

# Treatment of Acute & Chronic Rhinitis and Cough



## Objectives:

- ❖ 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)



**Important**



In male and female slides



Only in male slides



Only in female slides



Extra information

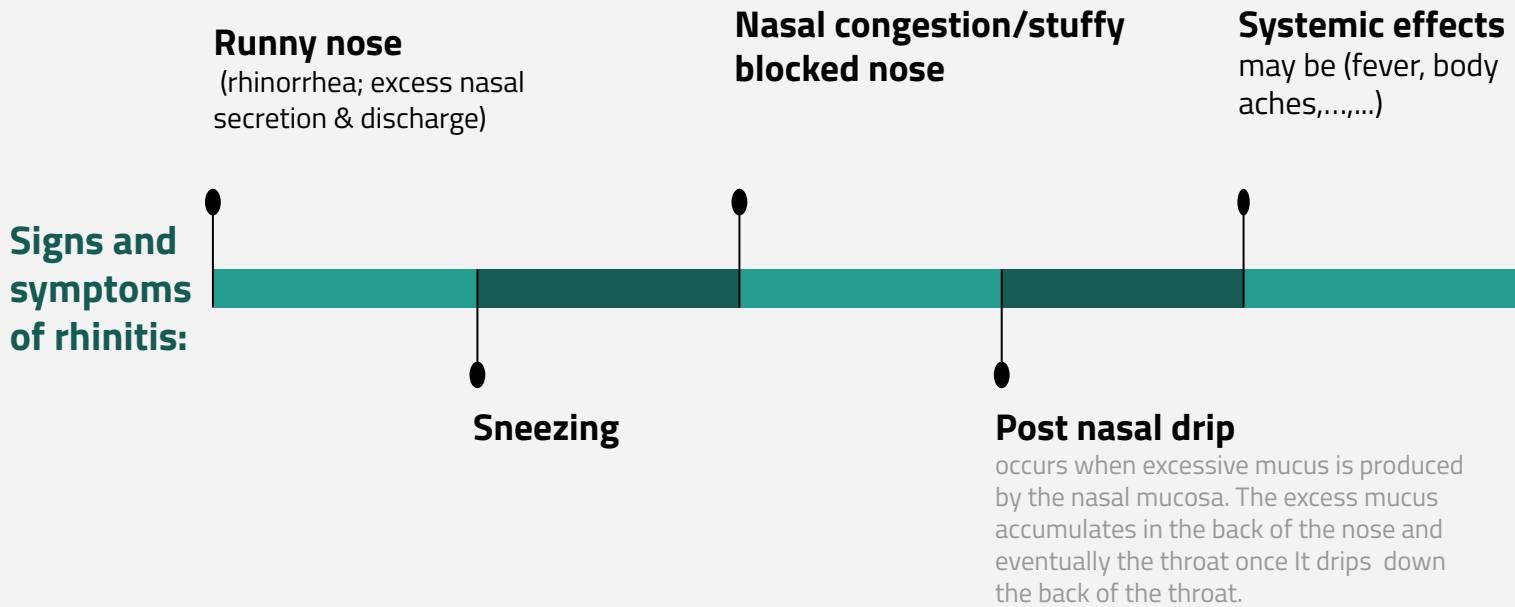
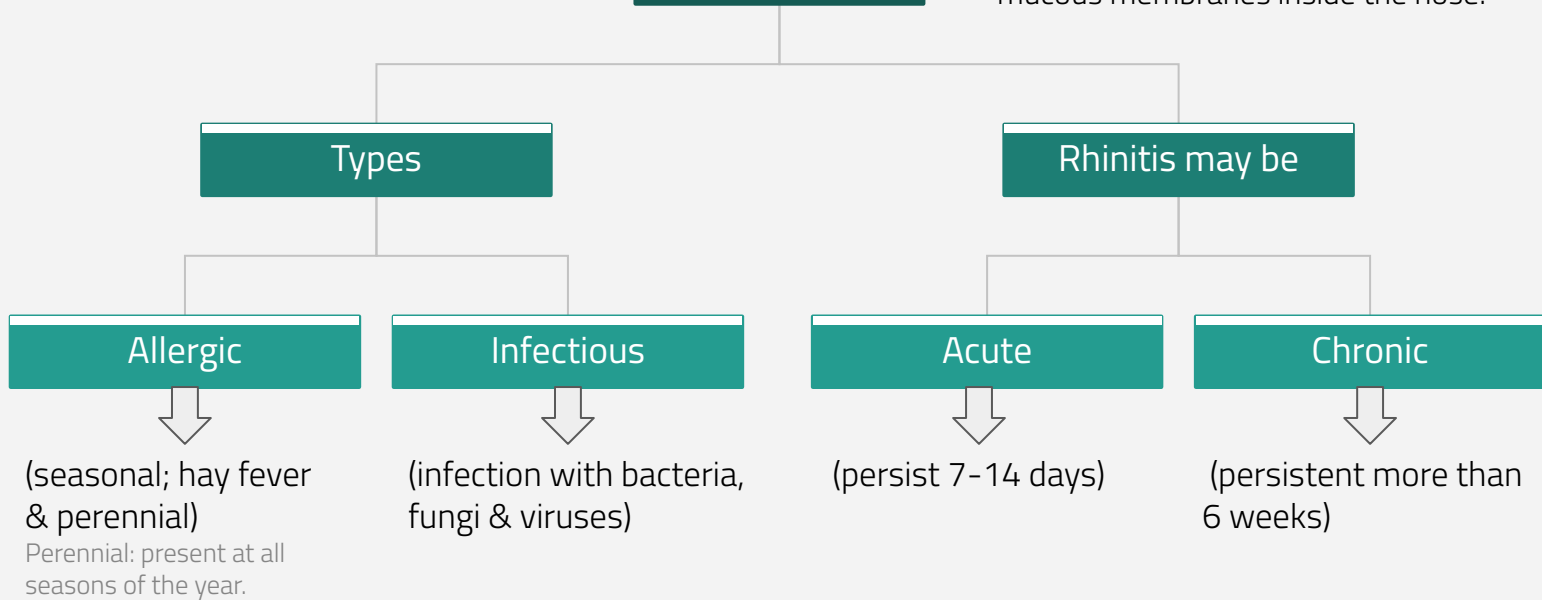


