



جامعة تبوك
University of Tabuk

- **Faculty of Medicine**
- **Department of pharmacology**
 - **respiratory module**
 - **2014-2015**

Treatment of cough

Objectives

- At the end of this lecture, the students should be able to:
- Describe the strategies of drug treatment of cough.
- List the major classes of drugs used for treatment of cough (antitussives, mucolytic, and expectorants) and describe the mechanism of action of each class.
- Describe the adverse effects of different classes of drugs used for treatment of cough.

Cough therapy

- Definition: cough is a protective mechanism to expel secretions and foreign bodies outside the respiratory tract.



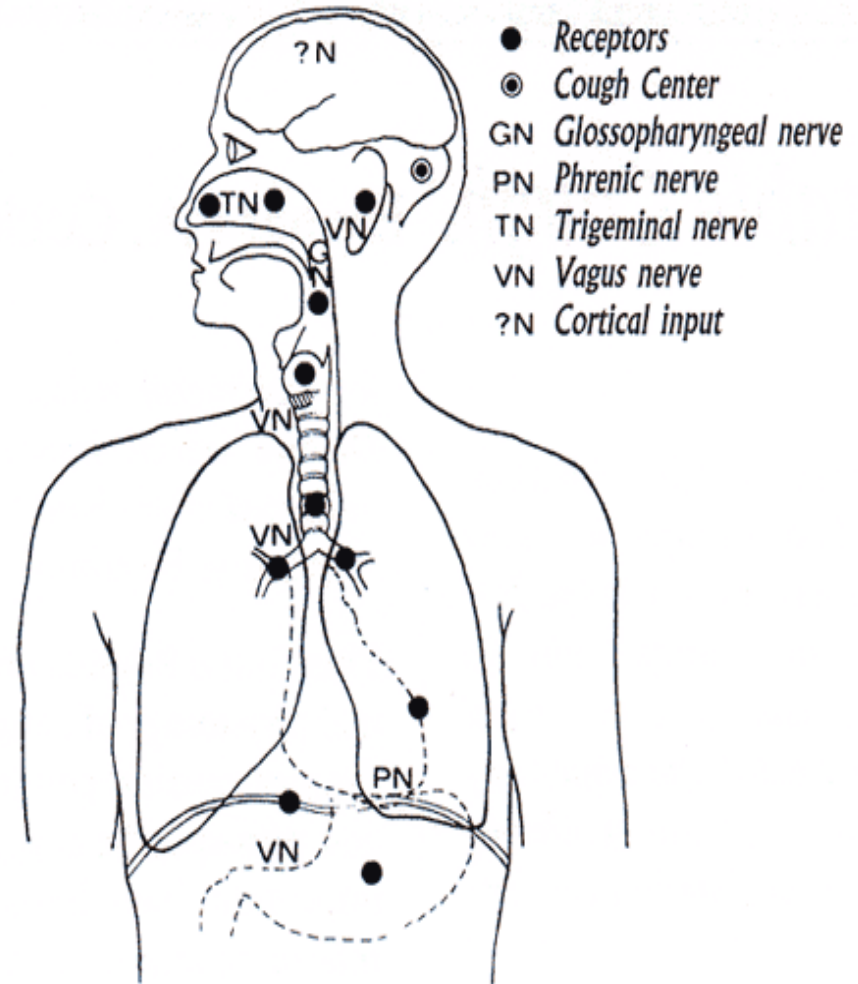
Type of cough

- A dry cough is a cough that does not produce any mucus.
- Irritate the lungs and throat.
- A sign of a viral infection or sinus problems.

