

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Pharmacology of respiratory system

Treatment of cough

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ILOs

- 1- Classify the antitussive drugs.
- 2- Mention the mechanism of actions of antitussive drugs.
- 3- List the indications and adverse effects of antitussive drugs
- 4- Identify expectorants and mucolytic agents and recognize their uses.
- 5- Summarize the treatment of cough.

Introduction

- **Acute cough** is the most common symptom for which patients seek medical care for common cold. .
- Acute cough following an upper respiratory tract infection is usually **self-limited** but it could impair the quality of life and needs medical treatment.
- **Antitussive** drugs aims to stop the cough reflex pathway.
- In most patients, acute cough is caused by **upper respiratory tract infections, acute bronchitis or trachea-bronchitis** due to bacterial or, more frequently, viral infections.
- Severe cough may be complicated with sleep disruption, exhaustion, headaches, and dizziness. More seriously rib fractures, urinary incontinence, and vomiting could occur.

❑ The airway mucosa shows hyperplasia and hypertrophy, with mucus hyper-secretion in response to infection and inflammation.

❑ Products of inflammation (e.g. neutrophil-derived (DNA) and filamentous actin, bacteria, and cell debris) contribute to mucus purulence. Expecterated mucus is called sputum.

❑ Mucus is usually cleared by ciliary movement, and sputum is cleared by productive cough.

❑ The medications that affect mucus properties and promote secretion clearance are called “mucoactive agents” which include expectorants, mucolytics and mucokinetic drugs.

Types of cough

1. **Productive cough** (associated with sputum): it is controlled by **mucoactive agents** (expectorants, mucolytics, etc).
2. **Dry, or non-productive cough**: it is not associated with sputum and controlled by **antitussive drugs**.

N.B: Treatment of the cause of cough must take place beside antitussive and muco-active drugs.

N.B: Untreated chronic cough could cause many problems like piles, uterine prolapse, hernia, etc.

Antitussive drugs

Classification:

1-centrally acting antitussives:

➤ Narcotic antitussives (opioids)

➤ Non-narcotic

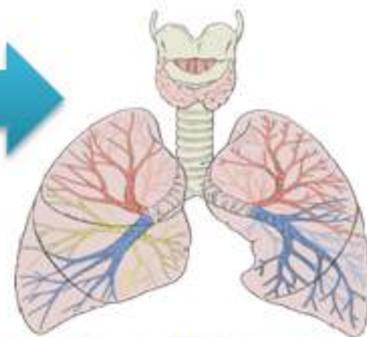
3-Peripherally acting antitussives.

4-Antihistamines

➤ Antitussives are drugs which decrease the frequency and severity of cough without impairing muco-ciliary defenses.



Inhibit cough center



Inhibit cough reflex

1-Narcotic antitussives

Examples:

1. Codeine

2. Hydrocodone

3. Morphine

- They activate central **opioid receptors** and **inhibit cough center**.
- These drugs are **potent analgesics**.
- They cause **euphoria** and may cause **dependence** and **addiction**.
- **Respiratory center depression** is the major side effect of these agents with high doses.
- These agents are used in **severe dry cough orally** .

2- Non-narcotic centrally acting antitussives

Examples:

1. Noscipine
2. Dextromethorphan
3. Benzonatate
- 4- Pipazetate (pipazethate)

- Have no analgesic effect
- They have little effects on opioid receptors
- Less dependence
- No euphoria
- No respiratory center depression.
- Used orally

1-Noscapine

A naturally occurring alkaloid with little dependence.

2- Dextromethorphan

- It is a **Synthetic codeine analog**.
- It antagonizes NMDA glutamate receptors.
- It has **mild opioid** effect when used in **excess doses**.
- Mild abuse potential.
- Dextromethorphan **has little toxicity** (respiratory center depression) compared to codeine.

3-Benzonatate

It inhibits cough center & pulmonary stretch receptors.

4-Pipazetate

Inhibits cough center and cough reflex

3 -Peripherally acting antitussives

Examples:

1. Inhaled **local anesthetics**

2. **Mucokinetics**

3. **Levodropropizine**

It is a non-opioid drug

It is a peripherally acting antitussive

It **inhibits the afferent** arm of the cough reflex arc itself by inhibiting vagal C-fibers (in the larynx, trachea, and bronchial tree).

4- First generation H1 blockers

- Antihistamines (like diphenhydramine) are **added to many cough and cold remedies** as both **antitussives** and to treat **rhinorrhea and nasal congestion**.
- Although some antihistamines may have an antitussive action, their clinical efficacy has not been well documented.
- The **anticholinergic** (atropine-like) action of antihistamines frequently causes a **drying sensation** in the **throat and nasal passages** and may result in **thickening of bronchial secretions**.

Uses of Antitussives

- 1- Cough due to **upper respiratory tract infections**.
- 2- Cough due to **chronic bronchitis**.
- 3- Cough due to **inoperable lung cancer**.
- 4- Used in cases in which an unproductive **cough interferes with sleep** or causes exhaustion.

NB: use of cough suppressants in children under six years of age should be avoided due to its safety profile.

Cough mixtures

Cough mixtures may be a combination of different active ingredients for treating cough which may include:

1-Antitussives

2-Antihistamines

3-Mucoactive agents (mucolytic, expectorants, or mucokinetics).

4-Natural antitussive agent like honey, ginger, Peppermint, Thyme, licorice root and others.

Mucoactive agents

1-Expectorants

Expectorants facilitate expulsion of mucous (making it easier to cough up) by making it less sticky to mucosal cells.

Examples: **Ammonium chloride** & **guaifenesin**

Guaifenesin acts through Increase the volume of watery airway secretions (so, reducing viscosity) of airway secretions and sputum.

2-Mucolytics

Drugs which degrade polymers in sputum.

1-N-Acetyl Cysteine: disrupts disulfide bond within the mucus glycoproteins making **mucus thinner** and easier to be expelled.

2- Dornase alfa (DNAse): ↓ leukocyte debris by degrading DNA polymers.

3-Bromhexine: it loosens and thins bronchial secretions by reducing surface tension and viscosity of mucus.

4- Ambroxol: Ambroxol might **stimulate surfactant secretion** and used in Europe (but not in USA and Canada) and other countries for the management of chronic bronchitis .

Uses of mucolytics:

1. Increases clearance of respiratory secretions (e.g., **common cold, pneumonia, COPD**).
2. N-acetylcysteine and DNase are used in **cystic fibrosis**.
3. N-acetylcysteine is used **for acetaminophen** overdose and hepatotoxicity.

Side effects of mucolytics:

- 1) GIT irritation (when given orally oral).
- 2) Burning sensation in airways (when given by inhalation).
- 3) Bronchospasm (when given by inhalation).
- 4) Allergic reactions.

3- Mucokinetic agents

Drugs that facilitate the removal of secretions from the respiratory tract by stimulating ciliary action

Examples:

1-Beta-2 adrenergic agonists (e.g. salbutamol) and Methylxanthines (e.g. aminophylline).

They are bronchodilators and increase ciliary movements.

2- Ambroxol

3- Surfactant

Thank you

