

Treatment of Acute & Chronic Rhinitis and Cough

Objectives:

- Define rhinitis and cough.
- Classify drugs used in the treatment of rhinitis.
- Expand on the pharmacology of different drug groups used in the treatment as; antihistamines, leukotriene antagonists, corticosteroids, decongestants and anticholinergics.
- Describe the pharmacology of different expectorants and mucolytics used in the treatment of productive cough.
- Describe the pharmacology of antitussives (cough suppressants).

Be positive

- Titles
- Very important
- Extra information
- Doctor's notes

Rhinitis

Rhinitis is the irritation and/or inflammation of the mucous membranes inside the nose.

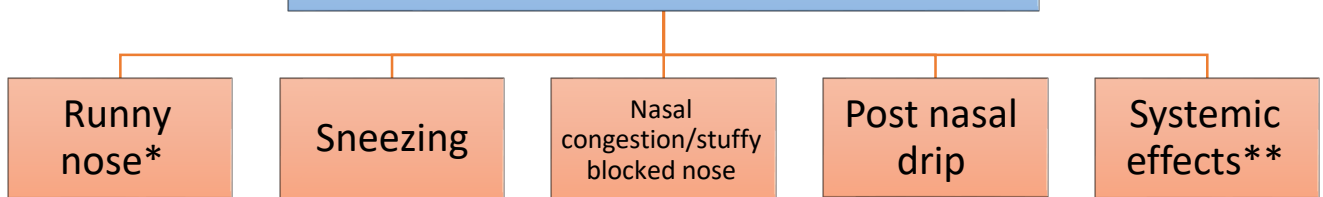
Types:

1. Allergic (seasonal ; hay fever and perennial)
2. infectious (infection with bacteria, fungi and viruses)

Rhinitis may be:

1. Acute (persist 7-14 days)
2. Chronic (persistent more than 6 weeks)

Signs and symptoms of rhinitis:



*rhinorrhea; excess nasal secretion & discharge

** fever, body aches

Treatment of Rhinitis

Preventive Therapy:

1. Environmental control
(dust control, pets).
2. Allergen immunotherapy .

Pharmacotherapy:

1. Anti-histamines (H1- receptor antagonists).
2. Anti-allergics .
 - a) Cromolyn sodium (mast cell stabilizer).
 - b) Leukotriene receptor antagonists (montelukast).
3. Corticosteroids.
4. Decongestants (alpha- adrenergic agonists).
5. Anticholinergics.
6. Antibiotics (if bacterial infection occur).

Histamine

What is Histamine ?

Histamine is a chemical messenger ,mostly generated in mast cell that mediates a wide range of cellular responses, including allergic and inflammatory reactions, gastric acid secretion and neurotransmission in parts of the brain.

- Histamine has no clinical application but antihistamines have important therapeutic applications.

1-Antihistamines (H1–receptor antagonists):

The term antihistamine, without modifying objective, **refers to the classic H1 – receptor blockers**. These drugs do not interfere with the formation or release of histamine, they only block the receptor-mediated **response** of a target tissue.

They are divided into 3 Generations:

The older first generation drugs still widely used because they are effective and inexpensive. These drugs **penetrate the blood brain barrier (BBB) ~non-polar~** and cause **sedation**. Furthermore, they tend to interact with other receptors (serotonin , adrenergic, cholinergic), producing a variety of **unwanted adverse effects**.

Second generation (Non-sedating) agents are specific for H₁ receptors and they carry polar groups, they **do not penetrate the BBB** causing less CNS depression

Extra information:

Polar: CNS لذلك ما لها تأثير على vessel يعني انها اغلب وصولها الى وسط واحد فقط

Non-polar: CNS ~ تتوزع في جميع الاوساط بما فيها >>>>> cause sedation

Antihistamines (H1 blockers):-

| 1st Generation | 2nd Generation | 3rd Generation |
|---|--|----------------|
| <u>Chlorpheniramine</u> | <u>Cetirizine</u> | Levocetirizine |
| <u>Dimenhydrinate</u> | | |
| <u>Diphenhydramine</u> | | |
| Antazoline | <u>Loratadine</u> | Fexofenadine |
| <u>Promethazine</u> | | |
| Cyclizine | | |
| Azatidine | | |
| Ketotifen | | |
| Cyproheptadine | | Desloratadine |
| <ul style="list-style-type: none"> - Short duration - Interactions; with enzyme inhibitors [as macrolides, antifungals, calcium antagonists] - Additive pharmacodynamic ADRs. Still use (if other generation don't give effect) | <ul style="list-style-type: none"> - Long duration (better control) - No drug interactions & minimal ADRs, since they are more specific for H1 receptors. Unless if given in toxic dose, which will then cause ADRs similar to those of the first generation blockers. | |