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Editing file

# Rhinitis

is the irritation &/or inflammation of the mucous membranes inside the nose.



## Treatment of Rhinitis:

### A. Preventive Therapy:

#### 1. Environmental control

(dust control, pets .....)

#### 2. Allergen immunotherapy

(desensitization immunotherapy):

What is the aim? to induce tolerance to the allergen by reducing its tendency to induce IgE production.

How? People are desensitized through the administration of escalating doses of allergen that gradually decreases the IgE-dominated response.

Why? to direct the immune response away from humoral immunity and toward cellular immunity, thereby encouraging the body to produce fewer IgE antibodies and more CD4+ T regulatory cells that secrete IL-10 and TGF- $\beta$ , which skews the response away from IgE production.

### 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).



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# 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 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.

team 434 overview

|                           | 1st generation   | 2nd Generation          | 3rd generation |
|---------------------------|--|-------------------------|----------------|
| <b>Duration of action</b> | Short  | Longer “Better control” |                |
| <b>Selectivity</b>        | Non-selective  | Selective               | More selective |
| <b>Crossing BBB</b>       | Cross  | No crossing             |                |
| <b>Drug interactions</b>  | with enzyme inhibitors [ macrolides, antifungals, calcium antagonists] | No drug interactions    |                |
| <b>Sedating effects</b>   | Sedating   | Non- sedating           |                |
| <b>Side effects</b>       | additive pharmacodynamics effects                                      | Minimal side effects    |                |



