



Pharmacological treatment of acute & chronic Rhinitis

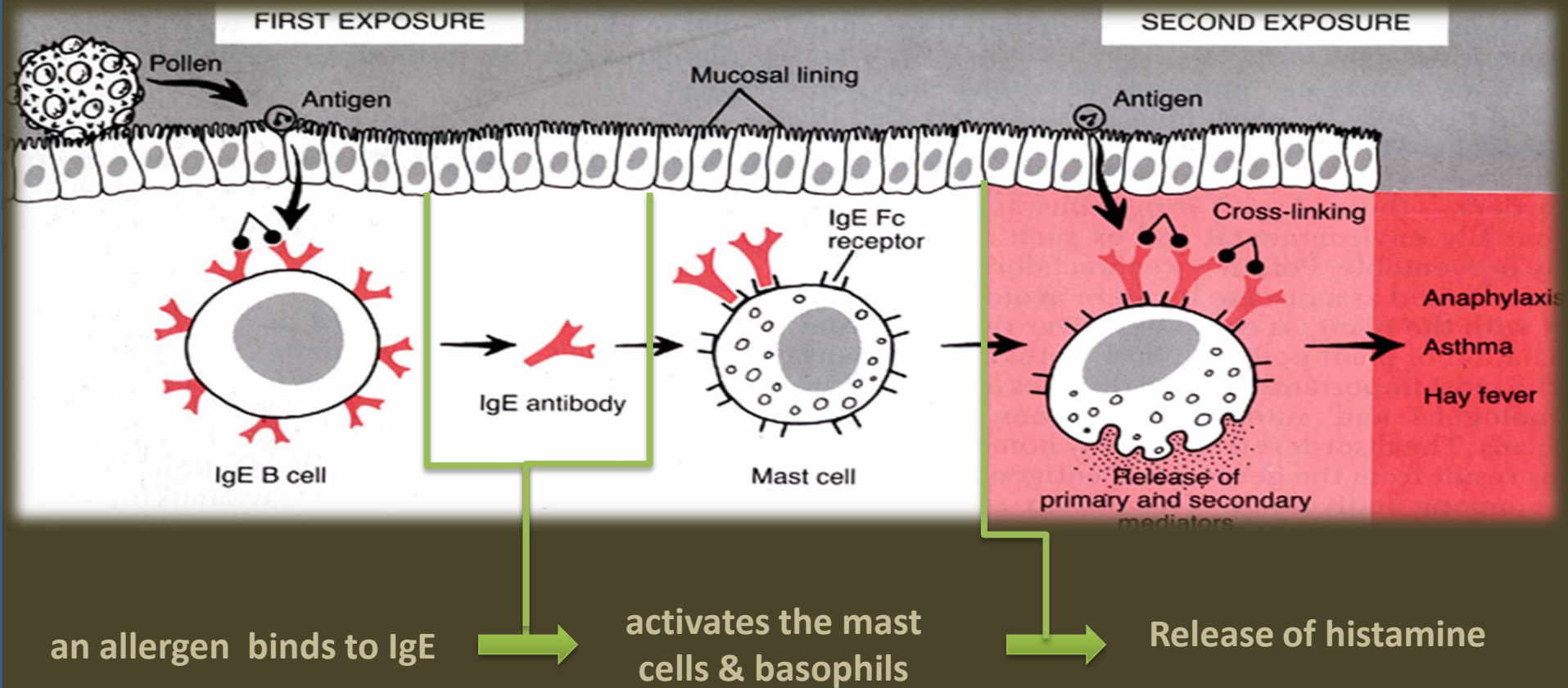
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Allergy: is a hypersensitivity reaction of the antibody class IgE



histamines lead to inflammatory responses ranging from runny nose to anaphylactic shock.

RHINITIS: A swelling & inflammation (mediated by IgE) of mucous membrane of the nose, eyes, ears, sinuses, & throat can also be involved.

Rhinitis

Symptoms

- 1) Runny nose (rhinorrhea)
- 2) Sneezing.
- 3) Itchy nose / eyes.
- 4) Stuffiness.

Causes

- 1) Cold .
- 2) Allergies .

Attack may be precipitated (تسرع) by inhalation of an allergen (dust, pollen, animal dander) .



1) Acute Rhinitis (7-14 days)

- Short lived
- Results from viral infections OR allergies
- Symptoms: runny nose, sneezing, congestion, post nasal drip, cough & low grade fever .

