



Lecture 4: Treatment of allergic rhinitis (AR) and cough

Respiratory system

Second year

Medical school

Hashemite University

2nd semester 23/24

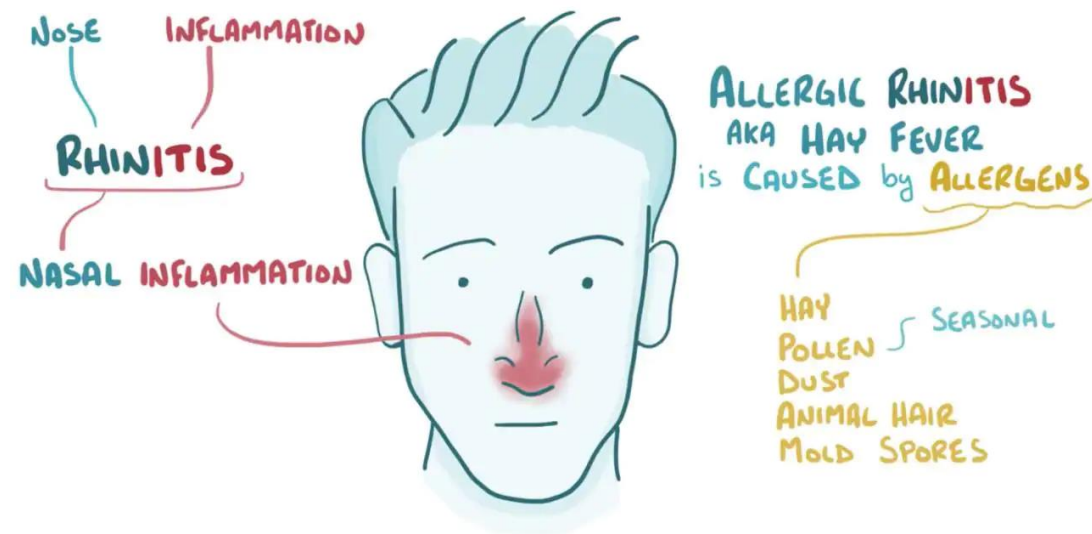
Sofian Al Shboul, MD, PhD.



Allergic rhinitis (AR)

- An **inflammation** of the mucous membranes of the **nose** and is characterized by:

1. Sneezing
2. itchy nose/eyes
3. watery rhinorrhea
4. nasal congestion/itching
5. sometimes a nonproductive cough.





Definition & symptoms

- Caused by immunoglobulin E (IgE)-mediated reactions to inhaled allergens (over-reaction of the immune system)
- It is often co-morbid with asthma and/or conjunctivitis.

Allergic rhinitis and asthma

If you have asthma, not treating your allergic rhinitis or hay fever symptoms adequately can lead to worsening of symptoms and increases the risk of a sudden asthma attack.

90% of people with asthma have allergic rhinitis



30% approximately of people with asthma have undiagnosed allergic rhinitis

Treating allergic rhinitis symptoms in people with asthma has been shown to reduce asthma exacerbations and A&E visits by up to

80%

 AllergyUK







Risk factors & triggers

- Known as “hay fever”
- An attack may be precipitated by inhalation of an allergen (such as dust, pollen, or animal dander).
- Genetic factors: IL33, IL33R and IL13.

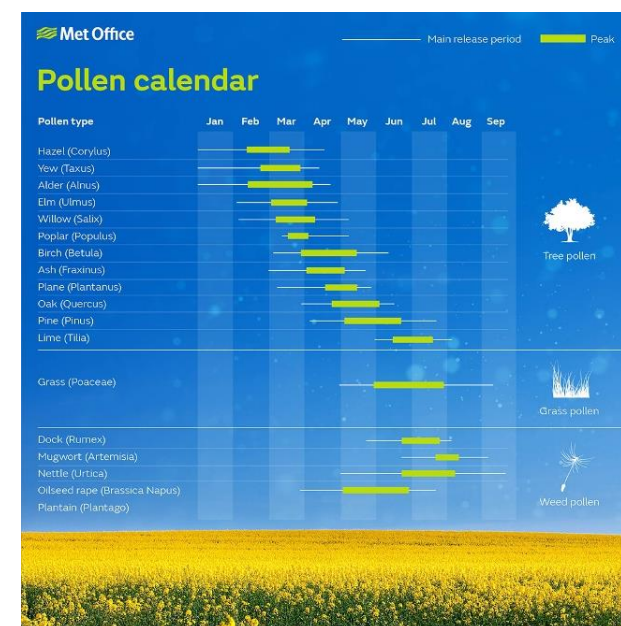
Allergic Rhinitis : Causes and Symptoms



- Pollen
- Animals
- Virus and bacteria
- Runny nose
- Red eye, lacrimation
- Sneezing
- Rash, itching



