

RESPIRATORY SYSTEM

PHARMACOLOGY



Title: Sheet 1+2 – Treatment of Cough

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Treatment of cough

First of all, it's important to know that coughing is an important spontaneous reflex (just like sneezing and blinking) that helps protect your airway and lungs from irritants. Basically, it's a defense mechanism for the respiratory system and a useful protective reflex. It can also be an indicator of an underlying illness.

The cough reflex can be stimulated **mechanically/physically** or **chemically** by cough receptors located in the lining epithelium of your respiratory airways.

- › **Mechanical stimulation** occurs in large respiratory passages
- › **Chemical stimulation** in alveoli (also occurs in large airways)

→ After receptor activation, impulses are carried through afferent vagal nerves to a medullary center to initiate deep inspirations, followed by strong expiratory effort against closed glottis (closed vocal cords); leading to increased pressure in the airways. Glottis suddenly relaxes, mouth opens, and air is released at high pressure.

Cough indicates that there is **something wrong** with the patient, and it is a common symptom of various diseases, so we have to investigate the underlying problem in order to give a proper treatment.

❖ **Problems and complications associated with coughing:**

- Exhaustion and insomnia (الأرق), especially in continuous cough
- Musculoskeletal pain, from continuous pressure on the thoracic cage
- Hoarseness of voice
- Urinary incontinence, patients tend to hide this symptom
- Dizziness, headache, syncope (الإغماء)
- Nausea, vomiting, and anorexia (فقدان الشهية)
- Could be associated with more serious diseases (Cancer / TB / AIDS)

✚ **Treatment of cough can be specific or non-specific.**

1- Specific treatment of cough :

→ Specific here means that it is directed to the **etiology** of the disease, or **Pathophysiological mechanism**, it simply means fixing the underlying cause = fixing the cough, as in :

- **Bronchial Asthma**
 - Should change the protocol used in treatment of asthma to make it suitable with cough medications
- **Allergic or perennial non allergic sinusitis + seasonal allergy**
- **Gastro-esophageal reflux disease (GERD)**
 - Proton pump inhibitors are classic treatment in this case
- **Chronic bronchitis**
 - Like asthma (change the used protocol)
- **Congestive heart failure**
- **ACE-inhibitors induced cough**
- **Sarcoidosis**
 - Sarcoidosis is a disease involving abnormal collections of inflammatory cells that form lumps known as granulomas. The disease begins in the lungs ,skin, or lymph nodes.

2- Non-Specific treatment of cough :

→ Directed at the symptom “only masks the cough”

→ Indicated when definitive therapy cannot be given either because:

- a. The cause is unknown
- b. Definitive therapy did not have the chance to work or will not work (like cancer metastatic to lung)

✚ Drug treatment is divided into two main categories :

Antitussive Drugs

Protussive Drugs

Therapy that controls, inhibits or eliminates cough. Useful to suppress intensity and frequency of coughing when it is distressing and unproductive (without sputum)

Protussive drugs are quite the opposite. A therapy that makes coughing more effective and productive for better excretion of larger amounts of mucus

Antitussive
Drugs

- ✚ **Drugs that may alter mucociliary factors**
 - associated with the initiation of cough stimulation
- ✚ **Drugs acting on the afferent limb**
 - On the nerves that send signals from receptors
- ✚ **Drugs acting on the cough center**
 - In the medulla where processing of the signal occurs
- ✚ **Drugs acting on the efferent limb**
 - On the nerves that send the signals back to receptors
- ✚ **Drugs acting on the respiratory skeletal muscles**

1- Drugs that may alter mucociliary factors.

- **These drugs work by :**

- Decreasing the production of mucus.
 - ✓ **To reduce the effort made by cilia in the respiratory passage.**
- Changing the consistency of mucus (i.e. Mucolytics)
 - ✓ **Which reduces the viscosity of mucus and thus easing its excretion.**
- Increasing mucociliary clearance.
 - ✓ **Increased washing out of mucus and therefore increasing the volume of secretions without increasing mucus production.**
- Increasing the volume of the secretions.

- ❖ Drugs from **natural sources** :

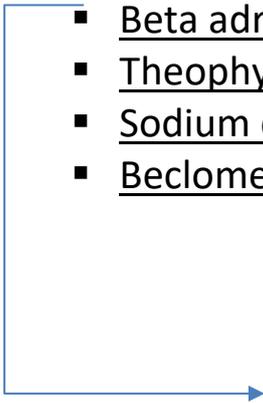
- ❁ **Ipecacuanha and Squill** : are natural products which have direct effect on CNS and locally (on the cilia) to principally cause emesis (vomiting) which is preceded by increased secretions.
- ❁ **Volatile oils (lemon, anise-يانسون, pine- صنوبر)** : have direct action on bronchi and cilia.
- ❁ **Iodinated glycerol**: is excreted through bronchial glands and stimulates secretions directly. Widely used but have doubtful efficacy. Can cause congenital hypothyroidism, so contraindicated in pregnancy and during lactation. So we can use volatile oils as an alternative
- ❁ **Aromatic chest rub** : known in traditional medicine and can have alternative mucociliary actions.

