TREATMENT OF RHINITIS & COUGH

ILOs

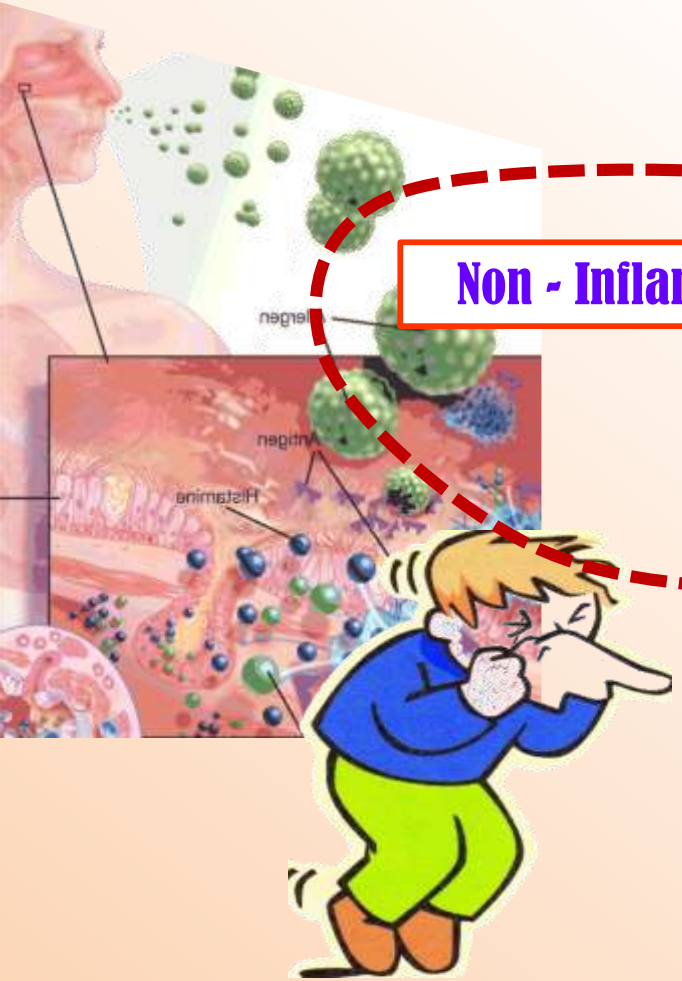
- Classify types of rhinitis
- Specify preventive versus pharmacotherapeutic strategies
- Expand on the pharmacology of different drug groups used in treatment as antihistamines, anti-allergics, corticosteriods, decongestants and anti-cholinergics
- Differentiate between productive versus dry irritant cough
- Compare pharmacology of different expectorants & mucolytics drugs used in treatment of productive cough
- Contrast between peripherally and centrally acting antitussives

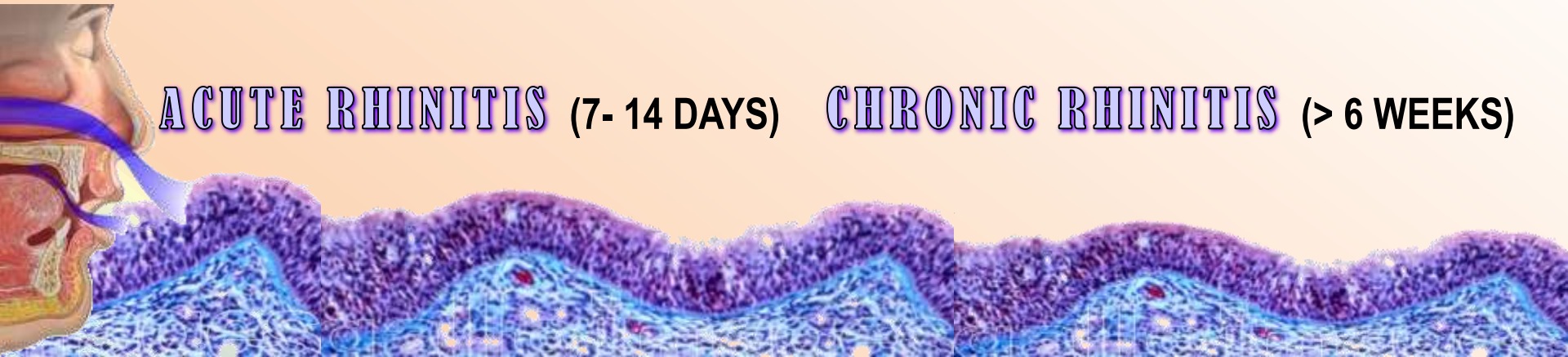
RHINITIS

Irritation &/or inflammation of the mucous membranes inside the nose

- **Non - Inflammatory**
  - **Infectious** → **NON-ALLERGIC**
- **Inflammatory**
  - **Allergic** → **ALLERGIC**
    - Seasonal
    - Perennial

