

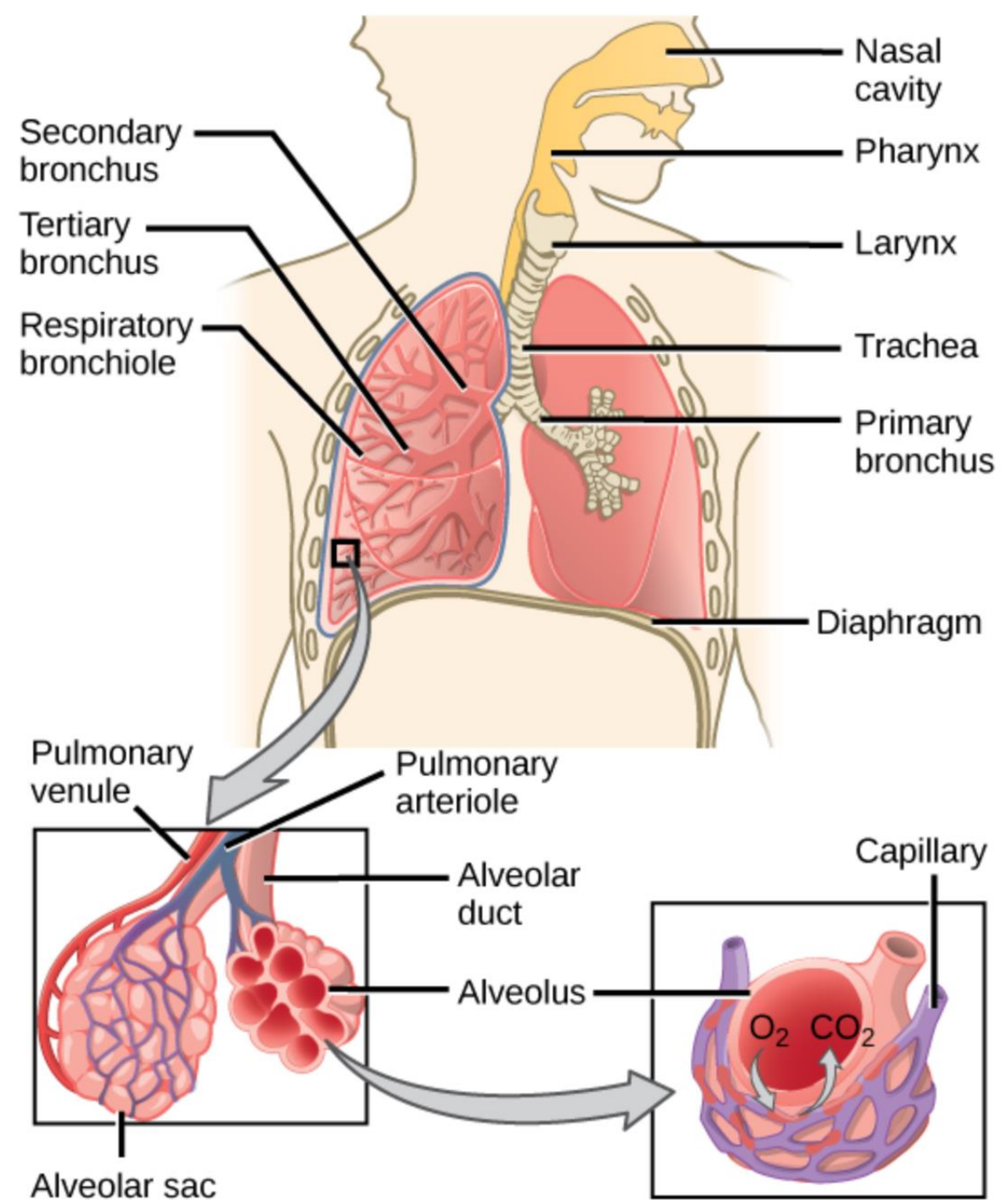
OTC تراپی علایم ریوی

دکتر شهیده امینی

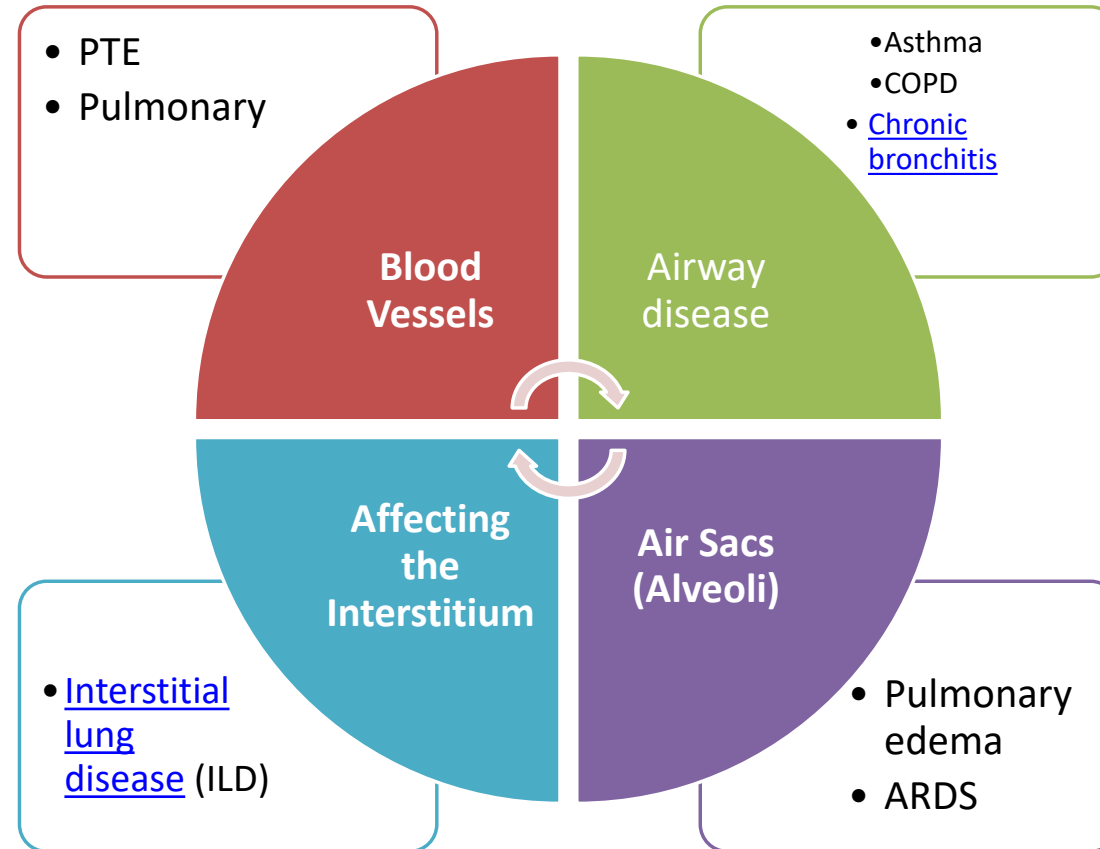
متخصص داروسازی بالینی

فلوشیپ فارماکوتراپی مراقبت های ویژه

Introduction



Introduction



Pulmonary symptoms

- Dyspnea
- Cough
- Fatigue
- Upper airway symptoms(sneezing, rhinorrhea, PND)



