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## Respiratory Block

# 2 Treatment of acute and chronic rhinitis and cough

## Objectives :

1. Define rhinitis and cough.
  2. Classify drugs used in the treatment of rhinitis.
  3. Expand on the pharmacology of different drug groups used in the treatment as; antihistamines, leukotriene antagonists, corticosteroids, decongestants and anticholinergics.
  4. Describe the pharmacology of different expectorants and mucolytics used in the treatment of productive cough.
  5. Describe the pharmacology of antitussives (cough suppressants).
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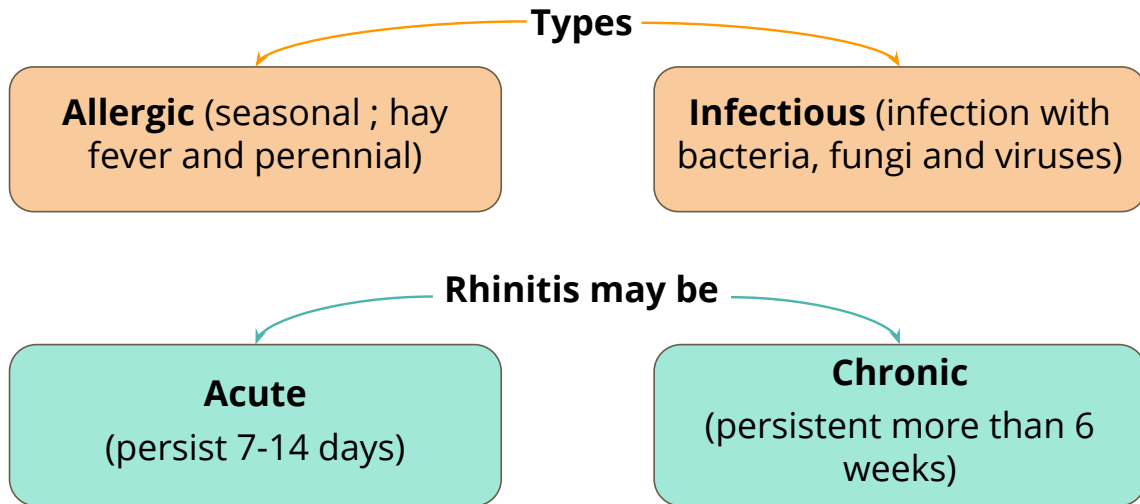
Red: important

Grey: Notes or extra information



# Rhinitis

**Rhinitis** is the irritation and/or inflammation of the mucous membranes inside the nose.



## 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:	B. Pharmacotherapy:
1. Environmental control (dust control, pets .....) 2. Allergen immunotherapy (e.g vaccines)	1. Anti-histamines (H1 - receptor antagonists) 2. Anti-allergics <ul style="list-style-type: none"> <li>a. Cromolyn sodium (mast cell stabilizer)</li> <li>b. Montelukast (Leukotriene receptor antagonists)</li> </ul> 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:

1. Allergic and inflammatory reactions
2. Gastric acid secretion
3. 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