LALLEMAND PHARMA

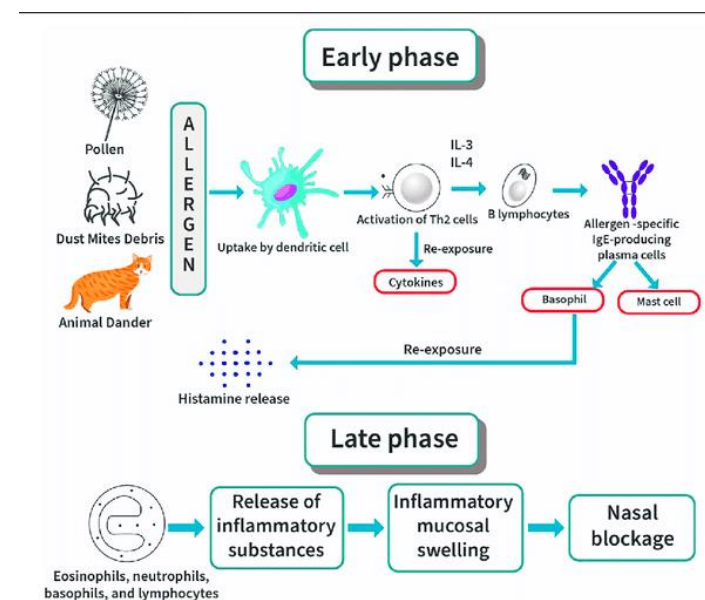




- Sensitization is a process by which the immune system will produce the IgE antibody in response to certain types of particles or allergens it considered abnormal

Pathophysiology

- First exposure to allergens (no symptoms) (Sensitization)
- DCs take up the allergen, process it present it to naive T cells which will activate and differentiate them into allergen-specific type 2 T helper cells (T_H2 cells) >> induce the activation of B cells >> plasma cells will produce allergen-specific IgE that binds to mast cells and basophils
- The mast cells release mediators, such as histamine, leukotrienes, and chemotactic factors that promote bronchiolar spasm and mucosal thickening from edema and cellular infiltration.





Histamine effects

- Histamine is present in all tissues
- Higher concentrations in mast cells and basophils
- Functions as a neurotransmitter in the brain
- **Released** by allergies, anaphylaxis and as a result of destruction of cells (cold, toxins from organisms, venoms from insects and spiders, and trauma)
- H1 receptor: **smooth muscle contraction** and **increasing capillary permeability**
- Can **enhance** the secretion of **proinflammatory cytokines**

H₁ Receptors

EXOCRINE EXCRETION

Increased production of nasal and bronchial mucus, resulting in respiratory symptoms.

BRONCHIAL SMOOTH MUSCLE

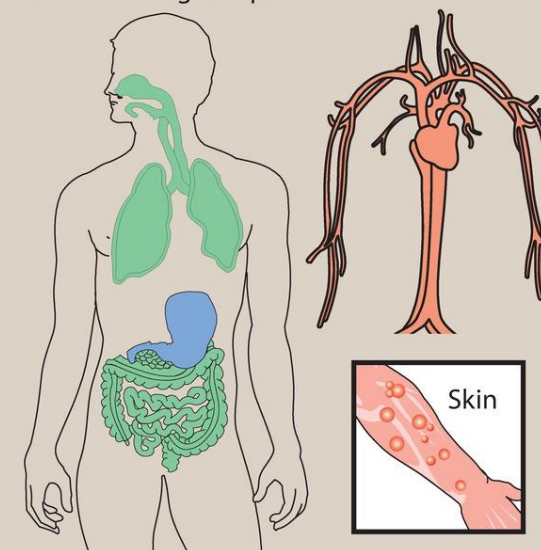
Constriction of bronchioles results in symptoms of asthma and decreased lung capacity.

INTESTINAL SMOOTH MUSCLE

Constriction results in intestinal cramps and diarrhea.

SENSORY NERVE ENDINGS

Causes itching and pain.