All are used systemically or topically

| | | |
|--------------------------------------|----------------------|--|
| 2 nd Generation | Cetirizine | (ثاني) مرة أشوفك كذا ترى (الستر) (زين) |
| | Loratadine | (لورا) (تدين) لي ب(ريالين) |
| 3 rd Generation | (Levo)(cetiri)(zine) | |
| نقدر نقسم اسم الدرق الى (ثلاث) مقاطع | (Deso)(lora)(tadine) | |
| | (Fexo)(fen)(adine) | (الفيكس) (فين) (اديني) هو |



Antihistamines (H1 blockers):-

| INDICATIONS linked to H1 block | INDICATIONS not linked to H1 block | |
|--|------------------------------------|---|
| | Receptor | Side effect interactions |
| <ul style="list-style-type: none"> Allergies : 1. GOOD CONTROL of Rhinitis, Conjunctivitis, Urticaria, Flu (cough & sneezing) 2. POOR CONTROL of Asthma, Otitis, Anaphylaxis, Sinusitis, Atopic dermatitis ITCHING: Even if non-allergic Others: Insomnia, Sleep aid, Vertigo, Anxiety, Cough | serotonin | appetite |
| | α -adrenergic | Hypotension , Dizziness , Reflex tachycardia |
| | cholinergic | Dry mouth , Urinary retention , Sinus tachycardia |

Side Effects & Interactions

GOOD CONTROL of Rhinitis, Conjunctivitis, Urticaria, Flu (cough & sneezing)
POOR CONTROL of Asthma, Otitis, Anaphylaxis, Sinusitis, Atopic dermatitis

INDICATIONS linked to H1 block

INDICATIONS not linked to H1 block

ANTIHISTAMINES

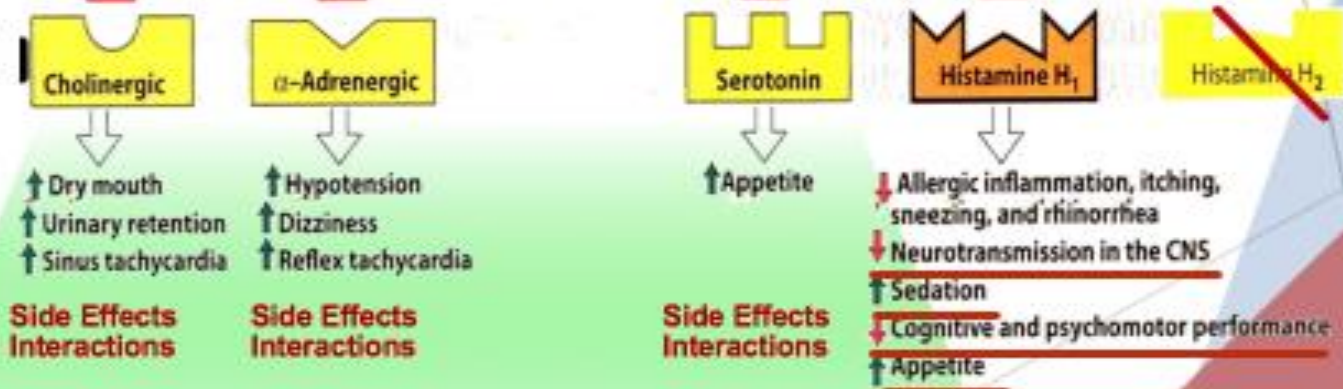
ALLERGIES

ITCHING

Even if non-allergic

Others

Insomnia
Sleep aid
Vertigo
Anxiety
Cough



Antihistamines (H1 blockers):-

| | |
|-------------------------|---|
| Actions | <ul style="list-style-type: none">- The action of all the H₁ receptor blocker is qualitatively similar.- <u>They are much more effective in preventing symptoms than reversing them once they have occurred.</u>- Most of these drugs have additional effects unrelated to their blocking H₁ receptors, which probably reflect binding of H₁ antagonists to: Cholinergic, Adrenergic or Serotonin receptors |
| Therapeutic uses | <ul style="list-style-type: none">• Allergic rhinitis: relieves rhinorrhea, sneezing, and itching of eyes and nasal mucosa• <u>Common cold</u>: dries out the nasal mucosa. Often combined with nasal decongestant and analgesics• <u>Motion sickness</u>.• Allergic dermatoses: can control <u>itching</u> associated with insect bites.• <u>Nausea and vomiting (Promethazine)</u> |
| Pharmacokinetics | <ul style="list-style-type: none">- H₁ receptor blockers are <u>well absorbed after oral administration</u>- Maximum serum levels occurring <u>at 1-2 hours</u>- Average plasma half life <u>is 4 to 6 hours</u>- H₁- receptor blockers <u>have high bioavailability</u> and distributed to all tissues Including CNS- Metabolized by <u>the hepatic cytochrome P450 system</u>- Excretion occur via kidney except <u>fenofenadine excreted in feces</u> unchanged |
| Adverse effects | Sedation , tinnitus "ear buzzing", fatigue, dizziness, blurred vision, dry mouth |
| Drug interaction | Interact with CNS depressants & cholinesterase inhibitors |
| Overdose | The most common and dangerous effects of acute poisoning are those on <u>CNS</u> ; including hallucinations, excitement, ataxia and convulsions |

