Pharmacology Team

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Red	**Important**
Purple	Extra Notes
Orange	General Explanation
Black	From the slides

Objectives

- Classify types & causes of rhinitis
- Specify preventive versus pharmacotherapeutic strategies
- Expand on the pharmacology of different drug groups used in treatment as antihistamines, anti-allergics, corticosteriods, decongestants and anti-cholinergics
- Differentiate between productive versus dry irritant cough
- Compare pharmacology of different expectorants & mucolytics drugs used in treatment of productive cough
- Contrast between peripherally and centrally acting antitussives

RHINITIS:

Irritation &/or inflammation of the mucous membranes inside the nose.

Irritation:

It could be irritate from:
Environment ,
Drug induced,
Dietary factors,
Sexual / Hormonal /
Emotional triggers
Foreign body / Trauma /
Structural Derangement.

inflammation:

- Non-Allergic:
  - In Certain season → Seasonal
  - Infectious:
    - -virus
    - - Bacteria
    - - Fungi
  - Non-Infectious:
    - - Environmental
    - - Drug inducer
    - - Food
    - - Hormonal
    - - Srtuctural derangement
- Allergic:
  - Seasonal
  - Perennial → Like cat allergy

Details…

Inflammation

Allergic:
High fever

1st exposure → **sensitization & Antibodies production.**

2nd exposure → **Hypersensitivity.**

ACUTE RHINITIS **(7- 14 DAYS)**

CHRONIC RHINITIS **(> 6 WEEKS)**

Non-Allergic:

Environmental;

-Airborne irritants; Smoke/ Strong odors/ Certain gases, Industrial pollution [Occupational]

-Non-irritants; cold / dry / air conditions → parasympathetic stimulation → change (Vasomotor) blood flow → Vasomotor

Drug-induced → Rh. Medicamentosa

Excess long term use of decongestants & nasal corticosteroid sprays → rebound congestion

Use of anti-hypertensives, anti-inflammatory, anti-anxiety, …

Food; Gustatory

Hormonal

Structural Derangement

اذا كان المرض
فالاساس سيستيميك و
جت معاه احد من
هذي الاعراض

Symptoms:

Runny nose (rhinorrhea)
Stuffy Blocked nose
Sneezing
Nasal congestion
Post-nasal drip
Itching
Catarrh

Sometimes with: systemic Manifestation

RHINITIS

TREATMENT

PREVENTIVE THERAPY

1- Environmental Control
2- Allergen Immunotherapy

PHARMACOTHERAPY

1- H_1 receptor antagonists; Antihistamines
2- Anti-allergics
   - Mast Cell Stabilizer; Cromolyn
   - Leukotriene receptor antagonists; Montelukast
3- Corticosteroids
4- Decongestants; α-Adrenergic agonists
5- Anticholinergics
6- Antibiotics
7- Mycolytics…..

} In infection, with chronicity & more if it is rhinosinusitis

1) ANTI-HISTAMINES: H1 RECEPTOR BLOCKERS ; All are used systemic or topical

Chemical / Functions	1st Generation	2nd Generation	3rd Generation
ALKYLAMINES	Chlorpheniramine		
ETHANOLAMINES	Dimenhydrinate Diphenhydramine		
ETHYLENEDIAMINES	Antazoline		
PHENOTHIAZINES	Promethazine		
PIPERAZINE	Cyclizine	Cetirizine	Levocetirizine
PIPERIDINES	Azatidine Ketotifen	Astemazole, Terfenadine	Fexofenadine
MISCELLANEOUS	Cyproheptadine	Loratidine	Desoloratidine

Short duration
Interactions; with enzyme inhibitors
[macrolides, antifungals, calcium antagonists]
ADRs due to additive pharmacodynamic actions

Longer duration = better control
No drug interactions & minimal ADRs

Red: Important to memorize
Yellow background: Strong sedating , Green Background: Anti-Allergic Effect,

Details…

ANTIHISTAMINIC ACTION

	1sr Generation	2nd generation	3rd Generation
Selectivity	Non selective	Selective	More Selective
BBB	Lipophylic Cross BBB SEDATING	Non-lipophylic Poor cross BBB NON-SEDATING High efficacy "ANTIALLERGIC" Little/Major Side effects.	NON-Lipophylic NOT cross BBB NON-SEDATING Higher efficacy ANTIALLERGIC. RARE side effects.

Itching + Insomnia
Sleep aid Vertigo
Anxiety..