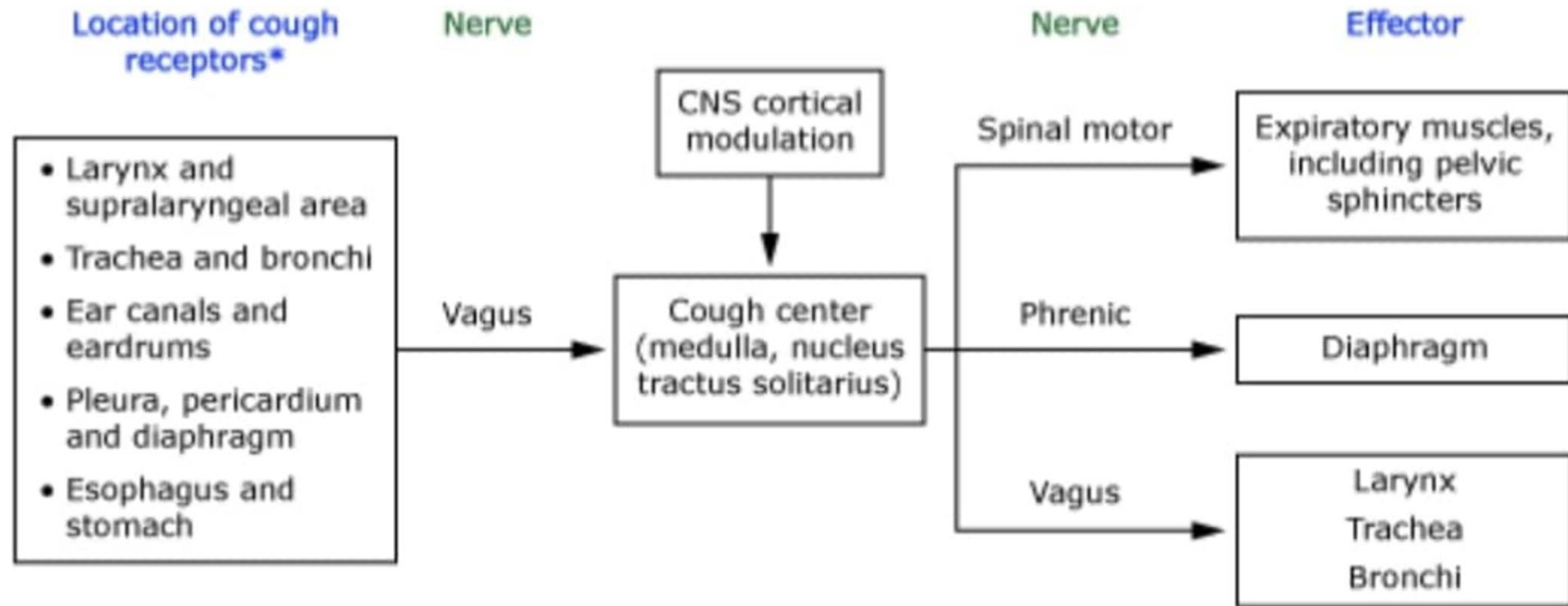
Cough

- The symptom of cough, which is responsible for approximately 30 million clinician visits annually in the United States, is one of the most common symptoms for which outpatient care is sought
- Cough can be classified based upon the duration of the cough; within each category are likely diagnostic possibilities.
- Acute cough exists for less than three weeks and is most commonly due to an acute respiratory tract infection. Other considerations include an acute exacerbation of underlying chronic pulmonary disease, pneumonia, and pulmonary embolism.
- Cough that has been present longer than three weeks is either subacute (three to eight weeks) or chronic (more than eight weeks)

Cough reflex arc

- Each cough occurs through the stimulation of a complex reflex arc.
- This is initiated by the irritation of cough receptors that exist not only in the **epithelium** of the **upper** and **lower** respiratory tracts, but also in the **pericardium**, **esophagus**, **diaphragm**, and **stomach**.
- Chemical receptors sensitive to acid, cold, heat, capsaicin-like compounds, and other chemical irritants trigger the cough reflex via activation of ion channels of the transient receptor potential vanilloid type 1 (TRPV1) and transient receptor potential ankyrin type 1 (TRPA1) classes

Cough reflex arc



Etiologies

- The most common etiologies of chronic cough are :
- Upper airway cough syndrome (due to postnasal drip),
- Asthma
- Gastroesophageal reflux