2) Chronic Rhinitis (> 6 weeks)

- Long- standing
- extension of rhinitis caused by inflammation or an infection & usually occurs with chronic sinusitis (inflammation in the paranasal sinuses)

Treatment of Rhinitis

Non-pharmacological therapy

- Avoidance of irritants .
- Dusting/vacuuming.
- washing of bed sheets .
- Intake of fluids .
- Rest .

Pharmacological therapy

1\ Antihistamines (H1 receptor antagonists) FOR sneezing & rhinorrhea .

2\ α -Adrenergic agonists AS decongestant .

3\ Corticosteroids AS anti-inflammatory .

4\ Cromolyn AS a prophylaxis . وقاية من المرض

5\ Antibiotics (not relieve symptoms of rhinitis)

6\ Leukotriene receptor antagonists (Montelukast).

What is Histamine..?

It is a neurotransmitter synthesized from histidine and produced by mast cells & basophils .

	Location	Type of receptor	Effect	Treatment
H1	Throughout the body, specifically in smooth muscles, vascular endothelial cells, heart & CNS	G-protein coupled, linked to intercellular Gq, which activates phospholipase C	Mediate an increase in vascular permeability at sites of inflammation induced by histamine	Allergies, nausea, sleep disorders
H2	In more specific locations in the body mainly in gastric parietal cells, low level can be found in vascular smooth muscle, mast cells, neutrophils, CNS, heart, uterus	G-protein coupled, linked to intercellular Gs	Increases the release of gastric acid	Stomach ulcers

Effects of Histamine

CVS	vasodilatation → ↓ B.P → ↑ Permeability → Edema
GIT	<ul style="list-style-type: none"> • stimulation of H1 : Contraction of smooth muscles . • stimulation of H2 : ↑ Acid production + ↑ intestinal secretion
Respiratory tract	stimulation of H1 : Bronchoconstriction
CNS	<ul style="list-style-type: none"> • Stimulation of H1: maintenance of wakeful states. • Stimulation of H1 & H2 : causes pain & itching by stimulation of peripheral nerve endings

Effects of histamine: # (intra-dermal injection)

triple response { 1. Red spot: due to capillary dilation
 2. Edema: due to exudation of fluid
 3. Flare formation: due to arteriolar dilation

itching may accompany these effects

Toxicity of histamine:

flushing, hypotension, tachycardia, headache, bronchoconstr. & GI upset.

Treatment of Rhinitis:-

1- Antihistamines:

They block H₁ receptors (reversible, competitive antagonists) of histamine.

Used locally/ orally.

Properties of Antihistamines

1st generation drugs

- lipid soluble .*
- easily cross into brain .*
- produce sedation & drowsiness .*

2nd generation drugs

- less lipid soluble .*
- not significantly pass into brain .*
- do not cause sedation & drowsiness.*

اسم العائلة غير مهم

اسم الدواء مهم جداً

1st Generation Drugs

1) Ethanolamine	e.g. Diphenhydramine, dimenhydrinate
2) Piperazine derivatives	e.g. Cyclizine, meclizine
3) Alkylamines	e.g. Chlorpheniramine
4) Phenothiazine derivatives	e.g. Promethazine
5) Miscellaneous (other drugs)	e.g. Cyproheptadine

2nd Generation Drugs

1) Piperidine	e.g. fexofenadine
2) Miscellaneous	e.g. Loratadine= Claritin® (longer acting), Cetirizine

Pharmacokinetics

- 1\ Rapid absorption
- 2\ Wide distribution
- 3\ metabolized by microsomal systems in liver (CYP_{3A4} system)
- 4\ 1st generation = 4-6 hours duration of action (except Meclizine)
2nd generation & (Meclizine) = 12-24 hours duration of action

Mechanism of action (MOA):

Inhibition of H₁- receptor.

however, **Many** of the **1st generation** drugs have effects that are **not** mediated by **H₁-receptors**, means they effect other receptors as:

- 1\ antimuscarinic
- 2\ α -adrenoceptors blocking
- 3\ serotonin receptors antagonism
- 4\ local anesthetic