# Antihistamine (H1-receptor antagonist)

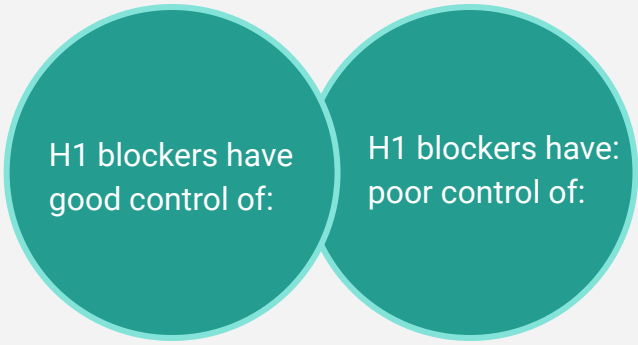
| First generation  | Second generation  | Third generation |                |
|---|--|------------------|----------------|
| Chlorpheniramine ★  | Cetirizine   | Levocetirizine   |                |
| Dimenhydrinate \ Diphenhydramine  |  | Loratadine ★     | Fexofenadine ★ |
| Antazoline  |  |                  | Desoloratadine |
| Promethazine  |  |                  |                |
| Cyclizine   |  |                  |                |
| Azatidine   |  |                  |                |
| Ketotifen   |  |                  |                |
| Cyproheptadine  |  |                  |                |
| <p><b>short duration</b></p> <p>1-Interactions with enzyme inhibitors (macrolides, antifungal, calcium antagonists).<br/>With enzyme inhibitors antihistamine effect will increase. (because cytochrome p450 inhibited → antihistamine metabolism will decrease → antihistamine effect will increase)</p> <p>2-Additive pharmacodynamic ADRs.</p>   | <p><b>long duration</b> (better control)</p> <p>1-No drug interaction</p> <p>2-Minimal ADRs<br/>since they are more specific for H1 receptors</p>  |                  |                |
| <p>-The older first generation drugs still widely used because they are effective and inexpensive.</p> <p>-These drugs <b>penetrate the blood brain barrier (BBB)</b> and cause <b>sedation*</b></p> <p>- Furthermore, they tend to interact with other receptors, producing a variety of <b>unwanted adverse effects.</b></p> <p>*they're not selective, they block the H1 receptor in the brain that is responsible for keeping you awake and alert</p> | <p>-Second generation <b>(Non-sedating)</b> agents are specific for H1 receptors</p> <p>-They carry <b>polar</b> groups, they <b>do not penetrate the BBB</b> causing less CNS depression.</p> |                  |                |

All are used systemically or topically

|                             |                      |  |
|-----------------------------|----------------------|--|
| 2nd generation              | Cetirizine           | (ثاني) مره اشوفك كذا ترى (الستر) (زين) |
|                             | Loratadine           | (لورا) (تدين) لي ب(ريالين)             |
| 3rd generation              | (Levo)(cetiri)(zine) |  |
| نقدر نقسم الدوا لثلاث مقاطع | (Deso)(lora)(tadine) |  |
|                             | (Fexo)(fen)(adine)   | (الفيكس) فين (اديني) هوا               |