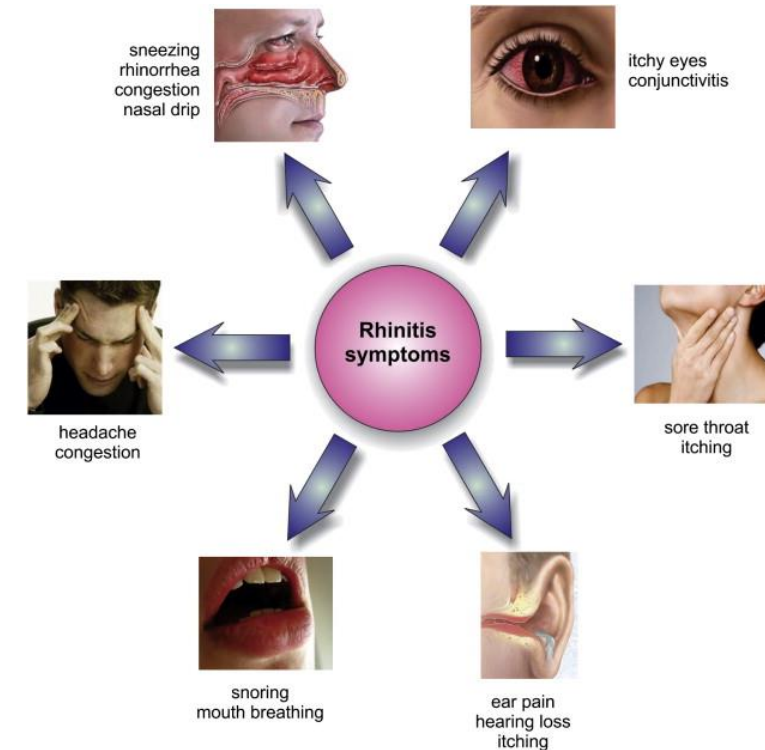
Pharmacological treatments

1. Intranasal corticosteroids
2. Antihistamines
3. Nasal decongestant sprays
4. Cromolyn and leukotriene receptor antagonists



Pharmacological treatments: Antihistamines

- Oral antihistamines (H1 receptor antagonists) have a **fast onset of action** and are useful for the **management of symptoms** of allergic rhinitis caused by **histamine release**, such as sneezing, watery rhinorrhea, and itchy eyes/nose.
- more effective for **prevention** of symptoms in **mild or intermittent** disease.





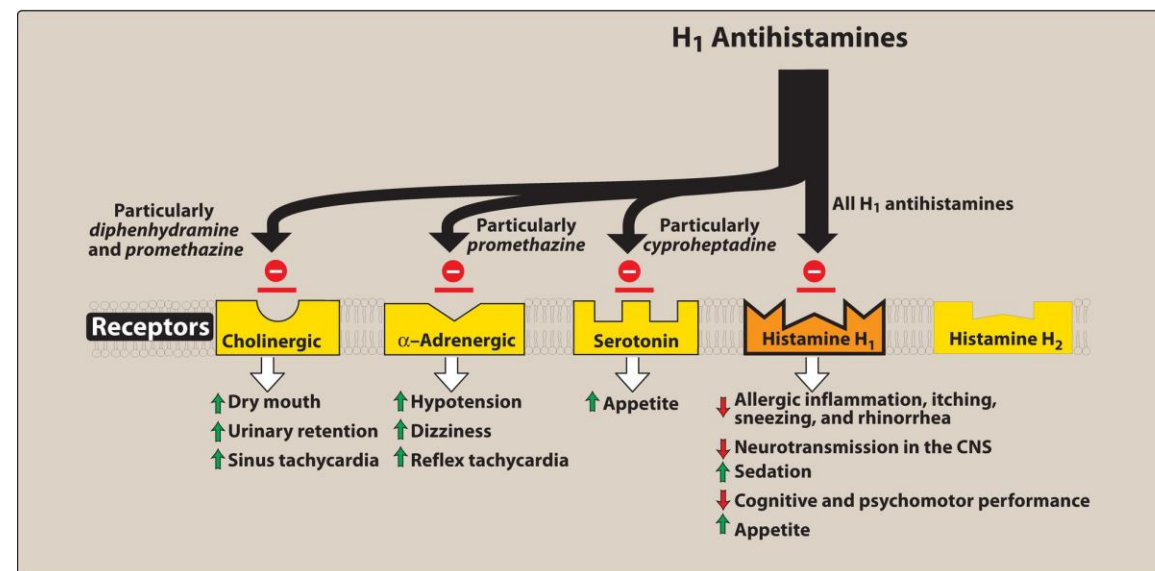
Pharmacological treatments: Antihistamines

- Ophthalmic and nasal antihistamine delivery devices are available for targeted, topical tissue delivery.
- Combinations of antihistamines with decongestants are effective when **congestion is a feature of rhinitis**, or when patients have **no response or incomplete control of symptoms with intranasal corticosteroids**.



