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
- Postnasal 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 (H_1- receptor antagonists)
2. Anti-allergics
    a) Cromolyn sodium (mast cell stabilizer)
    b) Montelukast (Leukotriene receptor antagonists)
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 (H_1-receptor antagonists):

- The term antihistamine, without modifying objective, refers to the classic H_1 – 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		→ Fexofenadine
		Loratadine	→ Desoloratadine
	Ketotifen		
7) MISCELLANEOUS	Cyproheptadine		

Short duration — *Longer duration = better control*

Interactions; with enzyme inhibitors — No drug interactions & minimal ADRs

[macrolides, antifungals, calcium antagonists]

+ additive pharmacodynamic 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 H_1 receptors and they carry polar groups, they **do not penetrate the BBB** causing less CNS depression

Actions:

- The action of all the H_1 receptor blocker is qualitatively similar
- **They are much more effective in <u>preventing symptoms</u> 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

ALLERGIES

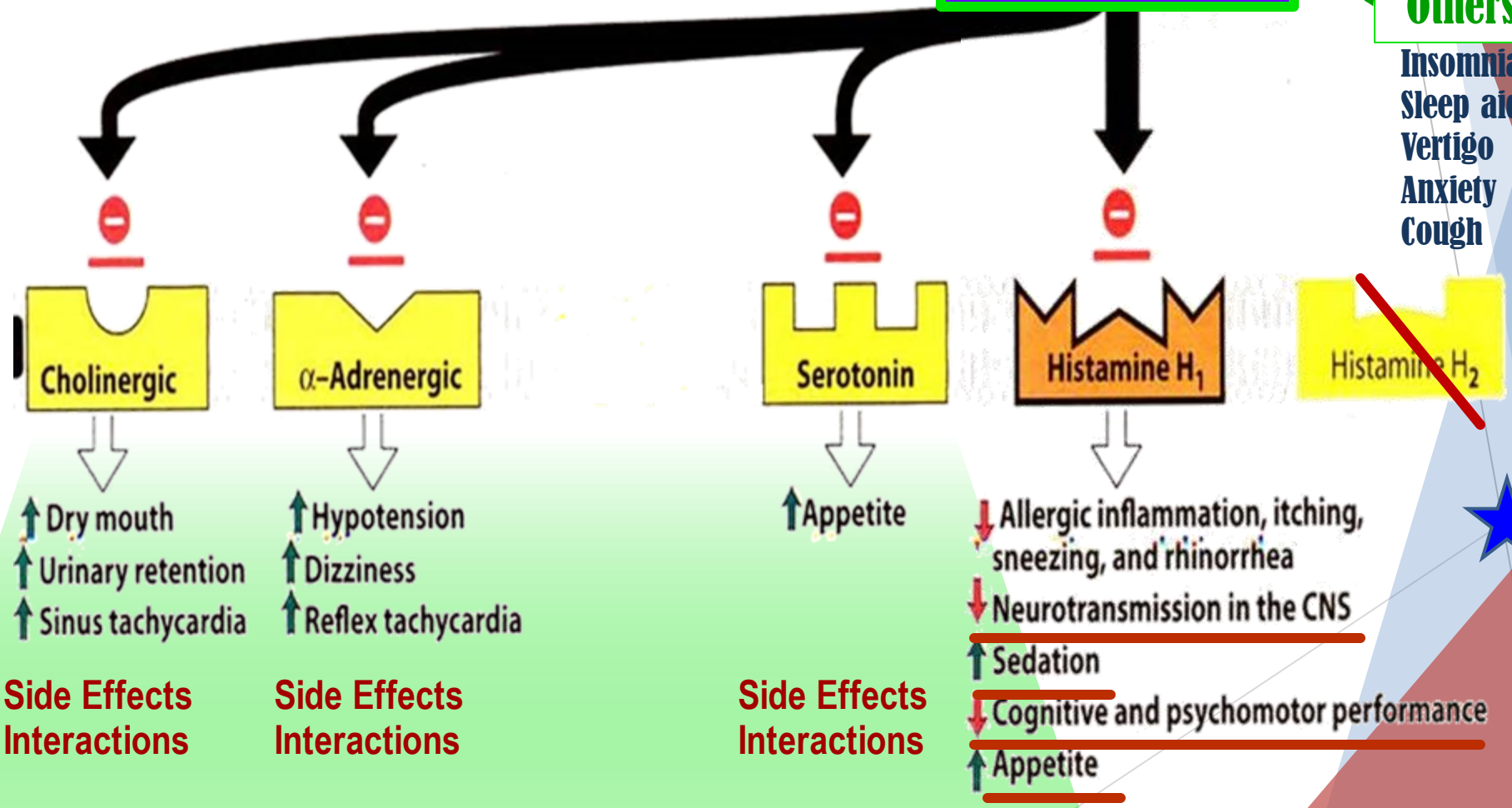
INDICATIONS linked to H1 block

ITCHING
Even if non-allergic

Others
Insomnia
Sleep aid
Vertigo
Anxiety
Cough

INDICATIONS not linked to H1 block

ANTIHISTAMINES



Side Effects
Interactions

Side Effects
Interactions

Side Effects
Interactions

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:

- H_1 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
- H_1- 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

2-ANTI-ALLERGICS

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.

