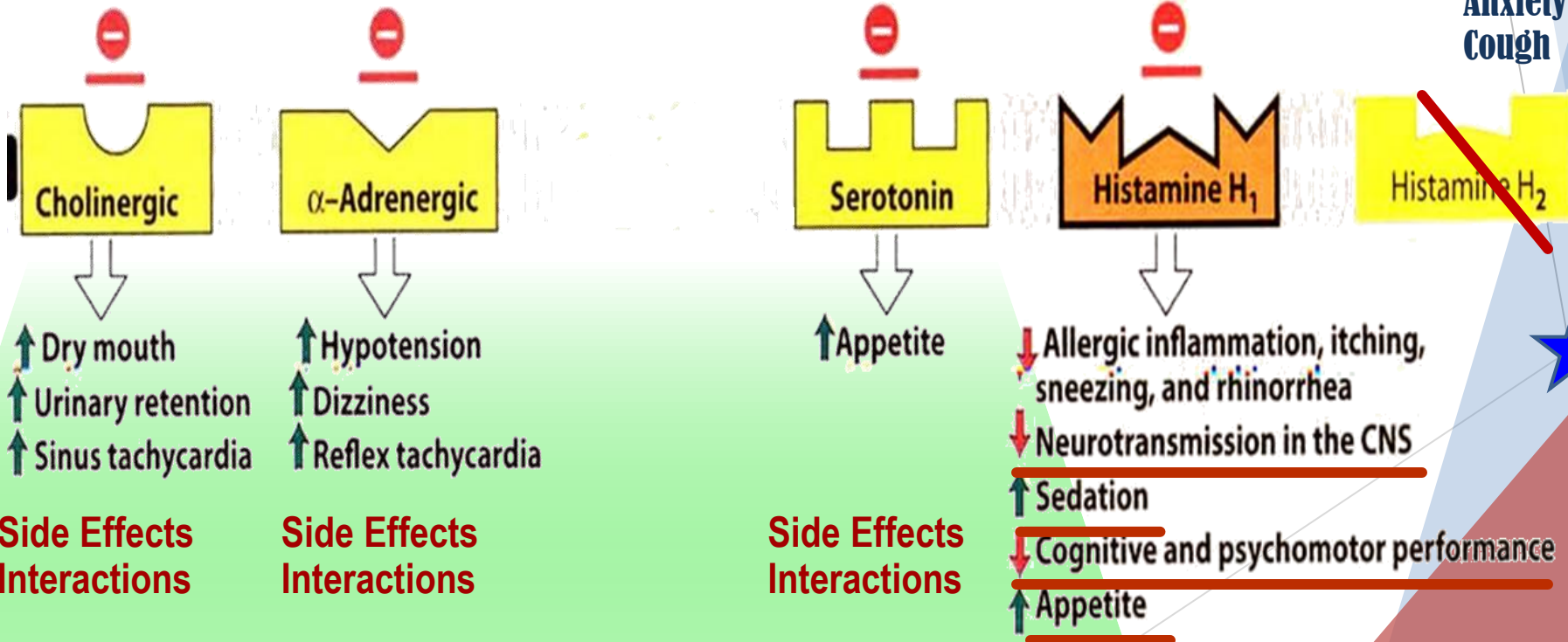
ALLERGIES

ITCHING

Even if non-allergic

Others

Insomnia
Sleep aid
Vertigo
Anxiety
Cough



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.
Can induce cough, wheezes, headache, rash, ...etc.

LEUKOTRIENE RECEPTOR ANTAGONISTS

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; steroid **spray**; beclomethasone, budesonide, & fluticasone

Given if severe intermittent or moderate persistent symptoms

ADRs; Nasal irritation, fungal infection, hoarseness of voice

4. DECONGESTANTS

α -Adrenergic agonists

→ For treatment of nasal stuffiness

SYSTEMIC

+ PSEUDOEPHEDRINE

TOPICAL

PHENYLETHYLAMINES

+ Phenylephrine
+ Methoxamine

IMIDAZOLINE

+ Naphazoline
+ Oxymetazoline HCl
+ Xylometazoline HCl

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

But 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



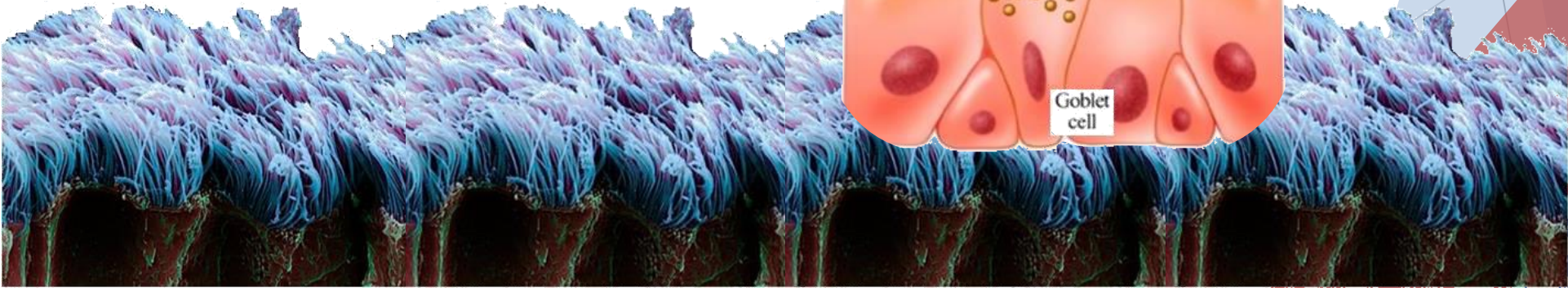
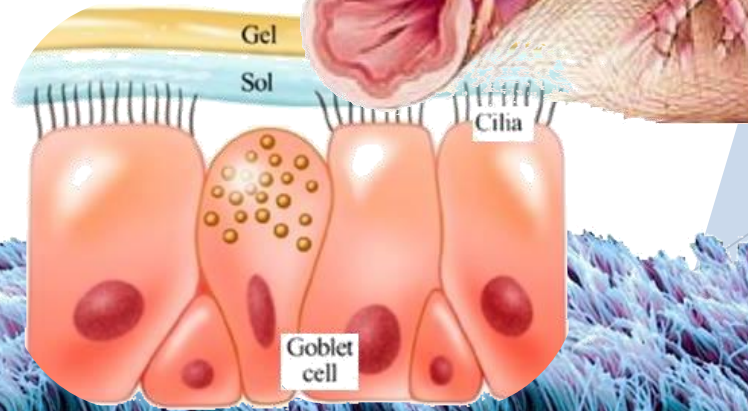
Effectiveness of different drug groups in controlling symptoms of RHINITIS