❖ Drugs from un-natural sources :



- **Bromhexine** : increase lysosome activity leading to increased enzyme secretion and hydrolysis of mucopolysaccharides, and thus decreasing the viscosity of mucus, which makes washing out of mucus easier .
- **Carbocisteine** : An aerosol, works through its SH group to reduce disulfide bonds in mucoproteins decreasing viscosity and leading to enhancement of flow. It may irritate the airways in some sensitive patients, so we should adjust the dose based on the condition.
- **Combination of H1-histamine antagonist and a decongestant** : they act to decrease mucus production, and they are usually combined as they have a synergistic effect together.
- **Ammonium chloride**
- **Hydration(natural ^^)**: either orally or intravenously, It is used to make the patient extra hydrated to decrease the viscosity of mucus by increasing the water content, which helps in washing out mucus.

- Ipratropium bromide
- Beta adrenergic agonists
- Theophylline
- Sodium chromoglycate
- Beclomethasone

 **Note :** These drugs are discussed in the treatment of **bronchial asthma**. They can help in the treatment of cough under the effect of altering mucociliary factors.

2- Drugs acting on the afferent limb=Sensory nerves

❖ Local anesthetics :

- **Lidocaine** : Applied topically on the chest, **has transient antitussive effect (temporal effect)**. Could have a central effect when applied intravenously.

❖ Opioids :

- this effect is beside their primary central effect.

3- Drugs acting on the cough center (cross BBB)

❖ Narcotics :

- **These drugs cause drowsiness**
- **Codiene** : **Is the standard and the most important one**, recently found no more effective than syrup vehicle
- Diamorphine
- Morphine

❖ Non-narcotic :

- **They don't cause addiction like narcotics**
- Dextromethorphan
- Glaucine
- Diphenhydramine
- **Pholcodine**

4-Drugs acting on the efferent limb

▪ **Ipratropium Bromide** :

- > **Given as an aerosol.**
- > Effective for asthma, chronic bronchitis, and persistent cough following Upper respiratory tract infections (URTI).
- > **Can also have effects on cough receptors by altering mucociliary factors.**

5- Drugs acting on the respiratory skeletal muscles :

- May be considered in patients **who can not be mechanically ventilated, because of uncontrollable continuous spasms of coughing, that other drugs couldn't treat.**
- **Nondepolarizing blockers** like pancuronium
 - › Explained by the dr. as : (block the depolarization of muscle cells, which blocks their contraction)



- ✚ This treatment increases cough effectiveness with or without increasing cough frequency.
- ✚ Cough effectiveness is enhanced by either an increase in **superficial velocity** (Explained by the dr. as an increase in the amount of collected mucus) Or alter mucus factors.
- ✚ Indicated when cough performs a useful function, and needs to be encouraged (e.g. bronchiectasis, cystic fibrosis, pneumonia and postoperative atelectasis).
- ✚ Protussive therapy is not only associated with drugs, as some cases require mechanical intervention.

➤ Hypertonic saline Aerosole :

- › Improves cough clearance but not pulmonary function or subjective assessment.

(Usually used with another kind of protussive therapy, because it's not sufficient when used alone)

➤ Amiloride Aerosol : For cystic fibrosis

➤ Bronchodilators :

- › Logically, dilation of respiratory airways gives more room for excretion of larger amounts of mucus. However, with too much relaxation, flow rates may actually decrease.

➤ Mechanical Measures :

> Mechanical measures and approaches could also be helpful in getting rid of excessive mucus, like :

- Positive insufflation followed by manual compression of the lower thorax and abdomen, which help skeletal muscles to contract and help the process of getting rid of mucus.
- Abdominal Push manoeuvre to assist expiration .
- Combining abdominal binding and muscle training of the clavicular portion of pectoralis major.
- Combination of Positive expiratory pressure and chest physiotherapy in patients with chronic bronchitis.

Note : underlined measures were skipped by the doctor

New Treatments

- **Opioids:** The opioids currently bind the OP3 receptor and are therefore associated with characteristic side effects, like affecting the CNS and causing addiction problems.
- **New Opioids:** they are peptides such as the endomorphins, that bind opioid receptor like-1 (ORL1), which has reduced effect on CNS and addiction (under testing)
- New drugs for the treatment of cough maybe directed at an extremely heterogeneous group of targets
- A major distinction in this regard is the ability of certain drugs to inhibit the underlying inflammatory process that under certain condition cause cough.

⚙ Examples:

- Anti-inflammatory drugs
- Drugs for the treatment of asthma or COPD
- Novel proton pump inhibitors as treatment for GERD
- Compounds that are targeted to inhibit sensory activity directly which should, in theory, inhibit cough of any etiology.