Pharmacological treatments: Antihistamines (Actions)

- They do **not influence** the formation or release of histamine
- They **block the receptor-mediated** response of a target tissue.
- They can bind to cholinergic, adrenergic, or serotonin receptors >> additional effects unrelated to their ability to block H1 receptors.





Pharmacological treatments: Antihistamines (Pharmacokinetics)

- Well absorbed after oral administration >> maximum serum levels occurring at 1-2 hours.
- First-generation half-life is 4 to 6 hours
- Second-generation half-life is 12 to 24 hours (once-daily dosing)
- First-generation distributed in all tissues (**CNS**)
- Metabolized by the liver



Pharmacological treatments: Antihistamines (Adverse effects)

- First-generation have a low specificity, interacting with histamine muscarinic cholinergic, α -adrenergic, and serotonin receptors:
 1. Sedation
 2. Tachycardia
 3. Hypotension
 4. Vertigo
 5. Increased appetite



Pharmacological treatments: Antihistamines

- First generation:

1. Diphenhydramine
2. Chlorpheniramine

- Second generation:

1. Fexofenadine
2. Loratadine
3. Cetirizine

- Internasal and/or eye drops:

1. Azelastine



Pharmacological treatments: Corticosteroids

<i>Budesonide</i> PULMICORT, RHINOCORT*	Allergic rhinitis, Asthma, COPD
<i>Fluticasone</i> FLONASE*, FLOVENT <i>Mometasone</i> ASMANEX, NASONEX* <i>Triamcinolone</i> NASACORT*	Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma Allergic rhinitis, Asthma

- Nasal CS are the most effective medications for treatment of allergic rhinitis.
- Onset of action that ranges from **3 to 36 hours** after first dose
- Systemic absorption is minimal, and adverse effects of treatment are localized (nasal irritation, nosebleed, sore throat, and, rarely, candidiasis)
- Patients should be instructed to **avoid deep** inhalation during administration into the nose, why?

To minimize systemic absorption

The target tissue is the nose



Pharmacological treatments: nasal decongestants

Phenylephrine
Oxymetazoline
pseudoephedrine



- Short-acting **constrict dilated arterioles** in the nasal mucosa and **reduce airway resistance**.
- **Rapid onset** of action and show few systemic effects.
- **Not recommended as monotherapy**
- Oral forms has been linked to **increased blood pressure, heart rate and insomnia**
- Effects of phenylephrine appear similar to those of placebo!!



Pharmacological treatments: Other agents

- **Cromolyn:**
 - regularly or as needed (ideally 30 minutes before an exposure).
 - helpful for brief exposures (minutes to hours).
 - For prolonged exposures: begin four to seven days in advance
 - Has very excellent safety profile
- **Leukotriene receptor antagonists may be a reasonable option in patients who also have asthma.**



Pharmacological treatments

Mild or episodic symptoms:

1. **Oral antihistamine** (cetirizine (≥ 6 months), fexofenadine or loratadine): regularly or as needed (two to eight hours before exposure)
2. **nasal spray antihistamine:** azelastine >6 years of age
3. **nasal spray glucocorticoid** (more effective than antihistamines): regularly or as needed (initiating therapy two days before, continuing through, and for two days after the end of exposure): Mometasone, fluticasone or triamcinolone
4. **nasal spray Cromolyn**



Pharmacological treatments

Persistent or moderate-to-severe symptoms

1. Nasal sprays glucocorticoid
2. Addition of an antihistamine spray
3. OR Addition of a minimally sedating oral antihistamine