Drug Groups	Main Symptom		
	Sneezing	Blockage Stuffiness	Secretions Rhinorrhea
Anti-histamines	++	-	+
Anti-allergics (cromolyns)	+	+	+
Topical corticosteroids	++	++	++
Decongestant	-	++	-
Anticholinergics	-	-	++

DRUGS USED IN



TREATMENT OF COUGH



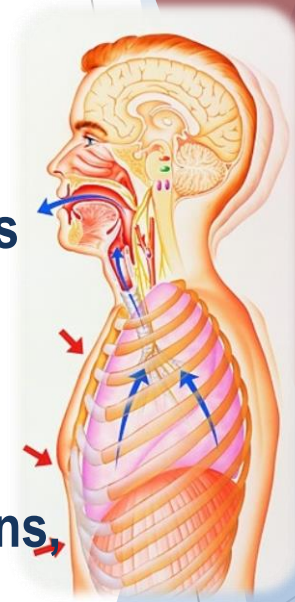
The respiratory tract is protected mainly by→

1. **MUCOCILIARY CLEARANCE** → ensures optimum tracheobronchial clearance → by forming sputum (in optimum quantity & viscosity) exhaled by ciliary movements
2. **COUGH REFLEX** → exhales sputum out, if not optimally removed by the mucociliary clearance mechanisms

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

Cough is meant to be useful → *“wet or productive”*

May not be useful & annoying 2ndry to irritant vapors, gases, infections, cancer → *“dry or irritant”*



EXPECTORANTS

Act by removal of mucus through



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

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; 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

Act by altering biophysical quality of sputum → becomes easily exhaled by mucociliary clearance or by less intense coughing



MECHANISM OF ACTIONS

Mucolysis occurs by one or more of the following;

- ✚ ↓ Viscoelasticity by ↑ water content; **Hypertonic Saline & NaHCO₃**
- ✚ ↓ Adhesiveness; **Steam inhalation**
- ✚ Breakdown S-S bonds in glycoproteins by reducing its SH Gp → less viscid mucous; **N-Acetyl Cysteine**
- ✚ Synthesize serous mucus (sialomucins of smaller-size) so it is secretolytic + activate ciliary clearance & transport; **Bromohexine & Ambroxol**
- ✚ Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of infection; **rhDNAase (Pulmozyme)**

INDICATIONS

- ✚ Most mucolytics → effective as adjuvant therapy in COPD, asthma, bronchitis, ...etc. (when there is excessive &/or thick mucus....)
- ✚ In bronchiectasis, pneumonia & TB → they are of partial benefit
- ✚ *Hardly any benefit in cystic fibrosis & severe infections* → Give rhDNAase



1. N-Acetylcysteine

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

ADRs; Bronchospasm, stomatitis, rhinorrhea, rash, nausea & vomiting

2. Bromhexine & its metabolite Ambroxol

They also ↑ immuno defence so ↓ antibiotics usage

They also ↓ pain in acute sore throat

ADRs; Rhinorrhea, lacrymation, gastric irritation, hypersensitivity

3. Pulmozyme (Dornase Alpha or DNase)

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

→ Full benefit appears within 3-7 days

ADRs;

Voice changes, pharyngitis, laryngitis, rhinitis, chest pain, fever, rash

ANTITUSSIVE AGENTS



Stop or reduce cough by acting either primarily on the peripheral or CNS components of cough reflex

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 benzoin compound & eucalyptol

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.

ADRS: drowsiness, dizziness, dysphagia, allergic reactions

Overdose → mental confusion, hallucination, restlessness & tremors

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

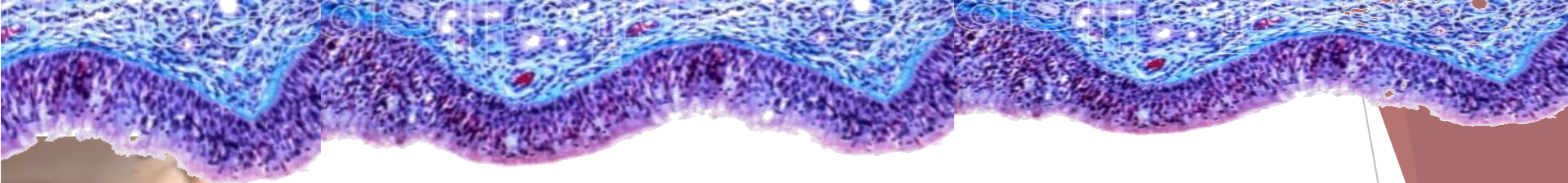
1. As potent as codeine
- 2- But no drowsiness
- 3- Less constipating
- 4- No respiratory depression.
- 5- No inhibition of mucociliary clearance
- 6- No addiction.

ADRs

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

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





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