HAY FEVER

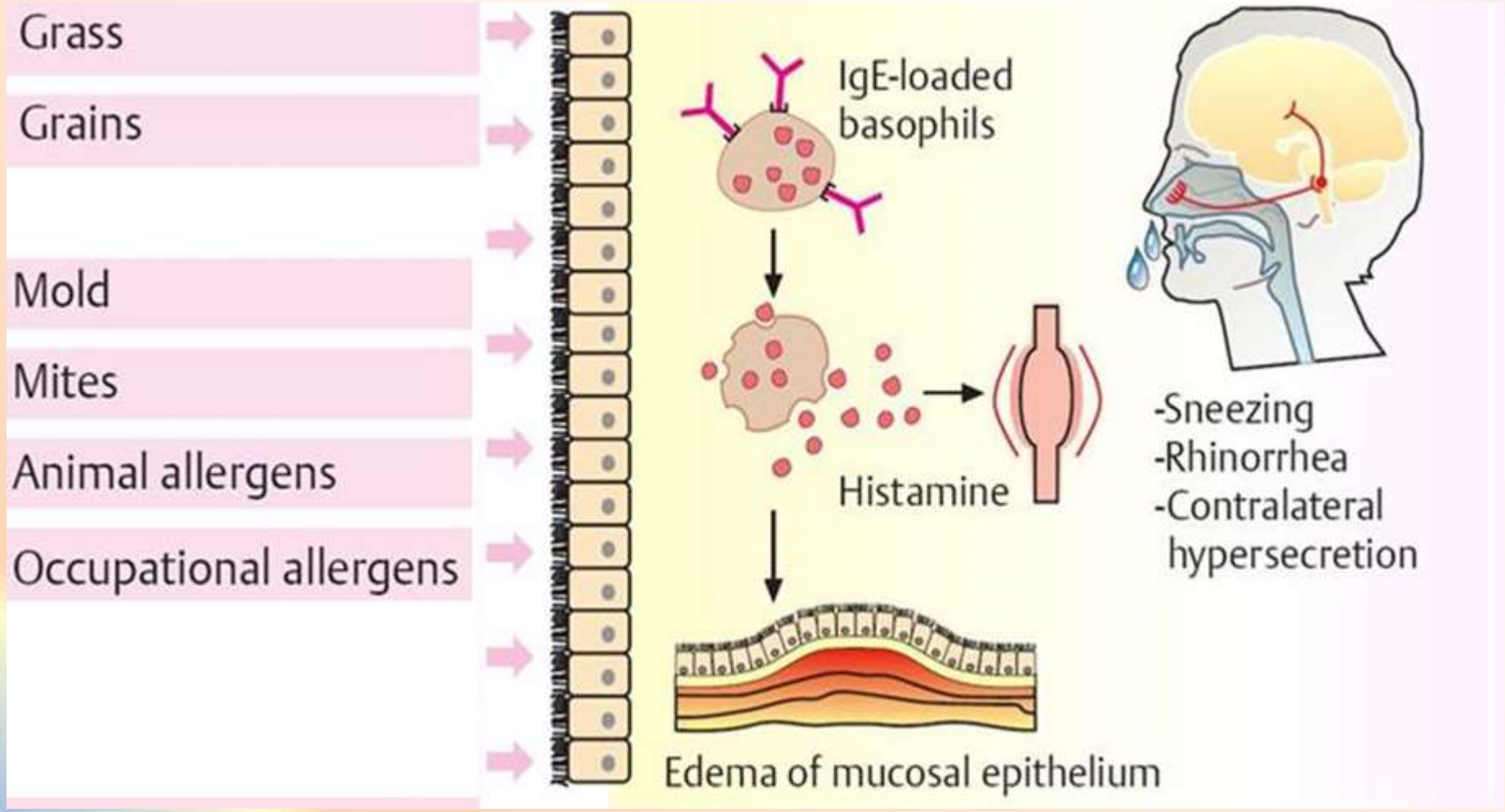




ACUTE RHINITIS (7- 14 DAYS) **CHRONIC RHINITIS** (> 6 WEEKS)

RHINITIS

Symptoms



TREATMENT

- **PREVENTIVE THERAPY**
  - 1- Environmental Control
  - 2- Allergen Immunotherapy
- **PHARMACOTHERAPY**