team 436

- Rhinitis
- Conjunctivitis
- Urticaria
- Flu



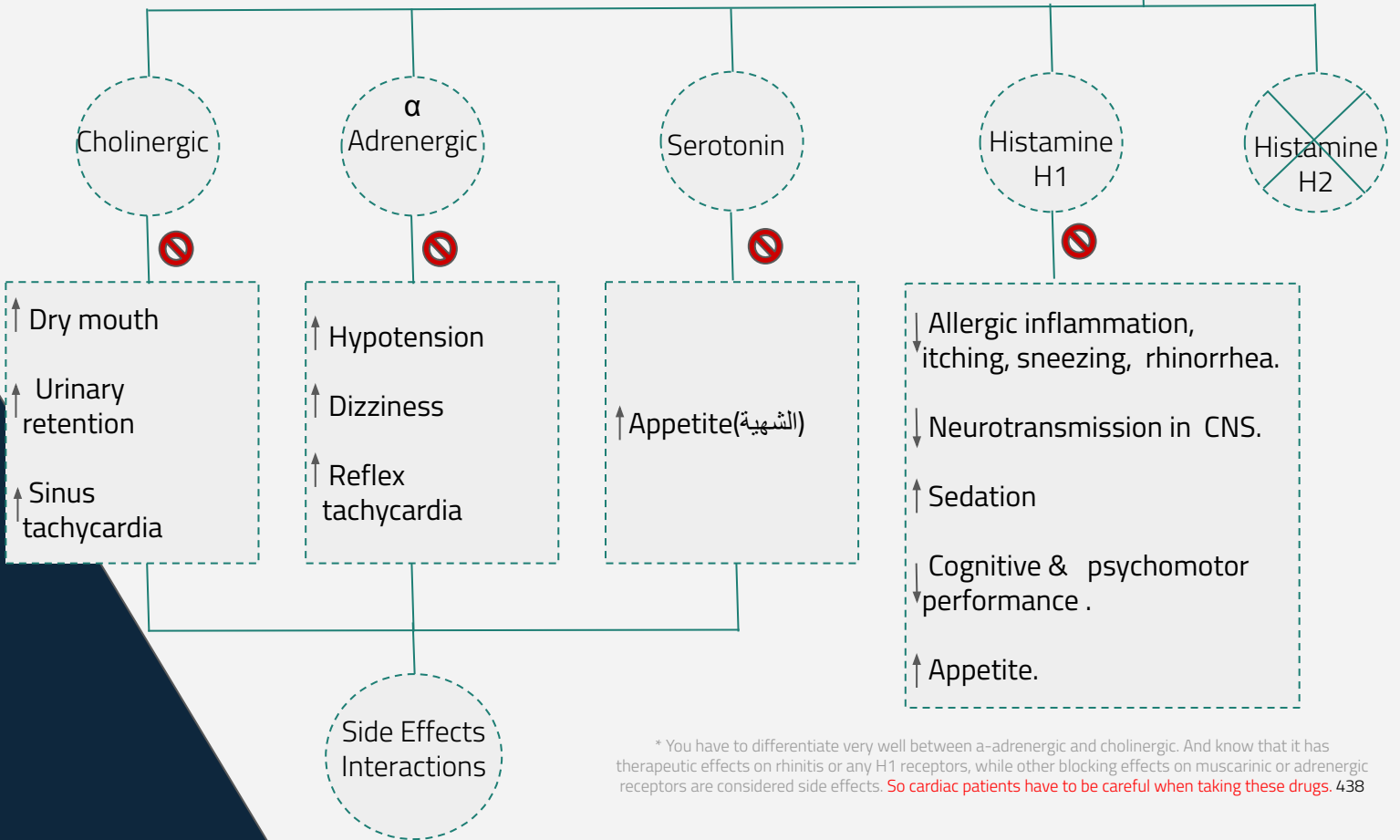
- Asthma
- Otitis
- Anaphylaxis
- Sinusitis
- Atopic dermatitis

- Allergies
- Itching (Even if non allergic)
- Others:
  - Insomnia
  - Sleep aid
  - Vertigo
  - Anxiety
  - Cough

Indications  
Linked to H1  
Block

# Antihistamines

Indications  
**Not** linked to  
H1 block



\* You have to differentiate very well between a-adrenergic and cholinergic. And know that it has therapeutic effects on rhinitis or any H1 receptors, while other blocking effects on muscarinic or adrenergic receptors are considered side effects. **So cardiac patients have to be careful when taking these drugs.** 438