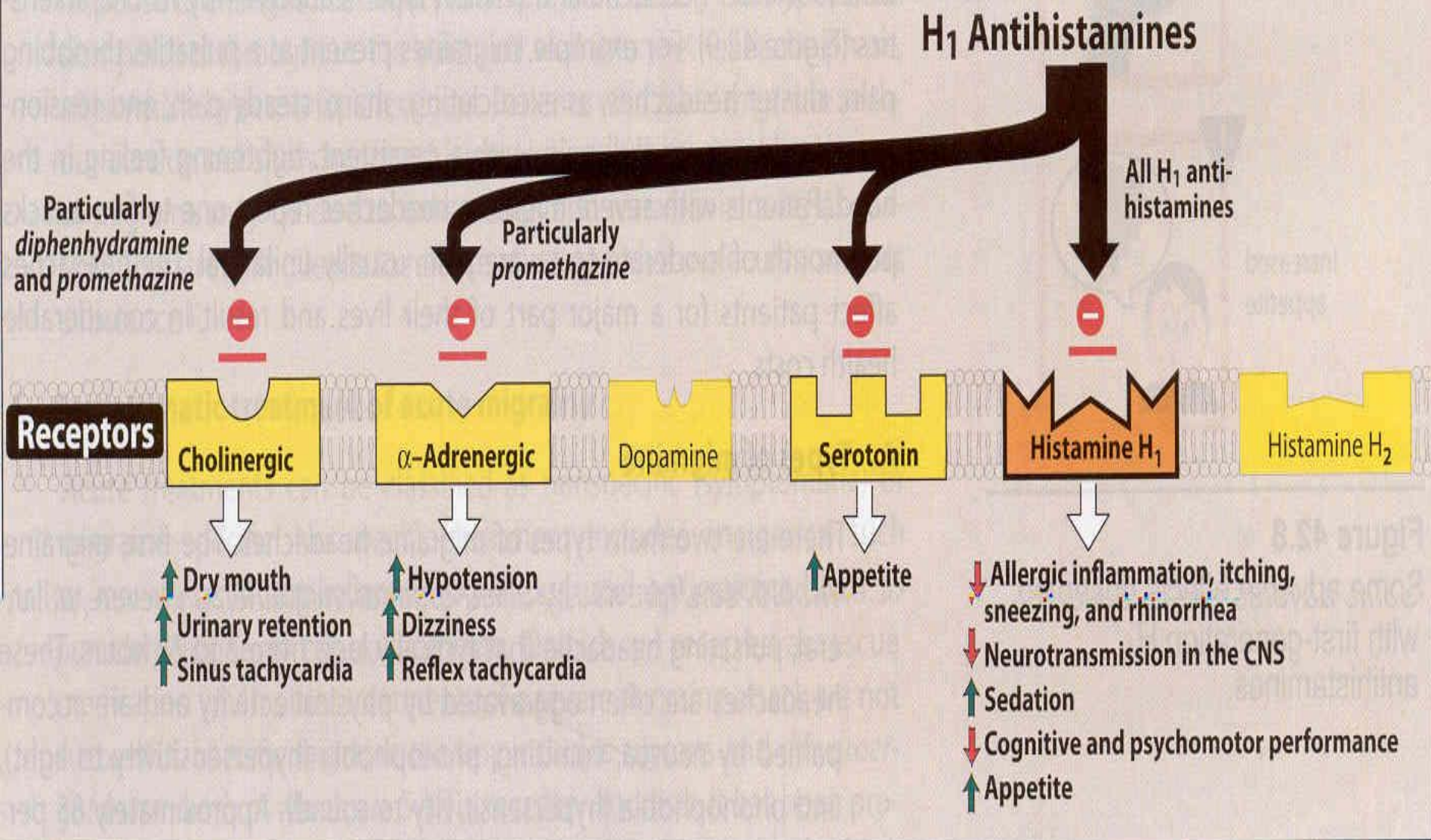


Figure 42.7

Effects of H₁ antihistamines at histamine, adrenergic, cholinergic, and serotonin-binding receptors. Many second-generation antihistamines do not enter the brain and, therefore, show minimal CNS effects.

Pharmacological actions

+ by acting on H₁ receptors +

1- Sedation

1st generation drugs

Common effect

Useful as “sleep aid” & unsuitable for daytime use.

(promethazine ↑) this is a drug that has the most (sedation) effect comparing with other 1st G-drugs

2nd generation drugs

little or no sedating effect.

2- Antinausea & Antiemetic actions (يمنع القيء)

1st generation drugs: significantly prevent motion sickness.

3- Antiparkinsonism effects (يخفف اعراض مرض باركنسون)

1st generation drug: (diphenhydramine)

4-Other actions

2nd generation drug: (cetirizine) it inhibits mast cell release of histamine & some other mediators of inflammation so it's useful for the treatment of allergies.