2- ANTI-ALLERGICS:

| | Mast cell stabilizers | Leukotriene receptor Antagonists |
|---------------------|---|---|
| Example | Cromolyn & Nedocromyl | Zafirlukast, Montelukast, Pranlukast |
| Mechanism of action | only prophylactic : It does not antagonize histamine that is already released, but it decreases Histamine release from the beginning (by inhibiting Cl channels) | Block leukotriene actions |
| Uses | - Used in children for prophylaxis of perennial allergic rhinitis. *Should be given on a daily basis and never stop abruptly. | - Prophylaxis of lower respiratory tract allergies * Acts on <u>lower</u> respiratory tract allergies more than on <u>upper</u> respiratory tract allergies. E.g., acts on perennial allergen, exercise or aspirin-induced asthma (LRT allergies) more than on chronic rhinosinusitis (URT allergy) |
| ADRs | Induce cough, wheezes, headache, rash | As in asthma: Elevation of liver enzymes, headache, dyspepsia |

3-Corticosteroids:

| Examples | beclomethasone, budesonide, & fluticasone |
|---------------------|--|
| Mechanism of action | Anti-inflammatory → blocks phospholipase A ₂ → decrease arachidonic acid synthesis → decrease prostaglandins & leukotrienes |
| uses | Administered Topically (inhaled) as steroid spray; - Given in severe intermittent or moderate persistent symptoms |
| ADRs | Nasal irritation, fungal infection, hoarseness of voice |

4-Decongestants(α -Adrenergic agonists):

| | SYSTEMIC | TOPICAL |
|------------------|--|--|
| Ex. | Pseudoephedrine | <ul style="list-style-type: none"> - Phenylethylamines: <ul style="list-style-type: none"> • Phenylephrine • Methoxamine - Imidazoline: <ul style="list-style-type: none"> • Naphazoline, • Oxymetazoline HCl • Xylometazoline HCl |
| Uses | <u>treatment of nasal stuffiness</u> | |
| ADRs | <ul style="list-style-type: none"> • nervousness, insomnia, tremors, palpitations, hypertension. | Rebound nasal stuffiness (repeated administration (10 days -2 weeks) |
| Contraindication | <p>Better avoided in</p> <ul style="list-style-type: none"> - hypertension, heart failure, angina pectoris, hyperthyroidism - glaucoma. | |

مقطع (azoline) يشبه فازولين=فازلين اللي يذكرنا بفيكس اللي يستخدم لعلاج (احتقان الأنف) أحيانا
 Or Xylo is oxy. Which asked in Arabic metazoline (نوف) naph (متى تزورين)

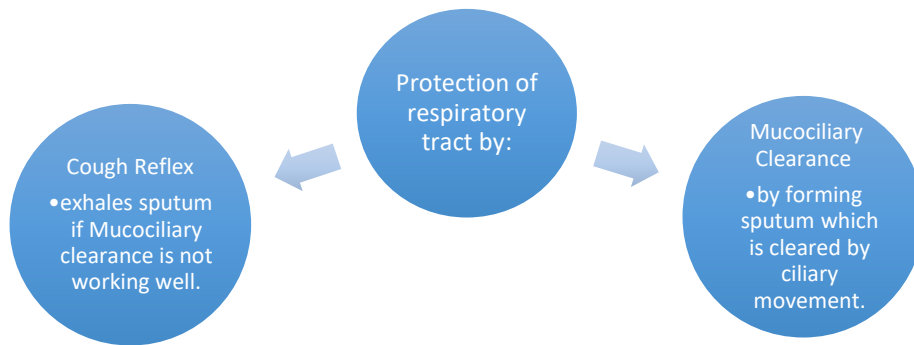
5-Anticholinergics:

| Ex. | Ipratropium The Ipra may fill with water |
|------|---|
| Uses | <ul style="list-style-type: none"> -Nasal drops to control rhinorrhea. * <u>So very effective in vasomotor rhinitis (watery hyper-secretion).</u> -bronchodilator in asthma . |
| ADRs | minimal systemic side effects (wheezing, bladder pain, cough producing mucous). |