1- H_1 receptor antagonists; Antihistamines

2- Anti-allergics

Mast Cell Stabilizer; Cromolyn
Leukotriene receptor antagonists; Montelukast

3- Corticosteroids
4- Decongestants; α-Adrenergic agonists

5- Anticholinergics

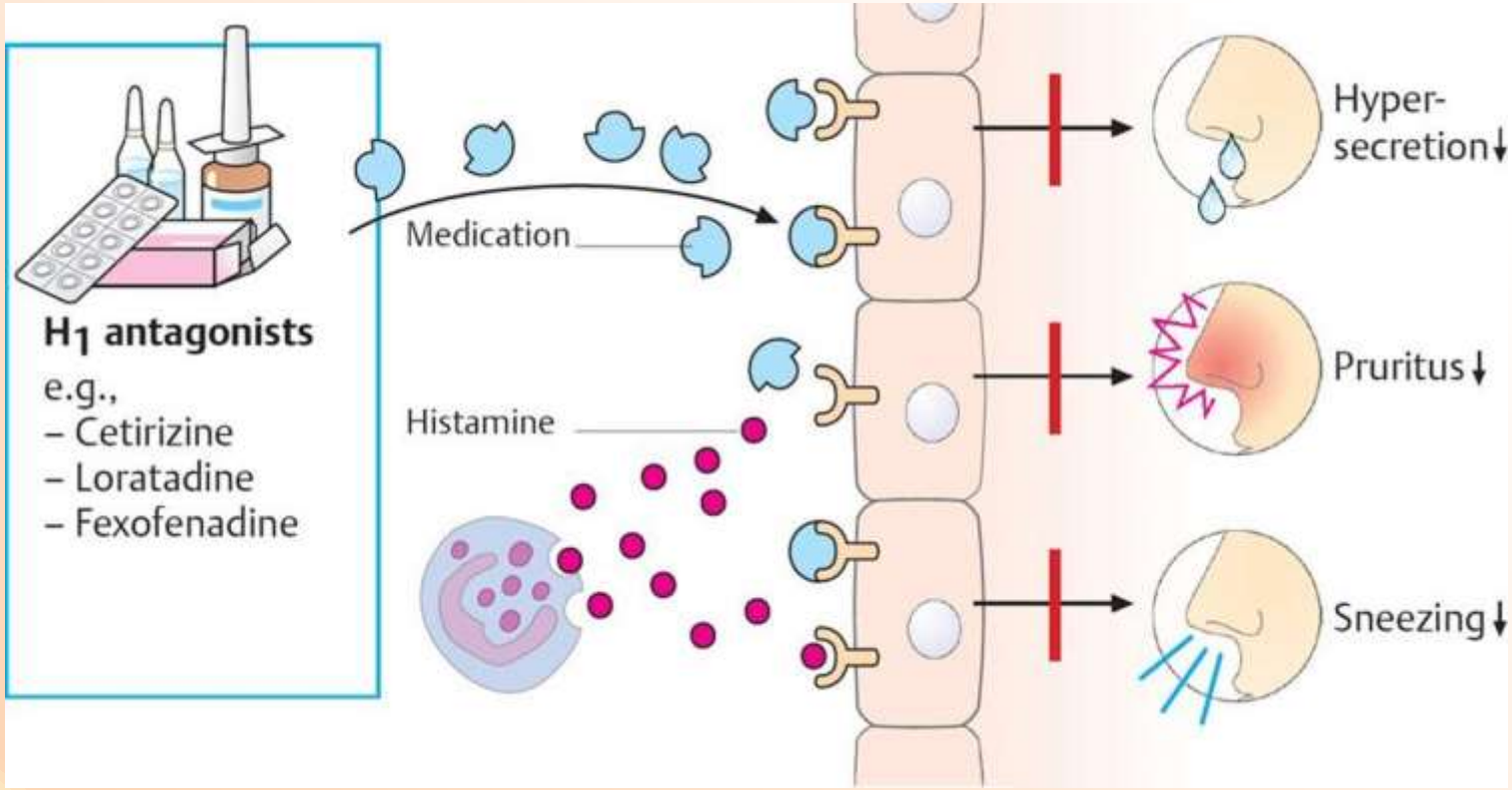
6- Antibiotics } In case of bacterial infection

ANTIHISTAMINES

First generation	Second generation	Third generation
Chlorphineramine Diphenhydramine Dimenhydranate Promethazine	Cetrizine Lortadine	Levocetrizine Desolortadine
Non-selective **Lipophylic** **Cross BBB** **SEDATING**	**Selective** **Non-lipophylic** **poor cross BBB** **NON - SEDATING** Metabolism inhibited by macrolides & antifungal drugs →serious arrhythmias	**More Selective** **Non-lipophylic** **not cross BBB** **NON - SEDATING**