Pharmacological actions

+ by acting on other receptors +

1- Anticholinceptor actions

1st generation drugs: (diphenhydramine & dimenhydrinate)

2- Alpha- adrenoceptor blocking actions

1st generation drug: (Promethazine) cause hypotension.

3-Serotonin blocking actions

1st generation drug: (Cyproheptadine) is an antiserotonin agent

4-Local anesthesia

1st generation drugs: (diphenhydramine & promethazine) by blocking Na^+ channels in excitable membranes

Clinical Uses

- 1- Allergic reaction.
- 2- Nausea & vomiting (Many 1st generation)
- 3- Motion sickness & vestibular disturbances (meniere's syndrome)
Many 1st generation with antimuscarinic activity.
- 4- sleep aid.

Adverse Effects

- Antimuscarinic effects

1st generation drugs: dryness of mouth, blurring of vision, retention of urine, constipation & ↓sweating

- α -Antagonist effects

1st generation drugs: hypotension

- CNS

1st generation drugs: sedation but may cause mental agitation & convulsion (toxic doses)

- Tolerance after prolonged administration.

2\ α -Adrenergic agonists (AS decongestant)

A- Short acting α -adrenergic agonist

constrict dilated arterioles in nasal mucosa, suppress swelling & ↓ airway resistance

e.g., pseudoephedrine

B- Longer acting

e.g., oxymetazoline

C- Alpha agonists + antihistamine

e.g., loratadine or fexofenadine + pseudophedrine

(Alpha agonists should not be used for longer time bec of rebound nasal congestion)

يعني لاتستخدمها اكثر من ثلاث ايام لانها ممكن ترجع لك الاحتقان

3\ Corticosteroids

AS anti-inflammatory .

Used to treat allergic nasal obstruction & chronic rhinitis (reduce: sneezing, itching, rhinorrhea & congestion).

Topical steroid sprays

e.g., beclomethasone, budesonide, fluticasone, flunisolide & triamcinolone.

Side effects:

Localized to intranasal (nasal irritation, nose bleed, sore throat, candidiasis) Due to the anti-inflammatory & immunosuppressive effect of steroids .

(Topical steroids more effective compared to systemic antihistamines for allergic & non allergic rhinitis)

4\ Cromolyn AS a prophylaxis

Antiinflammatory drug & Mast cell stabilizer

(prevent release of histamine & other mediators from mast cells)

Intranasal cromolyn= useful particularly as prophylactic when given before (1 to 2 weeks) contact with allergen

The only drug that work as a prophylaxis.

Effects:

Reduced allergic rhinitis & conjunctivitis

Reduces nasal pruritus, sneezing, rhinorrhea & congestion



Cough

Physiological Cough (Productive Cough)

With sputum

Is a protective reflex mechanism that removes foreign materials & secretions from the bronchi & bronchioles.

Unproductive Cough (dry cough)

Without sputum

occurs due to exposure to irritant vapors or gases or due to pathological conditions as chronic bronchitis.

Coughing can be provoked by:

Common cold

Pneumonia & pulmonary embolism

Asthma

Smoking

Gastroesophageal reflux

ACE inhibitors

Bronchitis.





Cough medicines

-cough suppressants

(for a dry cough)


-expectorants طارد للبلغم

(for a wet, productive cough that brings up mucous) are available OTC & by prescription.

Coughs

-Acute(not lasting longer than 2 -3 weeks)

-chronic (lasting longer than 4 weeks)



A productive cough should not be suppressed except •
in special circumstances (eg, when it exhausts the
patient or prevents rest & sleep) & generally not until
the cause has been identified.

An acute infection such as pneumonia may require •
antibiotics, an asthma-induced cough may be treated
with the use of bronchodilators, or an antihistamine
may be administered in the case of an allergy.

Pharmacological therapy



Antitussives (for dry cough.)

Expectorants

Mucolytics



Antitussives

central

- 1 - Narcotic analgesics .
- 2 - Synthetic narcotic analgesics .
- 3 - Antihistaminics (H₁-Blockers) .

Peripheral

- 1 - Demulcents .
- 2 - Local Anesthetics .
- 3 - Humidifying Aerosols .
- 4 - Steam Inhalations .



Narcotic analgesics

Are drugs used to suppress dry cough, used in doses below those required for pain relief.

Codeine (methyl-morphine)

opiate with less addiction liability.

Potent antitussive

Weak analgesic.

MOA

Suppress cough by **inhibiting** release of excitatory neuropeptides thru stimulation of μ receptors.