In children:
inappropriate dose can lead to :
Excitation, Agitation, Convulsions

Allergies
Are "drying agents"; ↓ secretions & localized inflammation
Act more on Upper and of limited effect on lower airway

Going to talk about (1st GENERATION)
Because:

- it has side effects and we are going to use its side effects AS (**THERAPUTIC**)

GOOD CONTROL of Rhinitis, Conjunctivitis, Urticaria, Flu (cough & sneezing) — Successful

POOR CONTROL of Asthma, Otitis, Anaphylaxis, Sinusitis, Atopic dermatitis — Poor

Important

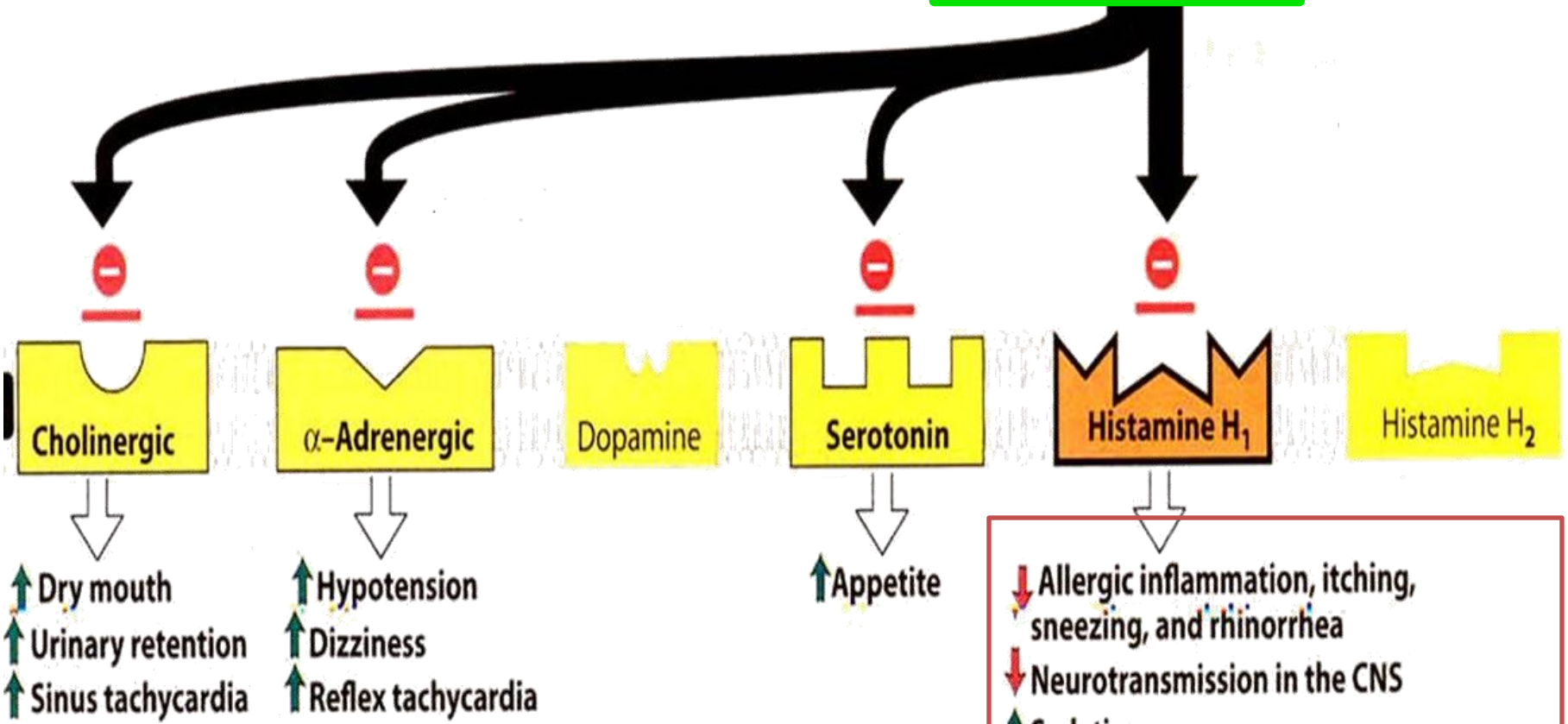
Indications linked to H1 blockers:

Allergey	-
Itching	Even not allergic
Others	Insomnia , sleep , aid vertigo , anxiety

Indications not linked to H1 blockers:

INDICATIONS not linked to H1 block

ANTIHISTAMINES



Side Effects
Interactions

Side Effects
Interactions

Side Effects
Interactions

Vertigo & Motion sickness	**Dimenhydrinate**, **Diphenhydramine**, **Promethazine**↓ firing from internal ear to vomiting center
Anti-emetic	**Promethazine** ↓ firing to vomiting center + Anticholinergic
Anticholinergic	**Chlorpheniramine**, **Dimenhydrinate** , **Promethazine** ↓ Extra-pyramidal effect [Antiparkinsonism] Vasoconstriction [non-inflammatory Rhinitis]
α-Adrenergic Block	**Promethazine** Orthostatic hypotension
5-HT modulation	**Cyproheptadine** ↑Appetite [Increase Appetite] ↑Sedation Prophylactic for Migraine
Na-Channel blocker	**Promethazine** , **Antazoline** Local anesthetic action / Anti-arrhythmic?

مانتعمق فيه بس نعرف < انها تصنف ضمن الاكشن الي h1مو متعلقه في blocker

2-ANTI-ALLERGICS

- CROMOLYN & NEDOCROMYL

↓ Histamine release [mast cell stabilizer by inhibiting Cl channels] i.e. can act only prophylactic but once released it does not antagonize its action Used more in children for prophylaxis of perennial allergic rhinitis [nasal drops] > than allergic or exercise induced asthma [as inhaled powder or neubilized solution] Should be given on daily base and never stop abruptly.
Can induce cough, wheezes, headache, rash, …etc.
Action : upper airway > lower airway

- LEUKOTRIENE RECEPTOR ANTAGONISTS

Block leukotriene actions
For prophylaxis of lower respiratory [i.e perennial allergen, exercise or aspirin-induced asthma] > upper respiratory allergies [chronic rhinosinusitis]
ADRs; as in asthma

3-CORTICOSTERIODS:

Anti-inflammatory → blocks phospholipase A_2 →
↓arachedonic a. synthesis → ↓ prostaglandins & leukotrienes
Topical; steroid spray; beclomethasone, budesonide, & fluticasone
Given if severe intermittent or moderate persistent symptoms
ADRs; Nasal irritation, fungal infection, hoarseness of voice

4. DECONGESTANTS:

α-Adrenergic agonists →For treatment of nasal stuffiness

PSEUDOEPHEDRINE

Systemic:
Can cause nervousness, insomnia, tremors, palpitations, hypertension.
Better avoided in hypertension, heart failure, angina pectoris, hyperthyroidism glaucoma.

(يعمل manifestation of sympathetic actions)

Topical :

PHENYLETHYLAMINES

- Phenylephrine
- Methoxamine

IMIDAZOLINE

- Naphazoline
- Oxymetazoline HCl
- Xylometazoline HCl

But can cause **Rebound** nasal stuffiness
(repeated administration (10 days -2 weeks)