ANTIHISTAMINES

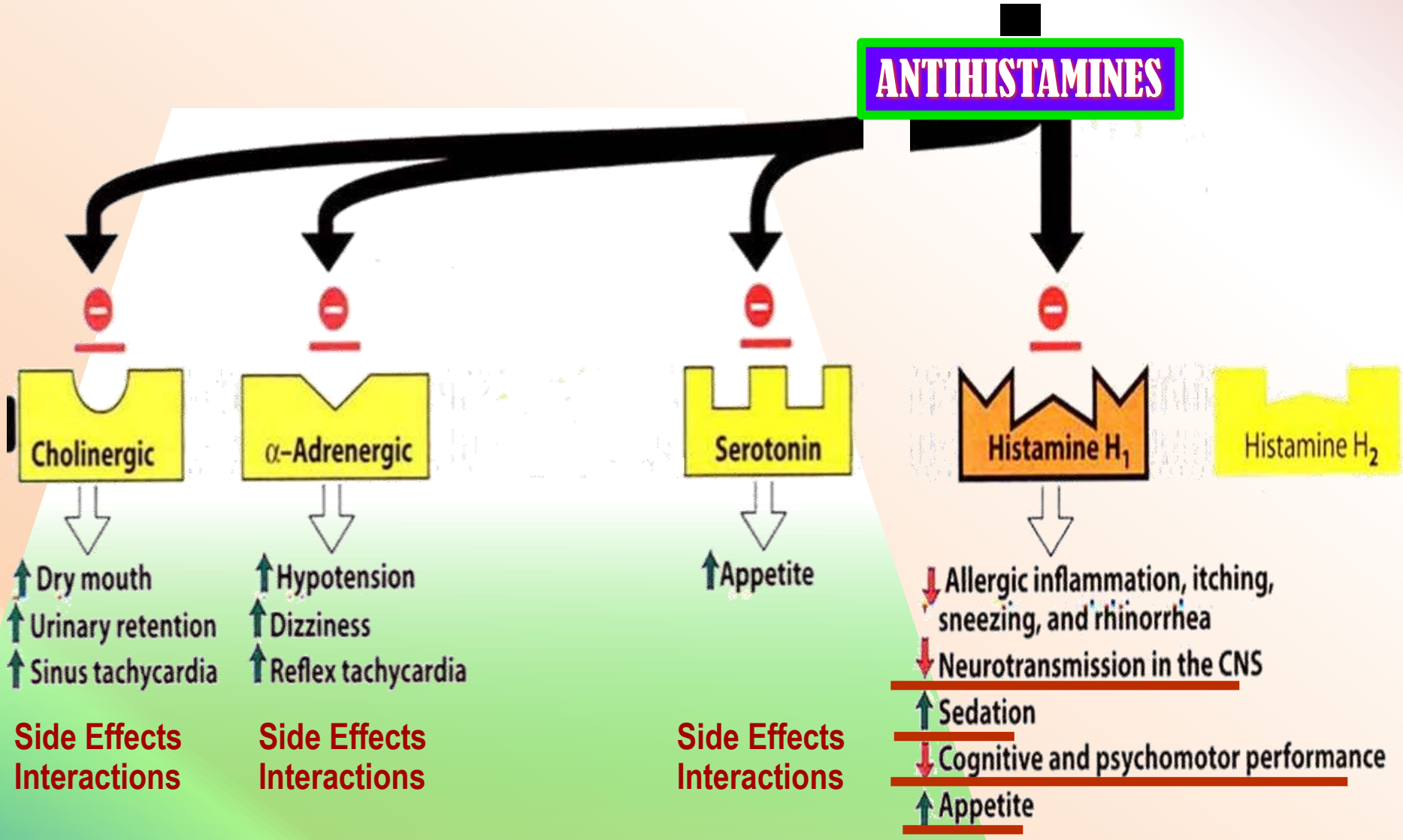
Effects in rhinitis



Not effective in relieving nasal congestion

Intranasal antihistamines ---more rapid onset

Pharmacodynamic Effects



ANTIHISTAMINES

INDICATIONS not linked to H1 block

1. Vertigo & Motion sickness — **Dimenhydrinate, Diphenhydramine, Promethazine**
   ↓ firing from internal ear to vomiting center

2. Anti-emetic — **Promethazine**
   ↓ firing to vomiting center + Anticholinergic

3. Anti-parkinsonism — **Chlorpheniramine, Dimenhydrinate , Promethazine**
   by anticholinergic action → ↓ Extra-pyramidal effects