# 1) Antihistamine Drugs

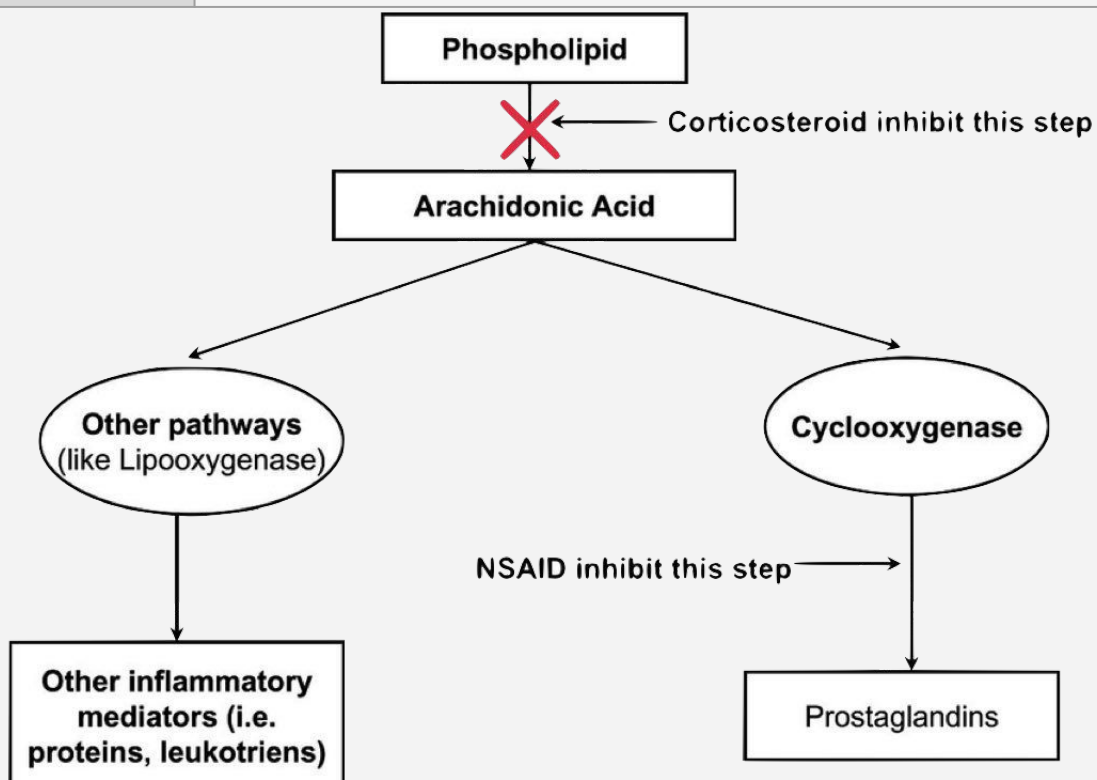
|                                |   |
|--------------------------------|---|
| <p><b>Actions</b></p>          | <p>- The action of all the H1 receptor blocker is qualitatively similar.<br/>         ★ -They are much more effective in <u>preventing symptoms</u> than <b>reversing them</b> once they have occurred.<br/>         - Most of these drugs have <b>additional effects</b> unrelated to their blocking H1 receptors (<b>not selective</b>), which probably reflect binding of H1 antagonists to:</p> <ul style="list-style-type: none"> <li>➤ Cholinergic receptors</li> <li>➤ Adrenergic receptors</li> <li>➤ Serotonin receptors</li> </ul> <p>(H1 antagonist can bind to these receptors and cause side effect)</p> |
| <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>P.K</b></p>              | <ul style="list-style-type: none"> <li>➤ H1 receptor blockers are well absorbed after → <b>oral</b> administration</li> <li>➤ Maximum serum levels occurring at → <b>1-2 hours</b></li> <li>➤ Average plasma half life is → <b>4 to 6 hours</b></li> <li>➤ H1- receptor blockers have high bioavailability and distributed to all tissues including <b>CNS</b> (lipid soluble can cross BBB)</li> <li>➤ Metabolized by → the hepatic <b>cytochrome P450 system</b></li> <li>➤ Excretion occur via <b>kidney except fexofenadine</b> excreted in <b>feces</b> unchanged.</li> </ul>                                    |
| <p><b>ADRs</b></p>             | <ul style="list-style-type: none"> <li>➤ Sedation.</li> <li>➤ Tinnitus.(ear buzzing)</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 (increased sedation effect)</li> <li>➤ Cholinesterase inhibitors<br/>             (Antihistamine blocks cholinergic receptor to stop Ach effect; whereas cholinesterase inhibitor tries to keep Ach effect. This opposing mechanism is considered as drug interaction)</li> </ul>  |
| <p><b>Over-dose</b></p>        | <p>The most common and dangerous effects of acute poisoning are those on <b>CNS</b>; including hallucinations, excitement, ataxia (loss of full control of bodily movements) &amp; convulsions.</p>   |