Side Effects

- 1- Constipation.
- 2- Inhibition of mucociliary clearance (thick sputum).
- 3- Decrease secretions in the bronchioles
- 4- Drowsiness & mild respiratory depression
- 5- Dependence.
- 6- Dry mouth.





Centrally acting:
2 - Synthetic narcotic analgesics

Dextromethorphan :

- 1- As potent as codeine.
- 2- No drowsiness. لا يسبب النعاس
- 3- Less constipating effect. لا يسبب الإمساك
- 4- No respiratory depression.
- 5- No inhibition of mucociliary clearance.
- 6- No addiction. لا يسبب إدمان

Contraindicated in :

chronic bronchitis

cough associated with asthma

(harmful sputum thickening & retention).

3 - Antihistaminics (H1-Blockers)

Diphenhydramine, Triprolidine.

Side Effects :

Anticholinergic actions

Sedation

Drowsiness

يسبب النعاس

Antitussives are
used for dry
cough



Second : Peripherally Acting Antitussives

Act on either the afferent or efferent side of the cough reflex.

1 -Demulcents

are (agents that form a soothing film (protective coating) over the irritated pharyngeal mucous membrane, relieving minor pain & inflammation of the membrane).

More explaining: These demulcents will coat the throat and relieve the irritation causing the cough.

*** Useful for coughs originating above the larynx**

They are usually given as syrups or lozenges & include acacia, licorice, glycerin, honey, & wild cherry syrups.

2 - Local anesthetics :

(lidocaine, benzocaine, and tetracaine) are used to inhibit the cough reflex in special cases such as before bronchoscopy or bronchography

Benzonatate: a congener of tetracaine, is a local anesthetic; its antitussive effect may be due to a combination of local anesthesia & depression/decrease sensitivity of pulmonary stretch receptors.

More explaining : Benzonatate is thought to act as a local anesthetic, decreasing the sensitivity of stretch receptors in the lower airway and lung, thereby reducing the drive to cough after taking a deep breath.

Stretch receptors are mechanoreceptors responsive to distention of the thorax, which are neurologically linked to the medulla via efferent nerve cells, joining them to the expiratory cells present there. Stretch receptors are also found in other organs and muscles, such as bowel wall.



3 - Humidifying aerosols and steam inhalations :

exert an antitussive effect by acting as a demulcent & by decreasing the viscosity of bronchial secretions

Inhaling water as an aerosol or as steam, with or without medicaments (sodium chloride, compound benzoin tincture, eucalyptol), is the most common method of humidification

Expectorants

- Drugs that aid in the expectoration (removal) of mucus & exudates from the respiratory passages by cough.
- Reduce the viscosity of secretions
- Disintegrate & thin secretions.

Mechanism of action:

Reflex stimulation

Agent causes irritation of the GI tract
Loosening & thinning of respiratory tract secretions occur in response to this irritation
Example: **guaifenesin**

Direct stimulation

The secretory glands are stimulated directly to increase their production of respiratory tract fluids
Examples: **iodine-containing products such as iodinated glycerol & potassium iodide.**

Final result: thinner mucus that is easier to remove.

Drug Effects

By loosening and thinning sputum and bronchial secretions, the tendency to cough is indirectly diminished.

Classification

1. Sedative Expectorants

They increase the fluidity of sputum & its expulsion by cough.

These drugs are used in chronic inflammation of respiratory mucosa (chronic bronchitis).

Examples: Potassium citrate, potassium acetate, Ammonium chloride, ipecacuanha, Na & K iodide, Guaiacol.

Guaifenesin

2- Stimulant expectorants

These drugs are used in chronic inflammation of respiratory mucosa

(chronic bronchitis).

Stimulating reflex expectorants in which person vomit thus ejecting the mucus & phlegm. They promote healing & repair of mucosal tissues.

thins the mucus which helps the body to cough it up.

e.g. terpene hydrate.

Mucolytics:

- Acts by reducing the viscosity of sputum.
- Acetyl cysteine (interfering with disulphide bonds in mucus).
- Bromohexine (destroy muco-polysaccharride structure of mucus).
- Steam inhalation

More explaining : An expectorant increases bronchial secretions and mucolytics help loosen thick bronchial secretions. Expectorants reduce the thickness or viscosity of bronchial secretions thus increasing mucus flow that can be removed more easily through coughing, Mucolytics break down the chemical structure of mucus molecules. The mucus becomes thinner and can be removed more easily through coughing

Uses :

Acute & chronic bronchitis
Asthma.