Less common causes of chronic cough

Bronchiectasis
Angiotensin-converting enzyme inhibitors
Nonasthmatic eosinophilic bronchitis
Bronchogenic carcinoma
Interstitial lung disease
Occult pulmonary infection
Occult heart failure
Occult aspiration
Tracheobronchial foreign body or mass (other than bronchogenic carcinoma)
Occupational asthma
Nasal polyps
Disorders of the external auditory canals, pharynx, larynx, diaphragm, pleura pericardium, esophagus, stomach, or thyroid
Psychogenic

Etiologies

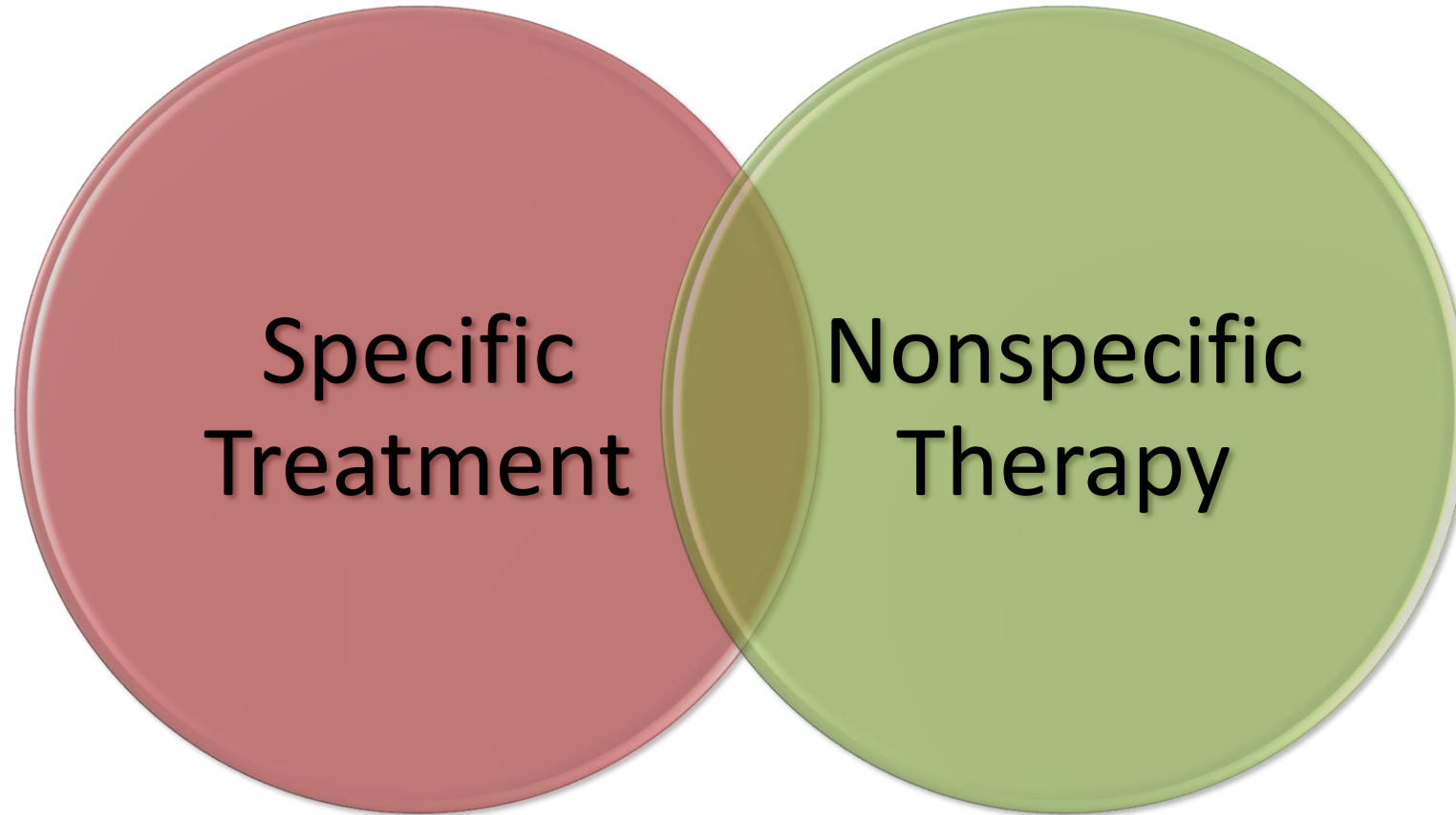
- A nonproductive cough is a well-recognized complication of treatment with angiotensin converting enzyme (ACE) inhibitors, occurring in up to 15 percent of patients treated with these agents .
- Although the pathogenesis of the cough is not known with certainty, it has commonly been hypothesized that accumulation of bradykinin, which is normally degraded in part by ACE, may stimulate afferent C-fibers in the airway
- **ACE inhibitor-induced cough has the following general features**
 - It usually begins within one week of instituting therapy, but the onset can be delayed up to six months.
 - It often presents with a tickling, scratchy, or itchy sensation in the throat.
 - It typically resolves within one to four days of discontinuing therapy, but can take up to four weeks.
 - It generally recurs with rechallenge, either with the same or a different ACE inhibitor.
 - It is a more common complication in women than in men, and is also more common in those of Chinese ancestry .
 - It does not occur more frequently in asthmatics than in non-asthmatics.
 - It is generally not accompanied by airflow obstruction