# Antihistamines (H1 receptor antagonists)

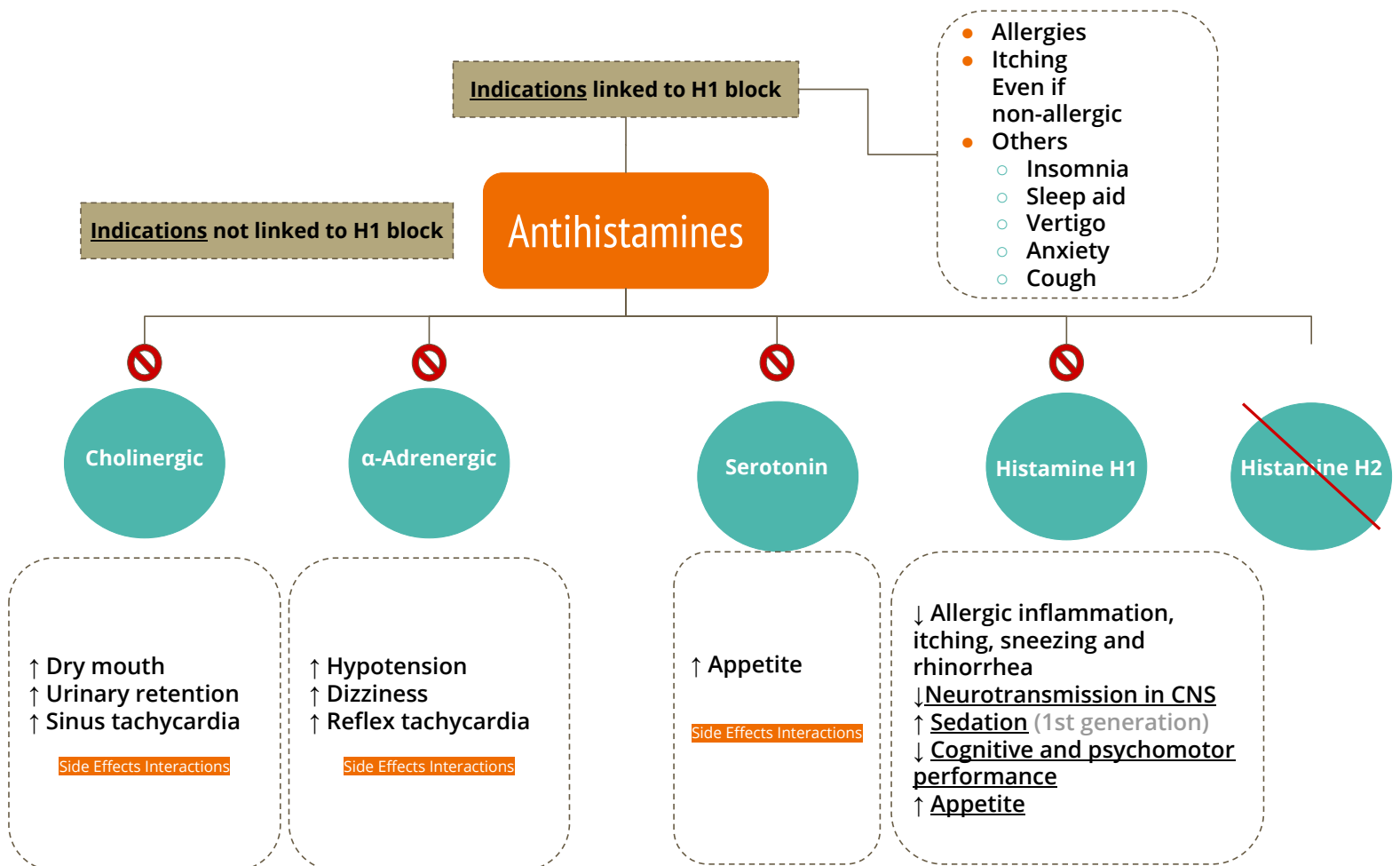
First generation	Second generation	Third generation	
Chlorpheniramine	Cetirizine	Levocetirizine	
Diphenhydramine			
Antazoline		Loratidine	Fexofenadine
Promethazine			
Cyclizine	Desloratidine		
Azatidine			
Ketotifen			
Cyproheptadine			
<ul style="list-style-type: none"> <li>- <b>Short</b> duration</li> <li>- Interactions with enzyme inhibitors ( as macrolides, antifungal, calcium antagonists)</li> <li>- Additive pharmacodynamic ADRs</li> </ul>	<ul style="list-style-type: none"> <li>- <b>Long</b> duration (better control)</li> <li>- No drug interactions and minimal ADRs since they are more specific for H1 receptors</li> </ul>		
<p>All are used systemically or topically</p>			

The old first generation	Second generation
<ul style="list-style-type: none"> <li>- still widely used because they are <u>effective and inexpensive</u>.</li> <li>- These drugs can penetrate the blood brain barrier (BBB) → cause sedation.</li> <li>- They tend to interact with other receptors → produce a variety of unwanted adverse effects</li> </ul>	<ul style="list-style-type: none"> <li>- Have no sedative effect</li> <li>- Specific for H1 receptors</li> <li>- They carry polar groups</li> <li>- They do not cross BBB → cause <u>less</u> CNS depression</li> </ul>

# Actions of H1 receptor blockers:

- The action of ALL H1 receptor blockers 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 to H1 receptors, which probably reflect binding of H1 antagonists to:
  1. Cholinergic receptors
  2. Adrenergic receptors
  3. Serotonin receptors