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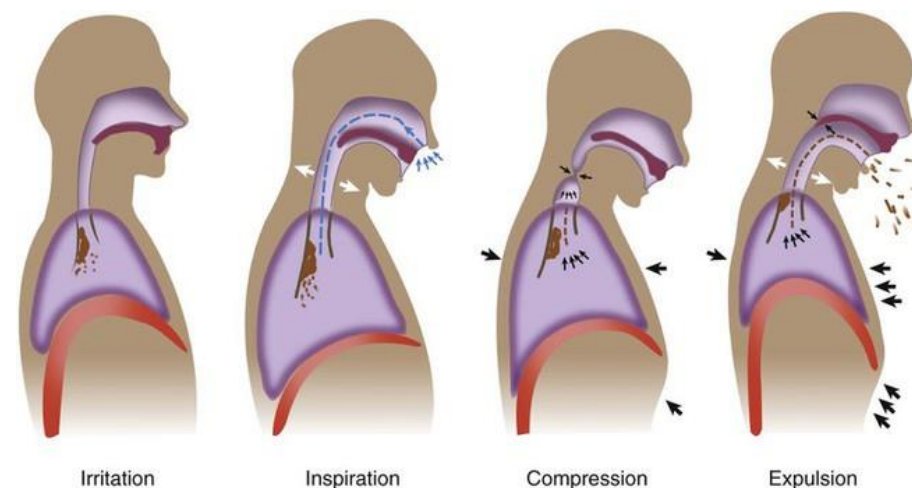
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Cough is a major Involuntary protective reflex

Overview

- ❖ A sudden expulsion of air through the large breathing passages that can help clear them of fluids, irritants, foreign particles and microbes.
- ❖ Not to be suppress- Indiscriminately
- ❖ Many situations do not serve any purpose
- ❖ Disturb patient ,its rest and sleep





Types and common causes of cough

- **Non-productive (dry):** No useful purpose, increases discomfort to the patient >> needs suppression
- **Productive (tenacious):** Presence of excessive sputum >> suppression not desired >> needs coughing/clearing out of the sputum

Clinical cough descriptor	Definition
Acute	Cough that lasts for < 3 weeks
Subacute	Cough that lasts 3 – 8 weeks
Chronic	Cough that lasts > 8 weeks
Refractory	Cough that does not respond to usual medical treatment such as the ADP
Chronic idiopathic	Cough with no underlying cause even after a thorough systematic review
Specific	A known underlying disease causing the cough

ADP: Anatomical diagnostic protocol.





Complications of coughing

- Acute:

1. cough syncope (fainting spells due to decreased blood flow to the brain when coughs are prolonged and forceful),
2. Insomnia
3. Cough-induced vomiting,
4. Subconjunctival hemorrhage or "red eye"

Chronic:

1. Abdominal or pelvic hernias
2. Fatigue fractures of lower ribs and costochondritis.
3. Chronic or violent coughing can contribute to damage to the pelvic floor and a possible cystocele.



Treatment

- Before treating cough, identification of its cause is important to ensure that antitussive treatment is appropriate.
- Priority should always be to treat the underlying cause of cough when possible.



- Antitussives:

Used when cough performs no useful function (i.e. is nonproductive), and its complications represent a real or potential hazard (i.e. distressing, painful, increasing airway damage or causing morbidity)

- Expectorants:

Used to get rid of excessive thick bronchial secretions

Table comparing
Cough Suppressant
&
Expectorant

Characteristics	Cough Suppressant	Expectorant
Definition	A medication that inhibits or suppresses a cough	A medication that makes it easier to cough up mucus
Ingredients	Dextromethorphan is the suppressant but often the medicine also has codeine and diphenhydramine	Guaifenesin is the expectorant but sometimes bromhexine and salbutamol are also added
Activity	Greatly reduces the reflex to cough	Increases the amount of water present in mucus so it can be coughed up
Uses	Used to treat coughs that are dry, with little mucus present	Used to treat coughs that are wet, with lots of mucus present
Side effects	Dizziness, fatigue, nausea, and constipation	Dizziness, fatigue, nausea, and vomiting



Guaifenesin

- an **expectorant**, is available as a **single-ingredient formulation** and is commonly found in **combination cough products** with codeine or dextromethorphan.
- ↑ Bronchial secretion, ↓ Viscosity



Codeine

- ✓ Decreases the sensitivity of cough centers in CNS to peripheral stimuli **and** decreases mucosal secretion.
- ✓ Doses to get these effects are lower than those required for analgesia.
- ✓ Adverse effects: constipation, dysphoria, and fatigue.
- ✓ **Codeine has addictive potential**



Dextromethorphan

Synthetic derivative of morphine with NO analgesic effects in antitussive doses.

- ❖ Better adverse effect profile than does codeine **and** is equally effective for cough suppression.
- ❖ In low doses = low addictive profile.
- ❖ It is also a potential drug of abuse, since it may cause **dysphoria at high doses**.
- ❖ Can trigger a histamine release (allergic reaction) >> children susceptible to allergic reactions should be administered dextromethorphan only if absolutely necessary
- ❖ AE: Nausea, vomiting