4. Increase appetite !!! — **Cyproheptadine**
   by 5-HT modulation
   ↑ Sedation

5. Anti-arrhythmic actions !!! **Promethazine, Antazoline**
   by Na channel blocking action & local anesthetic effects

CROMOLYN & NEDOCROMYL

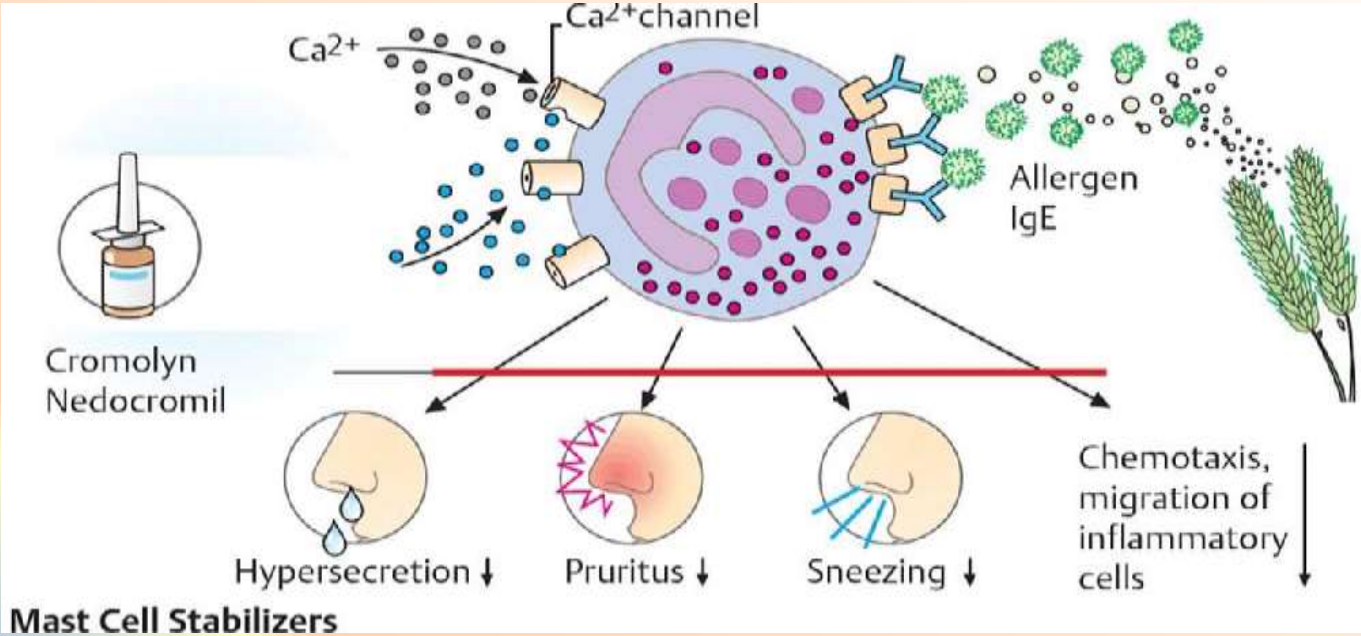
2-ANTI-ALLERGICS

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

Used more **in children** for prophylaxis of perennial allergic rhinitis [nasal drops]

Safe in pregnant women

Should be given on daily base and never stop abruptly.
Can induce cough, wheezes, headache, rash, …etc.



Mast Cell Stabilizers

Less effective in relieving congestion

LEUKOTRIENE RECEPTOR ANTAGONISTS

Montelukast

Efficacy compared to antihistamines

First line treatment for patients with rhinitis & bronchial asthma

3-CORTICOSTERIODS

Anti-inflammatory → blocks phospholipase A_2 →
↓arachedonic a. synthesis → ↓ prostaglandins & leukotrienes

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

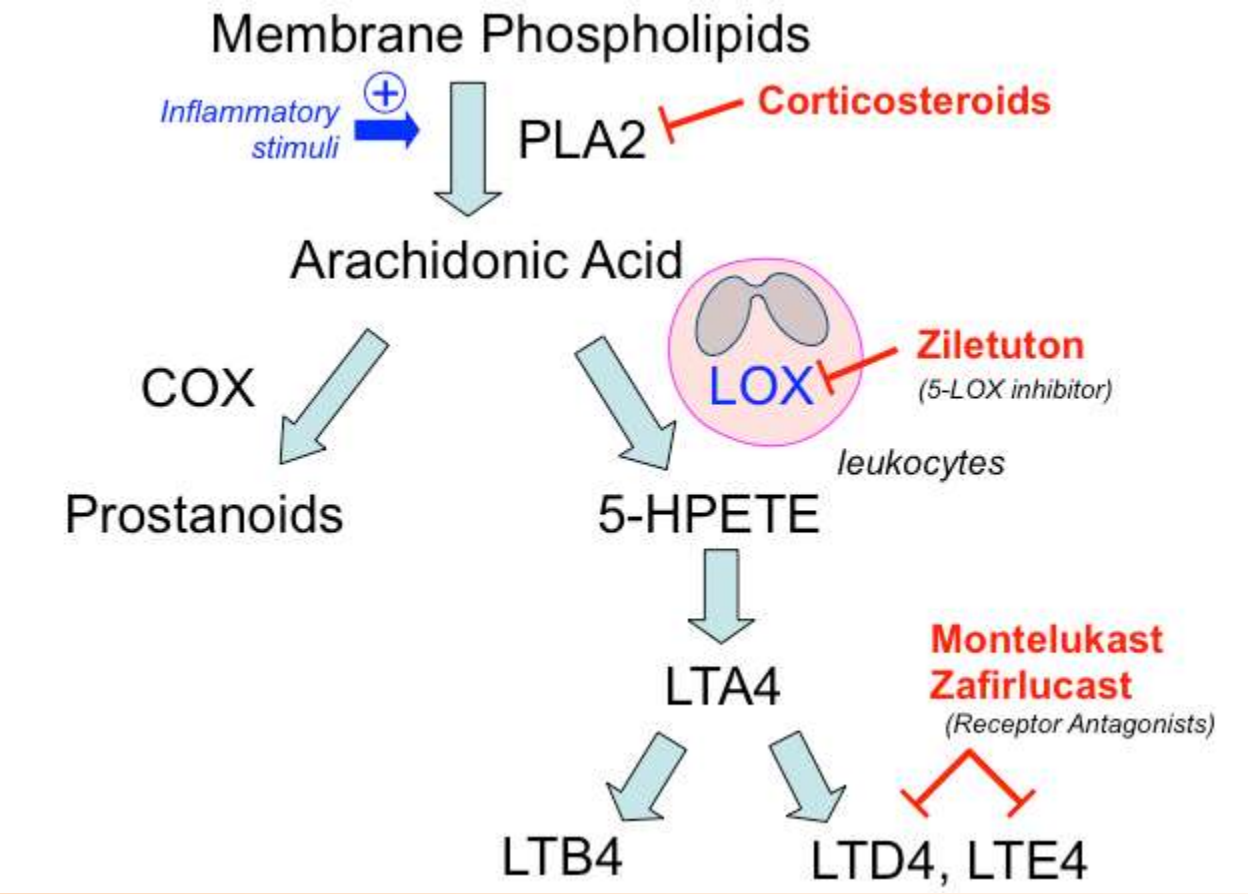
Most effective > antihistamines & leukotriene antagonists