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



# 1- Antihistamine Drugs

<p><b>Actions</b></p>	<ul style="list-style-type: none"> <li>• The action of all the H1 receptor blocker is qualitatively similar</li> <li>• They are much more effective in <b>preventing symptoms</b> than reversing them once they have occurred</li> <li>• Most of these drugs have additional effects unrelated to their blocking H1 receptors, which probably reflect binding of H1 antagonists to:             <ul style="list-style-type: none"> <li>○ <b>Cholinergic</b></li> <li>○ <b>Adrenergic</b></li> <li>○ <b>Serotonin receptors</b></li> </ul> </li> </ul>
<p><b>Therapeutic uses</b></p>	<ol style="list-style-type: none"> <li>1. <b>Allergic rhinitis</b>, relieves rhinorrhea, sneezing, and itching of eyes and nasal mucosa</li> <li>2. <b>Common cold</b>: dries out the nasal mucosa. Often combined with nasal decongestant and analgesics</li> <li>3. <b>Motion sickness</b></li> <li>4. <b>Allergic dermatoses</b>: can control itching associated with insect bites.</li> <li>5. <b>Nausea and vomiting</b> (Promethazine)</li> </ol>
<p><b>Pharmacokinetics</b> "Read it"</p>	<ul style="list-style-type: none"> <li>• H1 receptor blockers are well absorbed after oral administration</li> <li>• Maximum serum levels occurring at 1-2 hours</li> <li>• Average plasma half life is 4 to 6 hours "first generation"</li> <li>• have high bioavailability and distributed to all tissues including CNS "first generation"</li> <li>• Metabolized by the hepatic cytochrome P450 system</li> <li>• Excretion occur via kidney except <b>fexofenadine</b> excreted in feces unchanged</li> </ul>
<p><b>Adverse effects</b></p>	<ul style="list-style-type: none"> <li>• <b>Sedation</b></li> <li>• tinnitus</li> <li>• fatigue</li> <li>• dizziness</li> <li>• blurred vision</li> <li>• dry mouth</li> </ul>
<p><b>Drug interaction</b></p>	<ul style="list-style-type: none"> <li>• CNS depressants</li> <li>• cholinesterase inhibitors</li> </ul>
<p><b>Overdose</b></p>	<p>The most common and dangerous effects of acute poisoning are those on CNS; including hallucinations, excitement, ataxia and convulsions</p>

## 2- Anti-allergics

	Mast cell stabilizers	Leukotriene receptor antagonists
Example	<b>Cromolyn</b> and <b>Nedocormyl</b>	Zafirlukast, Montelukast, Pranlukast
Mechanism of action	<b>Only prophylactic :</b> It does not antagonize histamine that is already released but it decreases histamine release from the beginning ( by inhibition Cl channels)	Block leukotriene action
Uses	<b>Used in children for prophylaxis of perennial allergic rhinitis</b> ** should be given on daily basis and <u>never stop abruptly</u>	<b>Prophylaxis of lower respiratory tract allergies</b> <b>- Act on lower respiratory tract allergies more than on upper respiratory tract allergies</b> Eg: act on perennial allergen, exercise or aspirin induced asthma (LRT allergies) more than on chronic rhinosinusitis ( URT allergy )
ADRs	Induce cough , wheezes , headache , rash	As in asthma : elevation of liver enzymes, headache, dyspepsia

## 3- Corticosteroids

Example	<b>Beclomethasone, budesonide</b> and <b>fluticasone</b>
Mechanism of action	Anti-inflammatory , block phospholipase A2 , decrease arachidonic acid synthesis - decrease prostaglandins and leukotrienes
Uses	Administered topically ( inhaled) as steroid <b>spray</b> <b>Given is severe intermittent or moderate persistent symptoms</b>
ADRs	Nasal irritation, fungal infection, hoarseness of voice

## 4- Decongestants (Adrenergic agonists)

Systemic	Topical
<p><b>Ex:</b> Pseudoephedrine</p>	<p><b>Ex:</b>  <b>1-Phenylethylamines</b>                      -Phenylephrine                      -Methoxamine  <b>2-Imidazoline</b>                      -Naphazoline                      -Oxymetazoline HCL                      -Xylometazoline HCL</p>
<p><b>Uses:</b> Treatment of stiffness</p>	<p><b>Uses:</b> Treatment of stiffness</p>
<p><b>ADRs:</b> nervousness, insomnia, tremors, palpitations, and hypertension.</p>	<p><b>ADRs:</b> Can cause <b>Rebound nasal stuffiness</b> (repeated administration (10 days -2 weeks))</p>
<p><b>Contraindication:</b> Better avoided in hypertension, heart failure, angina pectoris, hyperthyroidism and glaucoma.</p>	

## 5- Anticholinergics

<p><b>Ex:</b> Ipratropium</p>
<p><b>Uses:</b>                      -Nasal drops to <b>control rhinorrhea</b> so very effective in <b>vasomotor rhinitis</b> (watery hyper-secretion).                      -bronchodilator in asthma.</p>
<p><b>ADRs:</b> minimal systemic side effects (wheezing, bladder pain, cough producing mucus).</p>



# 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

1-wet or productive

2-dry or irritant "secondary to irritant vapors, gases, infections, and cancer "