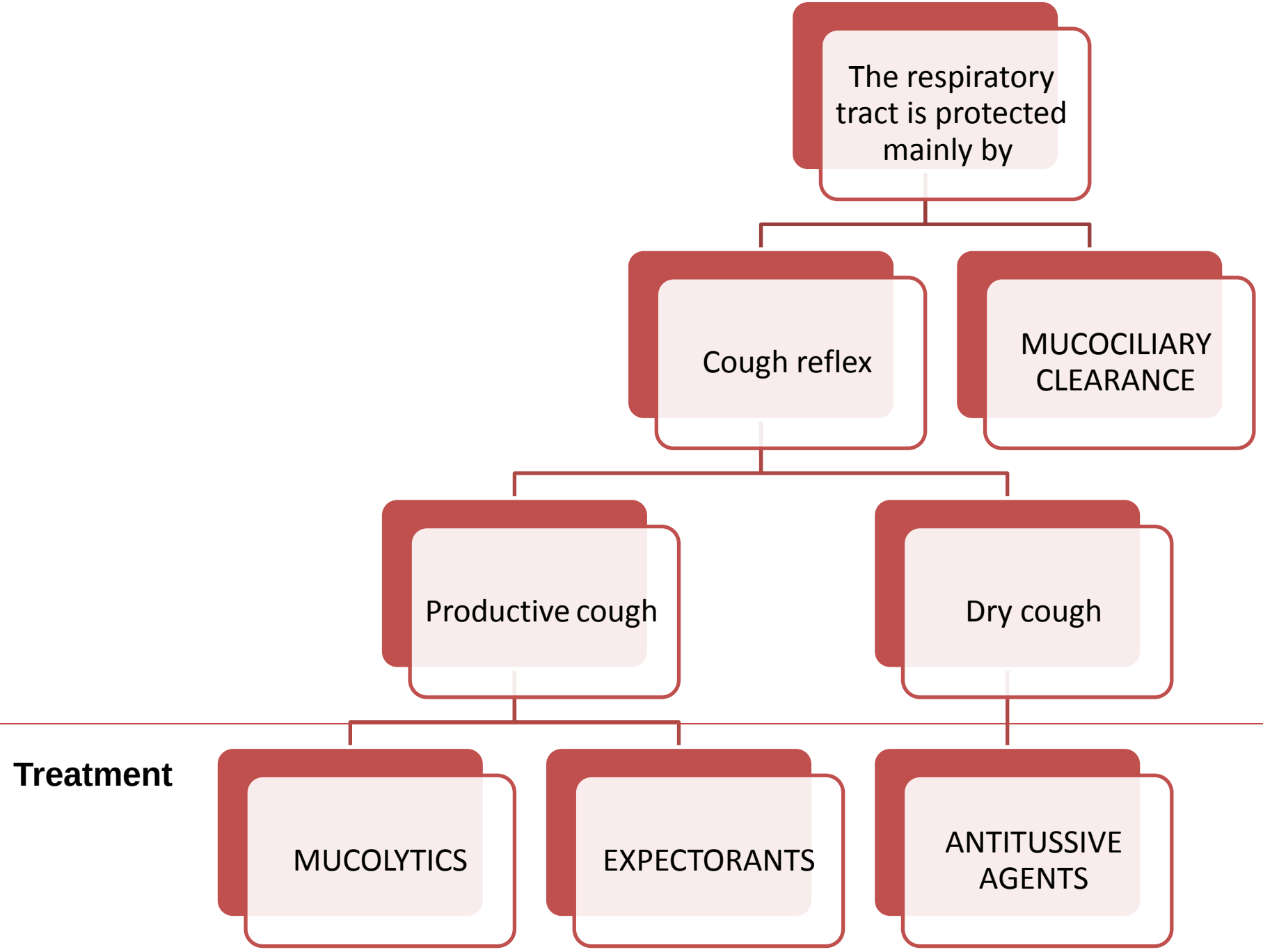
5. ANTICHOLINERGICS

Ipratropium

Given as nasal drops to control rhinorrhea (excess nasal secretion & discharge) So very effective in vasomotor rhinitis (watery hyper-secretion).

Its indication as bronchiodilator in asthma and ADRs ➔ see asthma

Drug used in Treatment of COUGH


The respiratory tract is protected mainly by
Cough reflex
MUCOCILIARY CLEARANCE
Productive cough
Dry cough
Treatment
MUCOLYTICS
EXPECTORANTS
ANTITUSSIVE AGENTS

EXPECTORANTS **Act by removal of mucus BY**

1/ Reflex stimulation

Guaifenesin

Irritate GIT by stimulate gastropulmonary vagal reflex

Adverse effect

risk of kidney stones due to increase uric acid excretion

2/Direct stimulation

Stimulate secretory glands it will increse respiratory fluids production by Iodinated glycerol, Na or K iodide / acetate , Ammonium chloride, Ipecacuahna

Adverse effect

Hyperthyroidism

Indication

- Common cold
- Bronchitis
- Laryngitis
- Pharyngitis
- Influenza
- Measles
- Chronic paranasal sinusitis
- Pertussis

MUCOLYTICS

Act by altering biophysical quality of sputum➔ becomes easily exhaled by mucociliary clearance or by less intense coughing

Note / Will dissolve the mucosa and make it easily to remove.

MECHANISM OF ACTIONS

1/ Decrease the Viscoelasticity by increase water content.
Drug : Hypertonic Saline & $NaHCO_3$ (sodium bicarbonate).

2/ decrease Adhesivness by Steam inhalation

يقلل الالتصاق عن طريق استنشاق البخار

3/ Breakdown S-S bonds in glycoproteins by its reducing SH Gp ➔ less viscid mucous.

Note / Will breakdown the SH group on the polysaccride (which the mucosa is made of) so it will change its structure and will be easily to exhaled

Drug: N-Acetyl Cysteine

4/ Synthesize serous mucus (sialomucins of smaller-size) so it is secretolytic + activate ciliary clearance & transport;

Drugs: Bromohexine & Ambroxol

Note/ Change the mucosa secretion to water secretion

CONT.

5/ Cleavage of extracellular bacterial DNA, that contributes to viscosity
of sputum in case of infection
Drug : rhDNAase (Pulmozyme)
Note/ in case of infection like (cystic fibrosis). The drug will breakdown the DNA of the bacteria.