Evaluation

Take a history

- Smoking
- Purulent
- Red sign
- Duration
- Drugs
- Age, PMH

Approach



Mucolytics Definition

The general term for medications that are meant to affect **mucus properties** and promote secretion **clearance** is “**mucoactive**.”

These include **expectorants**, **mucolytics**, mucoregulatory, mucospissic, and mucokinetic drugs.

Expectorants are defined as medications that improve the ability to expectorate purulent secretions

Guaifenesin (sold as cough medications) is usually considered an expectorant rather than a mucolytic.

Mucolytics, Expectorants, and Mucokinetic Medications

Bruce K Rubin

Respiratory Care July 2007, 52 (7) 859-865;

Mucolytics Definition

- Mucolytics are medications that change the biophysical properties of secretions by degrading the mucin polymers, DNA, fibrin, or F-actin in airway secretions, generally **decreasing viscosity**. This will not necessarily improve secretion clearance, because sputum that is more viscous but less sticky tends to clear better with cough
- The best known of these agents is N-acetyl L-cysteine (NAC) which with free thiol (sulfhydryl) groups, which hydrolyze disulfide bonds attached to cysteine residues of the protein core.

Mucolytics, Expectorants, and Mucokinetic Medications

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Mucolytics Definition

Mucoactive drug classes	Proposed mechanism of action (example)
Expectorants	Increase mucus secretion volume and/or hydration for more productive cough (e.g. guaifenesin)
Mucolytics	Reduce mucus viscosity by breaking down tertiary structures within mucus (e.g. N-acetylcysteine)
Mucokinetics	Increase mucus transportability by mucociliary transport and cough mechanisms (e.g. ambroxol)
Mucoregulators	Affect the regulation of mucus synthesis and reduce mucus hypersecretion (e.g. anticholinergic agents)

Guaifenesin

- **Brief history of guaifenesin and its regulatory path in the US**
- Guaifenesin exerts its expectorant activity via a neurogenic mechanism: a stimulation of vagal afferent nerves in the gastric mucosa activates the gastro-pulmonary reflex, and increases the hydration of airway mucus
- In support of this hypothesis, a study in rats demonstrated that oral but not intravenous guaifenesin administration increased respiratory secretions

Time	Key events
Pre-1500s	Used as natural remedy by Native Americans
1500s	Guaiaac extract used as stimulant remedies, e.g. for sore throat, syphilis
1800s	Guaiaac extract used to treat respiratory diseases in Europe
1952	First accepted by US Food and Drug Administration (FDA)
1989	Guaifenesin was reclassified to Category I (generally recognized as safe and effective) and was included in the Final Monograph (Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use, 21 CFR 341) as an expectorant for the symptomatic treatment of colds and stable chronic bronchitis.
2002	12-h extended-release (ER) guaifenesin bi-layer tablets were approved by the FDA. From 2007, the FDA removed all marketed, but unapproved, timed-release guaifenesin products from the market.