Montelukast 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-CORTICOSTERIODS

Anti-inflammatory → blocks phospholipase A_2 → ↓arachedonic 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

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)]

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5. ANTICHOLINERGICS

Ipratropium

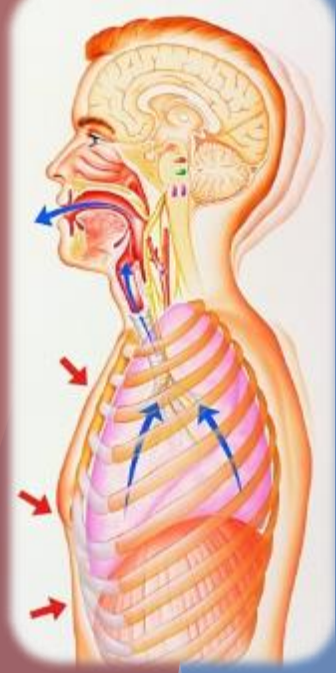
Given as nasal drops to **control rhinorrhea**
So very effective **in vasomotor rhinitis** (watery hyper-secretion).
Its indication as bronchodilator in asthma

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 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"*

TREATMENT → EXPECTORANTS, MUCOLYTICS ➔ For Productive Cough

ANTITUSSIVE AGENTS ➔ For Non-productive (dry) Cough

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, Ipecacuanha**

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

→ Final outcome is that cough is indirectly diminished

INDICATIONS

- Common cold
- Bronchitis
- Pharyngitis
- Chronic paranasal sinusitis

MUCOLYTICS

Mucolytic agents are used to dissolve or breakdown mucus in the respiratory tract ➜ becomes easily exhaled by mucociliary clearance (MCC) or by less intense coughing

MECHANISM OF ACTIONS

Mucolysis occurs by one or more of the following;

- ↓ Viscoelasticity by ↑water content; **Hypertonic Saline & $NaHCO_3$**
- ↓ Adhesivness; **Steam inhalation**
- Breakdown S-S bonds in glycoproteins ➜ less viscid mucous; **N-Acetyl Cysteine**
- Synthesize serous mucus + activate ciliary clearance & transport; **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 &/or thick mucus….)

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

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

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

They also ↑ immuno defence so ↓ antibiotics usage

They also ↓ pain in acute sore throat

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3. Pulmozyme (Dornase Alpha or DNAse)

➔ 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 on 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.

ANTITUSSIVE AGENTS

2. CENTRALLY ACTING ANTITUSSIVES

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

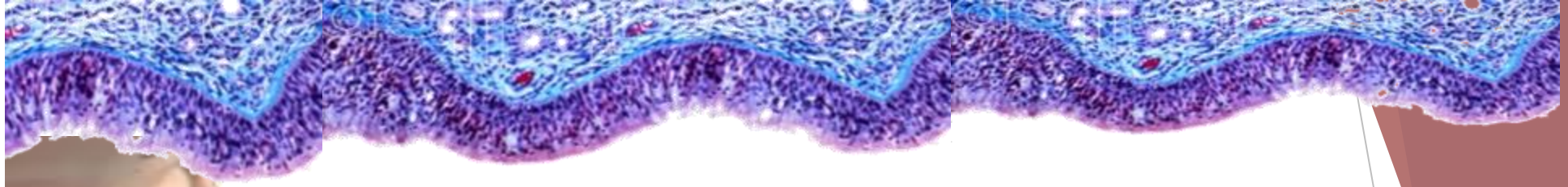
B. NON-OPIODS → Antihistaminics (>sedating)
↓
Dextromethorphan

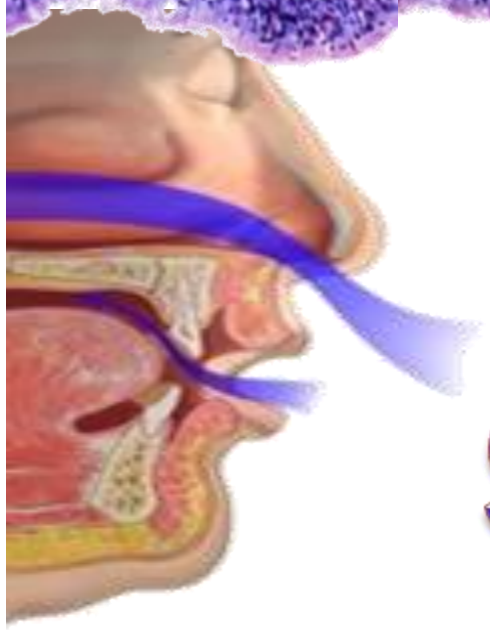
It ↑ threshold at cough center. It has benefits over opioids in being →

1. As potent as codeine but no drowsiness
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





GOOD LUCK