Indicated for perennial rhinitis & non allergic rhinitis

ADRs; Nasal irritation, fungal infection, hoarseness of voice

Systemic corticosteroids, role limited??

Short course To↓ nasal edema to facilitate penetration of intranasal preparation


Membrane Phospholipids
Inflammatory stimuli
PLA2
Corticosteroids
Arachidonic Acid
COX
LOX
Ziletuton
(5-LOX inhibitor)
leukocytes
Prostanoids
5-HPETE
LTA4
Montelukast
Zafirlucast
(Receptor Antagonists)
LTB4
LTD4, LTE4

4. DECONGESTANTS

α-Adrenergic agonists → For treatment of nasal stuffiness

SYSTEMIC

- PSEUDOEPHEDRINE

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

TOPICAL

PHENYLETHYLAMINES

- Phenylephrine
- Methoxamine

IMIDAZOLINE

- Naphazoline
- Oxymetazoline HCl
- Xylometazoline HCl

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

Used primarily to ↓nasal congestion in acute severe rhinitis

5. ANTICHOLINERGICS

Ipratropium

Useful in patients whom rhinorrhea is predominant

Given as nasal drops to control watery nasal discharge in perennial rhinitis

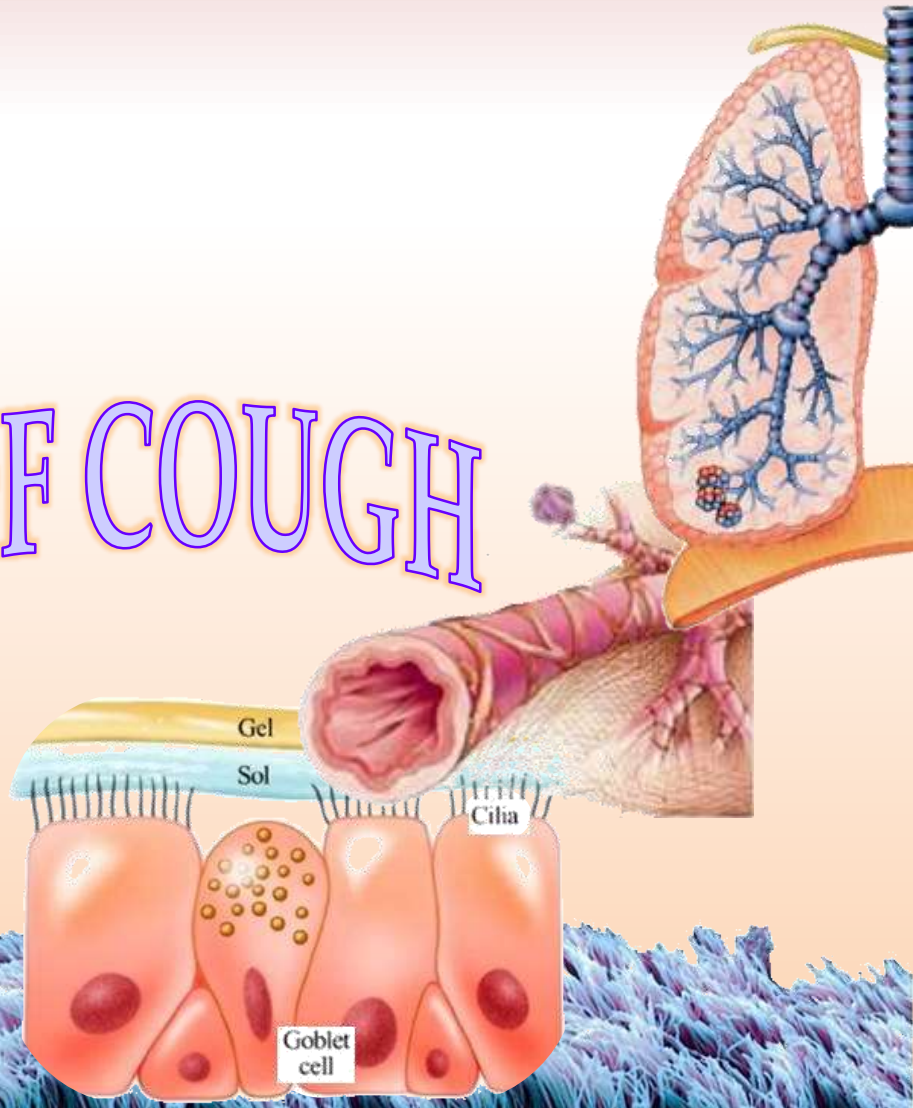
No effect on sneezing , itching & nasal congestion