Antitussive Agents

- **Dextromethorphan**

- Non-opioid to suppress cough via an action on the central cough center

- **Codeine**

- The traditional opiate used for cough, although evidence regarding its efficacy for chronic cough is limited.
- 30 mg every 4 to 6 hours as needed and increase to 60 mg, if the lower dose is insufficient.

Antitussive Agents

- Peripherally acting antitussive agents
- Benzonatate is a peripherally acting antitussive agent that presumably acts by anesthetizing stretch receptors in the lungs and pleura.

Protection of the Pharynx Mucosa

Nonpharmacological Modulation of Unpleasant Sensations and Irritative Stimulus Transmission from the Pharynx to the Cortical Neural Network:

- **Mucosal dehydration and mechanical stimuli**, caused by pharyngeal dripping of viscous nasal mucus, viruses, bacteria, inflammatory mediators, and irritant substances, play a decisive role in triggering the acute cough
- In this regard, up to 85% of the benefit of cough syrups depends on the physical and chemical effects of the syrup itself that exert a demulcent action, namely smoothing.
- A demulcent substance can form a soothing film over a mucous membrane, indirectly reducing pain and inflammation.

Protection of the Pharynx Mucosa

- From a practical point of view, the ideal physical and chemical characteristics of cough syrup can be obtained by a complex mixture of natural substances exerting lubricant, demulcent, and protective barrier effects.
- **Honey**, stimulate salivation and send sweet gustatory stimuli to the brain. The sweet
- taste and the viscous nature of the syrup are fundamental properties of ideal cough medication.
- In fact, sweet substances stimulate C fiber sensory neurons through transient
- receptor vanilloid-1 channels that are involved in cough reflex.
- **Mucilage** acts by accelerating healing of mucosa ulcers through 2 mechanisms: reinforcement of the resistance barrier and the oxygen radical scavenging activity

OTC Cough

- Over-the-counter (OTC) cough and cold medications contain a variety of active ingredients including acetaminophen, antihistamines, dextromethorphan, decongestants (eg, alpha adrenergic agonists such as phenylephrine or pseudoephedrine).

عصاره خشک ریشه پلارگونوم،

عصاره خشک برگ پیچک (**Hedera Helix**)

عسل



Plargonium



Zoufa



Antihistamines

Antihistamines are most effective for reducing sneezing, itching, and rhinorrhea.

They also diminish eye symptoms, but have minimal effects on nasal congestion. Although first generation antihistamines (FGA) are efficacious, their use is limited by anticholinergic and sedative effects which challenge their cost-effectiveness.

The magnitude of these effects is a subject of debate; nonetheless, newer antihistamines (second generation antihistamines, SGA) are recommended as first-line therapy for mild allergic rhinitis.

Antihistamines are available in oral, ophthalmic, and nasal formulations and can also be found in combinations with oral decongestants.

They are most effective when administered before allergen exposure.

Decongestants

Oral and nasal decongestants can effectively reduce nasal congestion produced by allergic and nonallergic forms of rhinitis.

Oral agents are often combined with antihistamines, but they can lead to profound side effects (e.g., insomnia, nervousness, urinary retention) and should be used with caution in elderly patients and in those with arrhythmias, hypertension, and hyperthyroidism.

Nasal agents are not typically associated with these effects, but should be limited to short-term use to avoid rebound nasal congestion.