-Treatment

1-Mucolytics and Expectorants for productive cough

2-Antitussive Agents for irritant cough

## Expectorants "Act by removal of mucus"

Stimulation type	Reflex Stimulation	Direct Stimulation
<b>Mechanism of Action</b>	Irritate GIT ↓ gastropulmonary vagal reflex ↓ loosening and thinning of secretions	Stimulate secretory ↓ increase glands respiratory fluids production
<b>Example</b>	Guaifenesin	Iodinated glycerol, Na or K iodide/ acetate, Ammonium chloride, Ipecacuahna.
<b>ADRs</b>	Dry mouth, chapped lips, risk of kidney stones(uric a. excretion).	Unpleasant metallic taste, hypersensitivity, hypothyroidism, swollen of salivary glands (overstimulation of salivary secretion), & flare of old TB.
<b>Indications (Uses)</b> "Final outcome is that cough is indirectly diminished"	<ol style="list-style-type: none"> <li>1. Common cold</li> <li>2. Bronchitis</li> <li>3. Pharyngitis</li> <li>4. Chronic paranasal sinusitis</li> </ol>	

# Mucolytics

Doctor Yieldez said : it's important to know the mechanism of action of each drug

**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.

Drug	Hypertonic Saline & NaHCO <sub>3</sub> NaHCO <sub>3</sub> = sodium bicarbonate	Steam inhalation	N-Acetyl Cysteine	Bromhexine (and its metabolite (ambroxol	Pulmozyme (Dornase Alpha or rhDNAase "recombinant human "deoxyribonuclease
<p><b>Mechanism of Action</b></p> <p>Mucolysis occurs by one or more of the following:</p>	<p>↑water content or secretion</p>	<p>↓Adhesivness</p> <p>يقلل من ترابط جزيئات البلغم من خلال استنشاق البخار ويعتبر حل مؤقت.</p>	<p>(antiagonist to paracetamol)</p> <p>Breakdown S-S bonds in glycoprotein less viscid mucous</p> <p>Glycoproteins are found in mucus</p>	<p>Synthesize serous mucus + activate ciliary clearance</p> <p>عشان تطرد البلغم</p>	<p>Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of infection</p> <p>In <u>bacterial infection</u> the sputum will be colored and thick so we give the patient this drug "enzyme "to breakdown the DNA of bacteria</p>
<p><b>Overview</b></p>	<p>—————</p>			<p>↑immuno defence so ↓antibiotics usage + ↓pain in acute sore throat</p>	<p>A recombinant human -deoxyribo nuclease-1 enzyme that is *neubilized + Full benefit appears within 3-7 days</p>
<p><b>Indications (Uses)</b></p>	<p><b>Most mucolytics</b> → effective as adjuvant therapy in COPD*, asthma, bronchitis. (when there is excessive, thick mucus)</p> <p>We use it when the sputum thick so we need to dissolve it and become easy to expel .</p> <p>*Chronic obstructive pulmonary disease</p> <p>*Expel = forced something to leave a place</p>				

\*Nebulizer: a device for producing a fine spray of liquid, used for example for inhaling a medicinal drug.

# Antitussive drug

Stop or reduce cough by acting either :

## 1- PERIPHERALLY

### 1- Inhibitors of airway stretch receptors

Location	Use	Drugs
In Pharynx	Demulcents “ form a protective coating”	1- Lozenges 2- Gargles
In Larynx	Emollients “ form a protective coating”	1- Menthol 2- Eucalyptus
In Tracheobronchial Airway	aerosols or inhalation of hot steam	1- Tincture benzoin compound 2-Eucalyptos
During bronchoscopy or bronchography	local anaesthetic aerosols	1-Lidocaine 2-Benzocaine 3-Tetracaine

### 2- Inhibitors of pulmonary stretch receptors in alveoli

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

## 2- CENTRALLY

	Mechanism	Drugs
1- OPIOIDS	activating $\mu$ opioid receptors	1- Codeine 2-Pholcodine
2- NON-OPIOIDS	_____	1- Antihistaminics (>sedating) 2- <b>Dextromethorphan</b>

### ADRs :

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

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

It increases threshold at cough center.

It has benefits over opioids in being :

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

# MCQs

1- Which of the following drugs block leukotriene action?

- A. Pulmozyme
- B. Loratidine
- C. Montelukast
- D. Dextromethorphan

2- Sedation is an adverse effect of :

- A. Antihistamine Drugs
- B. Anti-allergics
- C. Corticosteroids
- D. Anticholinergics Drugs

3- Which one of the following drugs is a second generation?

- A. Cyclizine
- B. Cetirizine
- C. Fexofenadine
- D. Cyproheptadine

4- Which one we use in children for prophylaxis?

- A. Pranlukast
- B. Zafirlukast
- C. Cromolyn and Nedocormyl
- D. Gargles

# SAQ

5-How can we treat productive cough?

6-List three therapeutic uses for antihistamine drugs.

7-Describe the mechanism of action for Bromhexine.

8- What is the MOA of Dextromethorphan?

Answers:

1-A

2-A

3-B

4-C

5- by Mucolytics and Expectorants.

6-allergic rhinitis, common cold, motion sickness, allergic dermatoses, nausea and vomiting.

7- Synthesize serous mucus + activate ciliary clearance.

8- It increases threshold at cough center

# Good Luck & Thank you !

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