## 2) Anti-Allergics

| Type                  | Mast cell stabilizer   | Leukotriene receptor antagonists   |
|-----------------------|--|--|
| Example               | <ul style="list-style-type: none"> <li>● <b>CROMOLYN</b> (another name for cromoglycate)</li> <li>● <b>NEDOCROMYL</b></li> </ul>   | <b>Montelukast</b>   |
| Mechanism of action   | Decrease histamine release (by inhibiting Cl channels) i.e. can act only prophylactic, it does <b>not</b> antagonize released histamine  | Block leukotriene actions<br><br>438 note: we can't use antihistamine in asthma because the chemical mediator is leukotriene not histamine.  |
| Uses                  | Used more in children for prophylaxis of perennial allergic rhinitis (even if they're not showing symptoms).<br><br>Should be given on daily base and <u>never stop abruptly</u> (because the mast cell is stabilized and this will cause massive release of histamine). | <b>for prophylaxis of lower respiratory tract allergies</b> (e.g. perennial allergen, exercise or aspirin induced asthma)<br><b>more than</b> on upper respiratory tract allergies (e.g. chronic rhinosinusitis) |
| Adverse drug reaction | <ul style="list-style-type: none"> <li>● cough</li> <li>● wheezes</li> <li>● headache</li> <li>● rash</li> <li>● etc.</li> </ul>   | Elevation of liver enzymes, headache, dyspepsia  |

# For **SEVERE** cases of rhinitis and asthma 3) Corticosteroids

|                       |  |
|-----------------------|--|
| Example               | Topical(inhaled);steroid spray; <u>beclomethasone</u> & <u>fluticasone</u>   |
| Mechanism of action   | Anti-inflammatory → block phospholipase A2 → decrease arachidonic acid synthesis → decrease prostaglandins & leukotrienes  |
| Uses                  | Given if severe* intermittent or moderate persistent symptoms<br><br>438 note: Why corticosteroids are important in <u>asthma</u> ? inhibits the synthesis of leukotrienes<br><br>*(because it causes many side effects) |
| Adverse drug reaction | <ul style="list-style-type: none"> <li>● Nasal irritation</li> <li>● <b>fungal infection</b></li> <li>● hoarseness of voice</li> </ul>   |





# 4) Decongestants

| Type                  | Systemic  | Topical  |
|-----------------------|---|--|
| Example               | <p><b>Pseudoephedrine</b></p> <p>438 note: *has many side effects because of the ephedrine which is a sympathomimetic (stimulating sympathetic nerves).</p>                             | <p><b>1-Phenylethylamines:</b></p> <ul style="list-style-type: none"> <li>● <b>Phenylephrine</b></li> <li>● <b>Methoxamine</b></li> </ul> <p><b>2-Imidazoline:</b></p> <ul style="list-style-type: none"> <li>● <b>Naphazoline</b></li> <li>● <b>Oxymetazoline HCL</b></li> <li>● <b>Xylometazoline HCL</b></li> </ul> |
| Mechanism of action   | <p><b><math>\alpha</math>-adrenergic agonists</b></p> <p>They cause vasoconstriction of blood vessels in nasal mucosa &amp; reduce the rhinorrhea (commonly known as a runny nose).</p> |  |
| Uses                  | <p>Treatment of nasal stuffiness</p>  |  |
| Adverse drug reaction | <p>nervous , insomnia, tremors, palpitations, and hypertension.</p>   | <p>Can cause Rebound nasal stuffiness (repeated administration &gt; 10 days -2 weeks)</p>  |
| Contraindication      | <p>hypertension, heart failure, angina pectoris, hyperthyroidism. glaucoma.</p>   | <p>—</p>   |

# 5) Anticholinergics

|                       |  |
|-----------------------|--|
| Example               | Ipratropium  |
| Uses                  | <ul style="list-style-type: none"><li>• Nasal drops to control rhinorrhea (excess nasal secretions &amp; discharge), so very effective in <b>vasomotor rhinitis*</b> (watery hyper-secretion).</li><li>• bronchodilator in asthma.</li></ul> |
| Adverse drug reaction | (discussed in the Asthma & COPD)   |

Reminder: An **anticholinergic** agent is a substance that blocks the action of the neurotransmitter acetylcholine at synapses in the central and the peripheral nervous system. These agents inhibit parasympathetic nerve impulses by selectively blocking the binding of the neurotransmitter acetylcholine to its receptor in nerve cells.

**\*Vasomotor Rhinitis** is chronic **rhinitis** that is characterised by intermittent (coming and going) episodes of sneezing, watery nasal drainage (rhinorrhea), and blood vessel congestion of the nasal mucus membranes.