Recent restrictions on the sale of nonprescription formulations containing pseudoephedrine and questions regarding the efficacy of phenylephrine have resulted in challenges to the optimal use of oral decongestants

Leukotriene Modifiers

Leukotriene modifiers are effective in relieving many of the nasal symptoms of allergic rhinitis.

In some studies, the efficacy of leukotriene modifiers is comparable to antihistamines however, they are generally recommended as adjunct treatment as opposed to monotherapy.

These agents may have a role in concomitant asthma and allergic rhinitis, particularly, if both diseases are relatively mild.

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- In patients with only mild, intermittent symptoms, saline irrigation (administered as frequently as needed) is helpful in soothing and moisturizing irritated nasal mucosa.
 - Antihistamines do little to relieve nasal congestion; therefore, patients with moderate to severe congestion may require a combination of an antihistamine with a decongestant. The combination of an antihistamine and an oral decongestant is more effective than either component alone in the treatment of allergic rhinitis.

Decongestant Therapy

Both the topical (nasal) and the oral decongestants are sympathomimetics that directly stimulate α_1 -adrenergic receptors, resulting in vasoconstriction.

Local effects on the nasal mucosa include decreased tissue hyperemia, decreased tissue swelling, decreased nasal congestion, and improved nasal airway patency.

Generic Name (Example Brand Product)	Adult Dose	Pediatric Dose
Oral^a		
Pseudoephedrine (<i>Sudafed</i>)	60 mg every 4–6 hrs (MAX 240 mg/day)	Children 6–12 yrs: 30 mg every 4–6 hrs (MAX 120 mg/day) Children 2–5 yrs: 15 mg every 4–6 hrs (MAX 60 mg/day)
Phenylephrine (<i>Sudafed PE</i>)	10–20 mg every 4 hrs (MAX 120 mg/day)	Children 6–11 yrs: 10 mg every 4 hrs (MAX 60 mg/day).
Topical^d		
Naphazoline (<i>Privine</i>)	1–2 drops or sprays/nostril every 6 hrs	Children <12 yrs: Avoid, unless under physician direction
Phenylephrine (<i>Neo-Synephrine</i>)	0.25–0.5% solution: 2–3 sprays or drops/nostril every 3–4 hrs	Children 6–11 yrs: 2–3 sprays or drops (0.25% solution)/nostril every 4 hrs Children 2–5 yrs: 2–3 drops (0.125% solution) into each nostril not more than every 4 hrs
Oxymetazoline (<i>Afrin</i>)	0.05% solution: 2–3 sprays or drops/nostril every 10–12 hrs	Children 6–12 yrs: 2–3 sprays or drops/nostril every 12 hrs
Xylometazoline (<i>Otrivin</i>)	0.1% solution: 1–3 sprays or 2–3 drops/nostril every 8–10 hrs	Children 2–12 yrs: 2–3 drops (0.05% solution) into each nostril every 8–10 hrs

Decongestant Therapy

Oral decongestants can cause systemic side effects, particularly those associated with CNS stimulation (e.g., nervousness, restlessness, insomnia, tremor, dizziness, and headache).

Cardiovascular stimulation (e.g., tachycardia, palpitations, increased blood pressure) also can occur, so patients with hypertension should be monitored carefully while taking oral decongestants. Because oral decongestants are not associated with the development of rebound congestion, in most patients, they are appropriate for chronic use. They are not recommended, however, for use during pregnancy.

Topical administration of decongestants generally does not lead to systemic side effects; however, these agents are not appropriate for chronic use in rhinitis because of their potential for causing rebound congestion

OTC



OTC



OTC

۳۲۵ میلی گرم استامینوفن به علاوه ۲
میلی گرم کلرفنیرامین مالئات به علاوه ۵
میلی گرم فنیل افرین هیدروکلراید



OTC

استامینوفن ۵۰۰mg، دکسترومتورفان هیدروبروماید ۱۵mg، فنیل افرین
هیدروکلراید ۵mg





پیکسنگز.ام