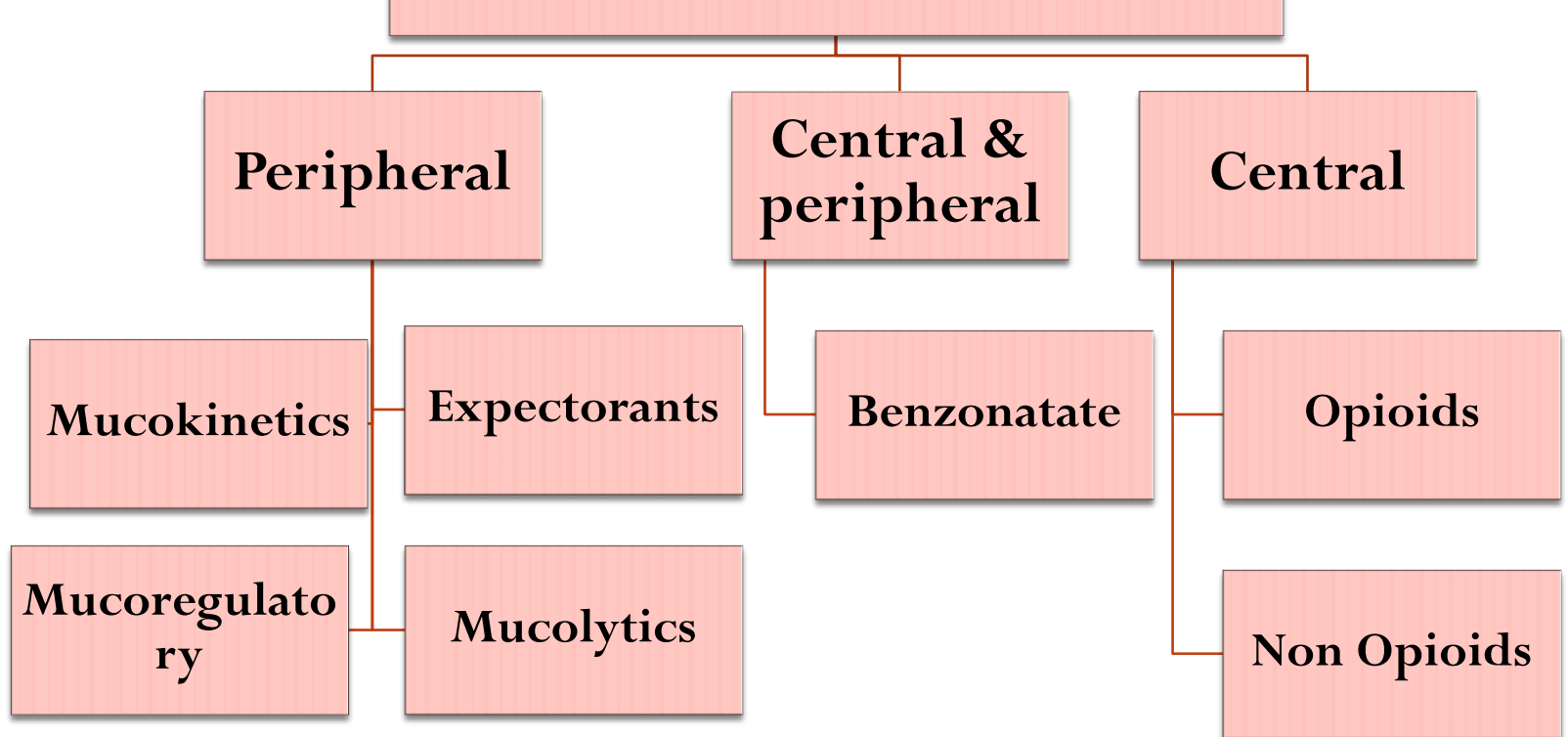
Antitussive drugs are useful

- A wet cough is a cough that produces mucus .
- May indicate a bacterial infection.