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

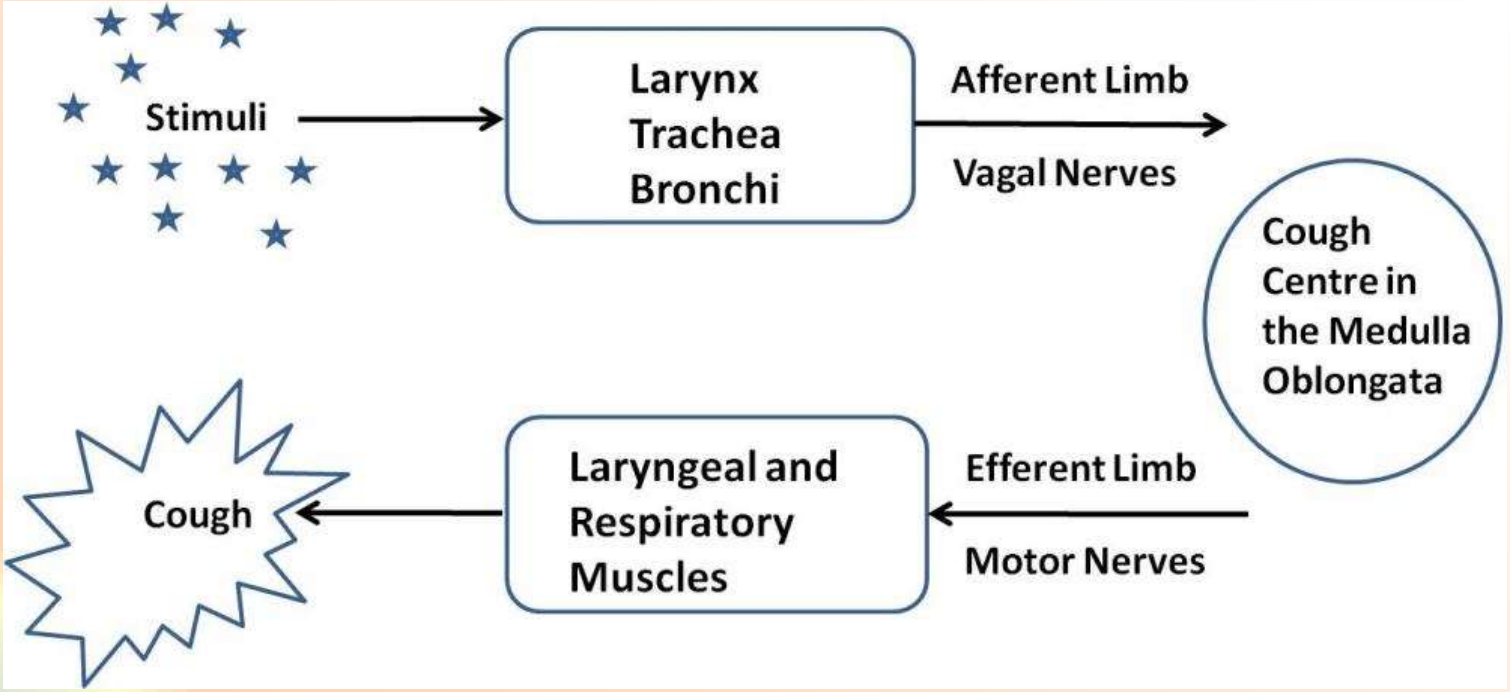
IN TREATMENT OF COUGH



Definition

Cough is an expulsive reflex that protect the lungs and respiratory system from foreign bodies

Cough reflex



Common causes of Cough:

- **1) Acute Respiratory Infection.**
  - Upper respiratory infection.
  - Pneumonia.
  - Bronchitis
- **2) Chronic Respiratory Infection.**
  - TB.
  - Postnasal drip.
- **3) Airway Diseases.**
  - Asthma.
  - COPD.
- **4) Irritants.**
  - Cigarettes smoking.
  - Inhaled foreign bodies.
- **5) Drug Induced.**
  - Inhaled drugs (aerosols).
  - ACE-inhibitors (anti-hypertensive).