Indication :
COPD
Asthma
Bronchitis
(in excessive or / and the mucus production)

1. N-ACETYLCYSTEINE

as dissolved powder taken orally.

A mucolytic & a free radical scavenger → used in acetominophin overdose

Adverse effect
1. Bronchospasm
2. Stomatitis
3. Rhinorrhea
4. rash,
5. nausea
6. vomiting

2. BROMHEXINE & ITS METABOLITE AMBROXOL

as tablets or nebulized solution.

Increase immuno defence mechanism . ↓ dis. duration
Long-term use → less antibiotics used for treatment of exacerbation.

Ambroxsol is also → very potent inhibitor of neuronal Na channels → decrease pain in acute sore throat (fast onset & long duration)

Drug	Guaifenesin	Iodinated glycerol, Na or K iodide / acetate , Ammonium chloride, Ipecacuahna	N-Acetyl Cysteine	Ambroxol	rhDNAase (Pulmozyme)
Type of teatment	EXPECTORANTS	EXPECTORANTS	MUCOLYTICS	MUCOLYTICS	MUCOLYTICS
	Reflex stimulation	Direct stimulation	breakdown the SH group on the polysaccride	Change the mucosa secretion to water secretion	breakdown the DNA of the bacteria
Side effect	kidney stones	Hyperthyroidism	Stomatitis rash	Rhinorrhea Lacrymation gastric irritation hypersensitivity	Voice changes Pharyngitis Laryngitis rhinitis chest pain fever rash
Indication	1/Common cold 2/Bronchitis 3/Laryngitis 4/Pharyngitis 5/Influenza 6/Measles 7/ Chronic paranasal sinusitis		COPD Asthma Bronchitis (in excessive or / and the mucus		cystic fibrosis (CF) Sever repiratory infection

ANTITUSSIVE AGENTS : (dry cough)
stop or Reduce the cough by acting on either peripheral (bronchi)
or act on CNS (cough center)

PERIPHERALLY ACTING ANTITUSSIVES

Drug	Tincture benzoin compound & Eucalyptol	Lidocaine, Benzocaine, and Tetracaine	Benzonatate
	Inhibitors of airway stretch receptors	Inhibitors of airway stretch receptors	Inhibitors of pulmonary stretch receptors in alveoli
General inf.	Act on trachiobronchial	Use local anaesthetic in case of bronchoscopy or bronchography	decrease sensitivity (numbing) of receptors by local anesthetic Action Taken oraly
Adverse effect			drowsiness, dizziness, dysphagia, allergic reactions

CENTRALLY ACTING ANTITUSSIVES

A. OPIOIDS (morphine family)

Very selective

Every product of morphine suppress the cough center
Codeine reduce the cough and inhibit the reparatory center
Those are not harmful unless if there over dose (it cause addiction)

They act directly on cough centre in the medulla by inhibiting release of excitatory neuropeptides via activating μ opioid receptors

e.g. Codeine (methyl-morphine) & Pholcodine

Morphine*, *only in bronchogenic carcinoma, because of its many side effects

CENTRALLY ACTING ANTITUSSIVES

B. NON-OPIOIDS

→ Sedating H_1-blockers
Diphenhydramine, Chlorphenaramine

↓

Dextromethorphan (used instead of codeine)

Mechanism

Multiple non-selective mechanisms; 5HT reuptake inhibition, s receptor agonist & NMDA receptor antagonist.

As antitussive; it ↑ threshold for coughing centrally

Its benefits :

1. As potent as codeine.
2- But no drowsiness.
3- Less constipating
4- No respiratory depression.
5- No inhibition of mucociliary clearance.
6- No addiction.

Questions :

تقريبا الاسئله من النقاط اللي ركزت عليها الدكتورة

- 1/ which one of these drugs Used more in children for prophylaxis of perennial allergic rhinitis ?

A. Ambroxol
B. Cromolyn
C. Loratidine
D. Diphenhydramine

- 2/ The antihistamine have a good control of which of the following diseases?

A. Asthma
B. Anaphylaxis
C. Otitis
D. Urticaria

- 3/ which one of these drugs act on NMDA receptors ?

A. Dextromethorphan
B. Guaifenesin
C. Levocetirizine
D. Lidocaine

- 4/ which one of these drugs is antitussive agents ?

A. N-Acetyl Cysteine
B. Tincture benzoin compound
C. Pulmozyme
D. Diphenhydramine

- Answers

1_ B

2_ D

3_ A

4_ B

THANK YOU

GOOD LUCK