Expectorant is useful



Treatment of cough



A. Central acting antitussive drugs

Only for non productive cough

❖ **Opioid**

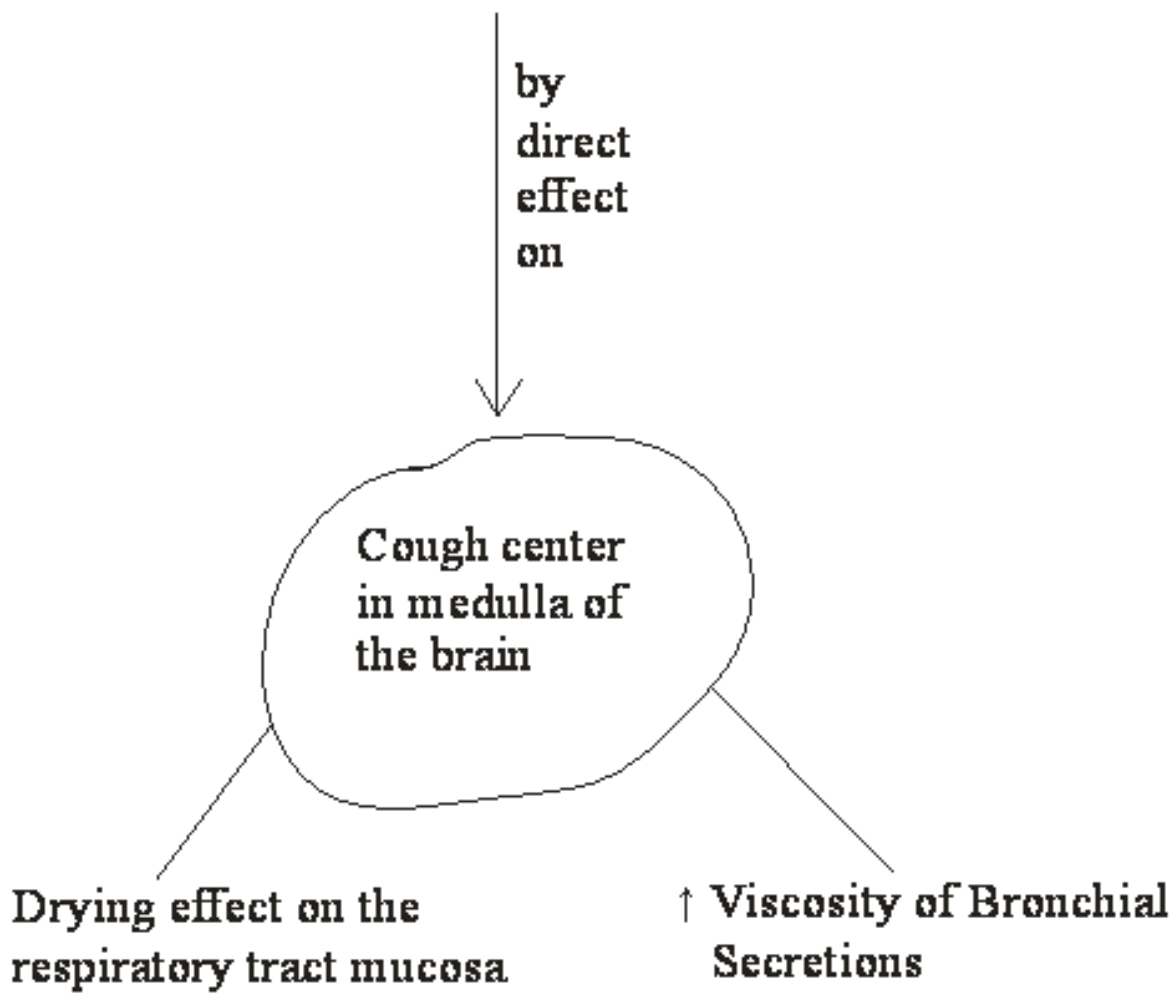
1. Codeine (methyldorphine) prodrug \Rightarrow metabolized to morphine.

- decreases the sensitivity of cough centers in the central nervous system to peripheral stimuli and decreases mucosal secretion.
- Side effect: constipation, dysphoria and fatigue.
- Potential cause of addiction.

Codeine mechanism of action

Lowering of the Cough reflex

by
direct
effect
on



Cough center
in medulla of
the brain

Drying effect on the
respiratory tract mucosa

↑ Viscosity of Bronchial
Secretions

Action of Codeine
(Jeepakistan.blogspot.com)

A. Central acting antitussive drugs

B. Dextromethorphan and pholcodine

- codeine analog.
- No analgesic effect.
- Low addictive profile.
- Mechanism of action: suppress the response of the central cough center.
- Side effects: dysphoria.
- **C-Morphine**
- used for palliative care in cases of lung cancer.

Antitussive agents

Acting peripherally

reduce the sensitivity of peripheral cough receptors to irritants

Acting Above larynx

- demulcents like lozenges and syrup (honey)
- form gelatinous protective and soothing coat on inflamed mucosa
- used for sore throat or pharyngitis.



Antitussive agents

Acting peripherally

Acting below larynx

- e.g. steam inhalation with or without menthol, eucalyptus or benzoin tincture)
- promote secretion of dilute mucus which protects inflamed mucosa.

Benzonatate **both centrally and peripherally**

- chemically related to local anesthetic such as procaine.
- Central  suppress cough center
- Peripheral  decreasing the sensitivity of stretch receptor.

Mucoactive agents

Mucus: secretion from goblet cells and submucous glands, composed of water, proteins and glycosylated mucins. The glycoproteins portion of the secretion is termed mucin.

Mucoactive agents: Any agent that help in airway clearance of mucus. These might act in one of the two ways:

- Increase ability to expectorate sputum or
- Decrease mucus hypersecretion.

Classification according to mechanism of action:

- I. Expectorants
- II. Mucolytics
- III. Mucokinetics
- IV. Mucoregulatory

Peripherally acting antitussive drugs

I. Expectorants

- Increase amount or hydration of airway secretions.
- e.g. Inhaled Na^+ or K^+ Iodide used in cystic fibrosis and bronchiectasis.
- e.g. **Guaifenesin** - inc. resp. sec. and dec. adhesiveness and surface tension of viscid sputum .
- used in chronic productive cough.