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# Treatment of cough

## What is Coughing?

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

Extra:

## 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 mechanism

## Types of cough

**Productive or wet (useful)**

Treatment by:  
1- **Mucolytics** (مذيب للبلغم)  
2- **Expectorants** (طارد للبلغم)

**Dry or irritant** (Not useful)  
secondary to irritant vapors,  
gases, infections, and cancer.

Treatment by:  
**Antitussive agents** (cough  
suppression))

# ★Expectorants:

Expectorants act by removal of mucous through different types of stimulations

| Stimulation Type      | Reflex Stimulation  | Direct Stimulation  |
|-----------------------|---|---|
| Example               | Guaifenesin   | Iodinated glycerol, Na or K iodide/ acetate, Ammonium chloride, Ipecacuanha.  |
| Mechanism of action   | <p>Irritate GIT</p> <p>↓</p> <p>stimulate gastropulmonary vagal reflex</p> <p>↓</p> <p>loosening and thinning of secretions</p>   | <p>Stimulate secretory glands</p> <p>↓</p> <p>Increase respiratory fluids production</p>  |
| Indications           | <p><b>Final outcome is that cough is indirectly diminished</b></p> <p>1.Common cold 2.Bronchitis 3.Pharyngitis</p> <p>4.Chronic paranasal sinusitis</p>                             |   |
| Adverse drug reaction | <p>Dry mouth, chapped lips, risk of kidney stones (<b>increases uric acid excretion</b>).</p> <p>*It is useful for patients with gout because it increases uric acid excretion.</p> | <p>Unpleasant metallic taste, hypersensitivity, hypothyroidism (IODIDE effect), swollen salivary glands (overstimulation of salivary secretion), &amp; flare(activation) of old TB.</p> |

# Mucolytics:

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

| Drug                | Hypertonic Saline & NaHCO <sub>3</sub>  | Steam inhalation  | N-Acetyl Cysteine  | Bromhexine & Ambroxol (Ambroxol is a metabolite of Bromhexine)                                       | Pulmozyme (Dornase Alpha or rhDNAase)<br><small>(مسؤول عن DNA sputum Synthesis)</small>  |
|---------------------|---|---|--|--|--|
| Mechanism of action | Decrease Viscoelasticity by increasing water content  | Decrease Adhesiveness<br><small>يقال من ترابط جزيئات البلغم من خلال استنشاق البخار ويعتبر حل مؤقت</small> | <b>Breakdown S-S bonds in glycoprotein</b> (in mucus) → less viscid mucous<br><br><small>(Glycoproteins are found in mucous)#438</small>   | Synthesize serous mucus (watery secretion from the submandibular gland) + activate ciliary clearance | Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum <u>in case of bacterial infection only</u>      |
| Overview            | —   |   | A free radical scavenger used in acetaminophen* overdose<br><br><small>(paracetamol toxicity) *medication used for children fever)</small> | Increase immune defence → decrease antibiotics usage + Decrease pain in acute sore throat            | A recombinant human-deoxyribo nuclease-1 enzyme genetically engineered that is neubilized + Full benefit appears within 3-7 days |
| Uses                | effective as adjuvant therapy in COPD, asthma, bronchitis,...etc. (when there is excessive &/or thick mucus...) |   |  |  |  |