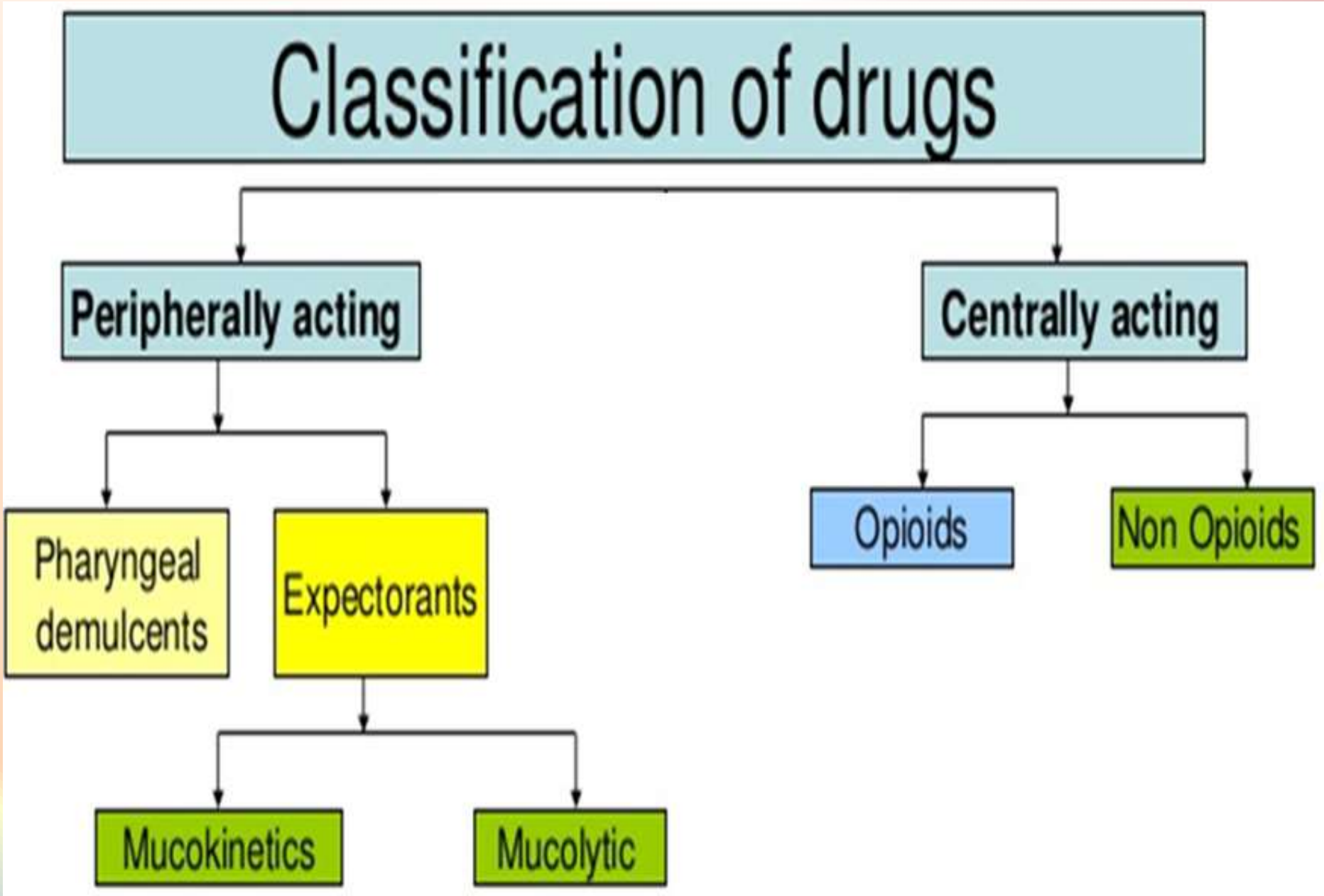
Types of cough

Productive Cough

- It clears the excess secretions & inhaled foreign matters.
- Expectorants are used.

Non-Productive Cough

- Dry cough has no useful function.
- Anti-tussives are used.



For Productive Cough

For Non-productive (dry) Cough

Demulcents

An agent that forms a soothing film over a mucous membrane, relieving minor pain and inflammation of the membrane

Glycerin, honey, liquarice

EXPECTORANTS

mucokinetics

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)

EXPECTORANTS

mucokinetics

Act by removal of mucus through

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 of salivary glands(overstimulation of salivary secretion), & flare of old TB.

INDICATIONS

Final outcome is that cough is indirectly diminished

- Common cold
- Bronchitis
- Laryngitis
- Pharyngitis
- Influenza
- Measles
- Chronic paranasal sinusitis
- Pertussis

MUCOLYTICS

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

MECHANISM OF ACTIONS

- ↓ Viscoelasticity by ↑water content; **Hypertonic Saline & $NaHCO_3$**
- ↓ Adhesivness; **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

2. CENTRALLY ACTING ANTITUSSIVES

A. OPIOIDS

activating μ opioid receptors **e.g. Codeine & Pholcodine**

B. NON-OPIODS

Dextromethorphan

Antihistamines

Opioids

Acts on morphine receptor in the medullary cough center↑ threshold for cough

Also induces peripheral action on cough receptors by ↓ cough impulses

Codeine:- little evidence for efficacy especially in post viral cough

ADRs:- sedation, constipation, low abuse liability

Morphine:- effective, indicated for intractable cough associated with bronchial carcinoma

Dextromethorphan

Centrally acting NMDA receptor antagonist, it may antagonize opioid receptors

Poorly effective despite common use

Uses:- dry non productive cough & tiring cough disrupting sleep

No addiction or constipating effect

Does not impair muocilliary function

ADRs

In high doses, hallucinations