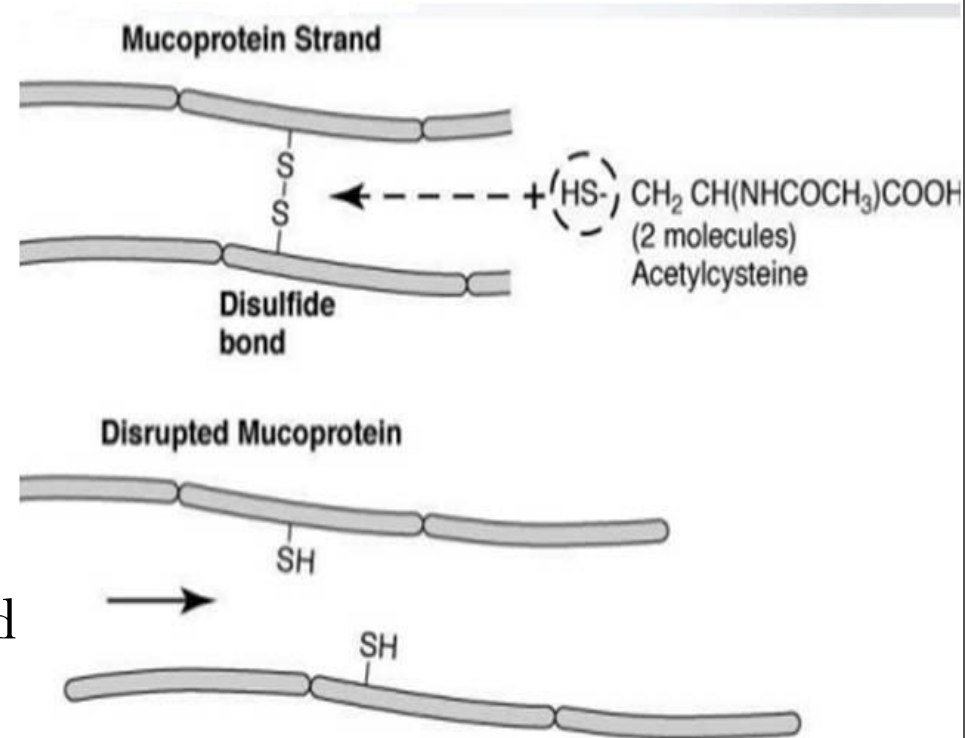
Mucolytics

- These decrease viscosity and elasticity of airway secretions and increase mucociliary or cough clearance. Main types:
- I. Classical mucolytics: Disrupt disulfide bond of mucin, break cross linkage. Ex. N acetyl cysteine (NAC), carbocysteine, methycysteine
- ii. Peptide mucolytics: Which lyses DNA acting polymer (derived from neutrophil). Ex. Dornase alpha.
- iii. Others: sodium bicarbonate.

Classical mucolytics

➤ **N- Acetyl cysteine:** Disrupt disulfide bond of mucin therefore both viscosity and elasticity of mucus lost.

- Effective orally or by inhalation (nebulisation).
- use in conditions associated with viscous mucus secretion such as chronic bronchitis and cystic fibrosis.
- Main adverse reaction is GIT irritation



B. Peptide mucolytics

- e.g **Dornase alpha** (recombinant human deoxyribonuclease).

- **Uses:** by nebulisation for **cystic fibrosis**

- **Mechanism of action:**

hydrolyzes the DNA present in mucus and reduces viscosity in the lungs. promoting clearance of secretions.

Adverse effects: allergic reactions

Other

I. Bromohexine

- It is an expectorant and mucolytic agent.
- Oral, parenteral and inhalation.
- Reduces viscosity of bronchial secretions by depolymerization of mucopolysaccharides as well as liberating lysosomal enzymes , network of fibers in tenacious sputum is broken.
- Used in acute and chronic bronchitis, COPD.
- AR: rhinorrhea, gastric irritation

II. Ambroxol is an active component of bromhexine –less gastric irritant

Mucokinetic agents

- increase mucociliary clearance

I. Increasing expiratory airflow: ex:bronchodilators

II. decreasing the surface adhesion between mucus and airway epithelium ex:surfactants.

Mucoregulatory agents

Decrease airway mucus hypersecretion by goblet cells and submucosal glands.

i. Antiinflammatory agents:

- **corticosteroids** decrease inflammatory stimulus that leads to hypersecretion.

ii. Anticholinergic agents:

- **Ipratropium** decreases volume secreted in chronic bronchitis.
- **Atropine** used preanesthetically decreases mucus hypersecretion due to endotracheal intubation.