# Antitussive agents : stop or reduce cough by acting either :

|  |  | Location  | use  | drug  |
|--|--|---|--|---|
| <b>Peripherally acting</b><br><small>*acts on the receptors of the respiratory center.</small> | <b>1- Inhibitors of airway stretch receptors</b>               | <b>In Pharynx</b>   | Demulcents (forms a protective coating)  | 1- Lozenges<br>2- Gargles (المضضة)  |
|  |  | <b>In Larynx</b>  | Emollients (forms a protective coating)  | 1- Menthol<br>2- Eucalyptus   |
|  |  | <b>In Tracheobronchial Airway</b>   | Aerosols or inhalation of hot steam  | 1- Tincture benzoin compound.<br>2-Eucalyptus   |
|  |  | <b>During bronchoscopy or bronchography</b>   | local anaesthetic aerosols   | 1- <u>Lidocaine</u><br>2- <u>Benzocaine</u><br>3- <u>Tetracaine</u>   |
|  | <b>2- Inhibitors of pulmonary stretch receptors in alveoli</b> | <b>M.O.A</b> .Decrease sensitivity (numbing) of receptors by local anesthetic action.             |  | Benzonatate   |
| <b>Centrally acting</b><br><small>* (acts on the cough center itself.)</small>                 | <b>OPIOIDS</b>   | <b>1-Codeine (very potent)</b> <b>2-Pholcodine</b><br>Have similar effects to morphine but weaker |  | activating $\mu$ opioid receptors   |
|  | <b>NON-OPIOIDS</b>   | <b>1- Antihistamines</b> (>sedating)<br><br><b>2-Dextromethorphan</b>                             | <b>Dextromethorphan</b> increases threshold at cough center.<br><br>It has benefits over opioids in being:<br>1- As potent as codeine.<br>2- Less constipating.<br>3- No respiratory depression.<br>4- No inhibition of mucociliary clearance.<br>5- No addiction. | ADR for <b>Dextromethorphan</b><br><br>Normal dose:<br>Nausea, vomiting, dizziness, rash & pruritus.<br><br>High dose:<br>Hallucinations + opiate like side effects on respiration & GIT. |

# MCQ

1-a patient suffers from travel sickness, nausea and vomiting, your drug of choice will be:

A- Promethazine

B- levocetirizine

C-fexofenadine

D-Codeine

2- H1 receptor blockers Excretion occur via kidney except for:

A- fexofenadine

B-cyclizine

C-azatidine

D- ketotifen

3- Which drug is the best for Vasomotor rhinitis ?

A-Lozenges

B- Ipratropium

C-menthol

D-cetirizine

4- patient suffering from nasal stiffness and he has hypertension. What's the decongestant that should be avoided.

A-Phenylephrine

B-Methoxamine

C-Naphazoline

D-psuedoephedrine

5-Inhibitors of pulmonary stretch receptors in alveoli?

A-Benzonatate

B-benzocaine

C-tincture benzoin

D-eucalyptus

6-Antitussive works by increasing the threshold at cough center?

A-Codeine

B-Pholcodine

C-Dextromethorphan

D-Lidocaine

7-one of of the following statements is true about fexofenadine

A-Cause sedation

B-carry a polar group

C-Binds to serotonin receptors

D-antitussive

## Answers

|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| A | A | B | D | A | C | B |

# SAQ

Q1) The classic H1 receptor antagonists mechanism of action:

Q2) List the ADRs of using corticosteroids?

Q3) What's the M.O.A for **Bromhexine & Ambroxol**?

Q4) list three peripherally acting antitussive agents and their location:

Q5) Dextromethorphan has benefits over opioids for being:

Q6) what are the side effects produced when antihistamines inhibit cholinergic receptors?

## Answers

A1) They block the receptor mediated response of a targeted tissue

A2) Nasal irritation, fungal infection, hoarseness of voice

A3) Synthesize serous mucus + activate ciliary clearance and increases the immune defence

A4) Slide 14

A5) as potent as codeine, less constipating, no respiratory depression

A6) dry mouth, urinary retention, sinus tachycardia





# GOOD LUCK!

## Team Leaders

**Tarfa Alsharidi**

**Khaled Alsubaie**

**Revised by** Dana Naibulharam Bandar Alharbi

## Team Members

Ghada Alothman  
Ghadah Alsuwailem  
Rawan Bagader  
Noura Bamarei  
Sadem Alzayed  
Yasmin Alqarni  
Ghaida Almarshoud  
Shayma Alghanoum  
Leen Almadhyani  
Noura Alsalem  
Noura alsalem  
May barakah  
Banan Alqady  
Reem Aldossari  
Nouf Alsubaie

Mohamed Aquhidan  
Meshal Alhamed  
Abdulaziz Alsalem  
Feras Alqaidi  
Musab Alamri  
Mohammed Alkathiri  
Abdullah Alburikan  
Mohammed Al-Shamrani

any suggestions or Complaints :

 [TeamPharma439@gmail.com](mailto:TeamPharma439@gmail.com)

 [Pharmacology439](https://twitter.com/Pharmacology439)