Summery:

| Drug Groups | Main Symptom | | |
|------------------------------|--------------|------------------------|--------------------------|
| | Sneezing | Blockage Stuffiness | Secretions Rhinorrhea |
| 1-Anti-histamines | ++ | - | + |
| 2-Anti-allergics (cromolyns) | + | + | + |
| 3-Topical corticosteroids | ++ | ++ | ++ |
| 4-Decongestant | - | ++ | - |
| 5-Anticholinergics | - | - | ++ |

Treatment of Cough



- ✓ Coughing is a sudden expulsion of air from the lungs through the epiglottis at an amazingly fast speed (~100 miles/ hr) to rid breathing passage ways of unwanted irritants.
- ✓ Abdominal & intercostal muscles contract, against the closed epiglottis → pressure ↑ → air is forcefully expelled to dislodge the triggering irritant.
- ✓ Cough is may be useful "**wet or productive**". Sometimes, it may not be useful & annoying secondary to irritant vapors, gases, infections, cancer "**dry or irritant**"

Treatment

Productive Cough (wet cough)

Non-Productive Cough (Dry or irritant cough)

Mucolytics

Expectorants

Antitussive Agents

N-Acetylcysteine

Bromhexine

Pulmozyme

Reflex Stimulation

Direct Stimulation

Peripherally Acting

Centrally Acting

Expectorants

Act by removal of mucus (sputum)

Final outcome is that cough is indirectly diminished

| Stimulation type | Reflex Stimulation | Direct Stimulation |
|---------------------|---|---|
| Mechanism of Action | <u>Irritate GIT → stimulate gastropulmonary vagal reflex → loosening & thinning of secretions</u> | <u>Stimulate secretory glands → ↑ respiratory fluids production</u> |
| Drug example | <u>Guaifenesin</u> | <u>Iodinated glycerol, Na or K iodide, acetate, Ammonium chloride, Ipecacuahna is plant</u> |
| ADRs | Dry mouth, chapped lips, risk of kidney stones (due to ↑ uric acid excretion). | ADRs of iodine preparation: Unpleasant metallic taste, hypersensitivity, hypothyroidism, swollen of salivary glands (overstimulation of salivary secretion), & flare of old TB. |
| Indications (Uses) | Common cold, Bronchitis, Pharyngitis, and Chronic paranasal sinusitis. | |

Mucolytics

- ✓ Mucolytic agents are used to dissolve or breakdown mucus in the respiratory tract. They make the mucus less viscous so that it can be coughed up with more ease.
- ✓ Act by altering biophysical quality of sputum → becomes easily exhaled by mucociliary clearance or by less intense coughing (Thick mucus → Thin mucus)

Mucolytics

| Drug | <u><i>N-acetylcysteine</i></u> | <i>Bromhexine</i> (and its metabolite <i>ambroxol</i>) | <u><i>Pulmozyme</i></u> (Dornase Alpha or rhDNAase*) | <u>Hypertonic saline and NaHCO₃</u> | <u>Steam inhalation</u> |
|---|---|--|--|--|-------------------------|
| Mechanism of Action occurs by one or more of the following; | <u>Breakdown S-S bonds in glycoproteins → less viscid mucous</u> <i>ذرة النيتروجين تغار من الرابطة بين ذرتي الكبريت فتروح تكسرها</i> | - Synthesize serous mucus (sialomucins* of smaller-size) so it is secretolytic* - Activate ciliary clearance & transport | <u>Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of infection</u> | ↓Viscoelasticit* by water content ↑ | ↓Adhesiveness* |
| Overview | A free radical scavenger used in acetaminophen overdose (paracetamol overdose) | - <u>They increase immune defense → Antibiotics usage</u> - ↓ <u>pain in acute sore throat</u> | That is nebulized. Full benefit appears within 3-7 days | <i>هذا الدرق مرتبط بالبكتيريا انفيكشن فممكن نقرا اسم الدرق كذا بل (Pul) هو موسم (mozyme) البكتيريا (in case of Bacterial_) infection</i> | |
| ADRs | Bronchospasm, stomatitis*, rhinorrhea, rash, nausea & vomiting | Rhinorrhea*, lacrimation*, gastric irritation, hypersensitivity | Voice changes, pharyngitis, laryngitis, rhinitis, chest pain, fever, rash | | |
| Indications (Uses) | <ul style="list-style-type: none"> - Most mucolytics are effective as adjuvant* therapy in COPD, asthma, bronchitis, ...etc. when there is excessive &/or thick mucus. - In bronchiectasis, pneumonia & TB → they are of partial benefit - Hardly any benefit in cystic fibrosis & severe infections → Give rhDNAase (pulmozyme) | | | | |

Glossary

Viscoelasticity: لزوجة مطاطية

Adhesiveness: التصاق

Sialomucins: a component of airway secretions of the lungs.

Secretolytic: breaks up secretions

Recombinant: Synthetic DNA

Lacrimation: tears

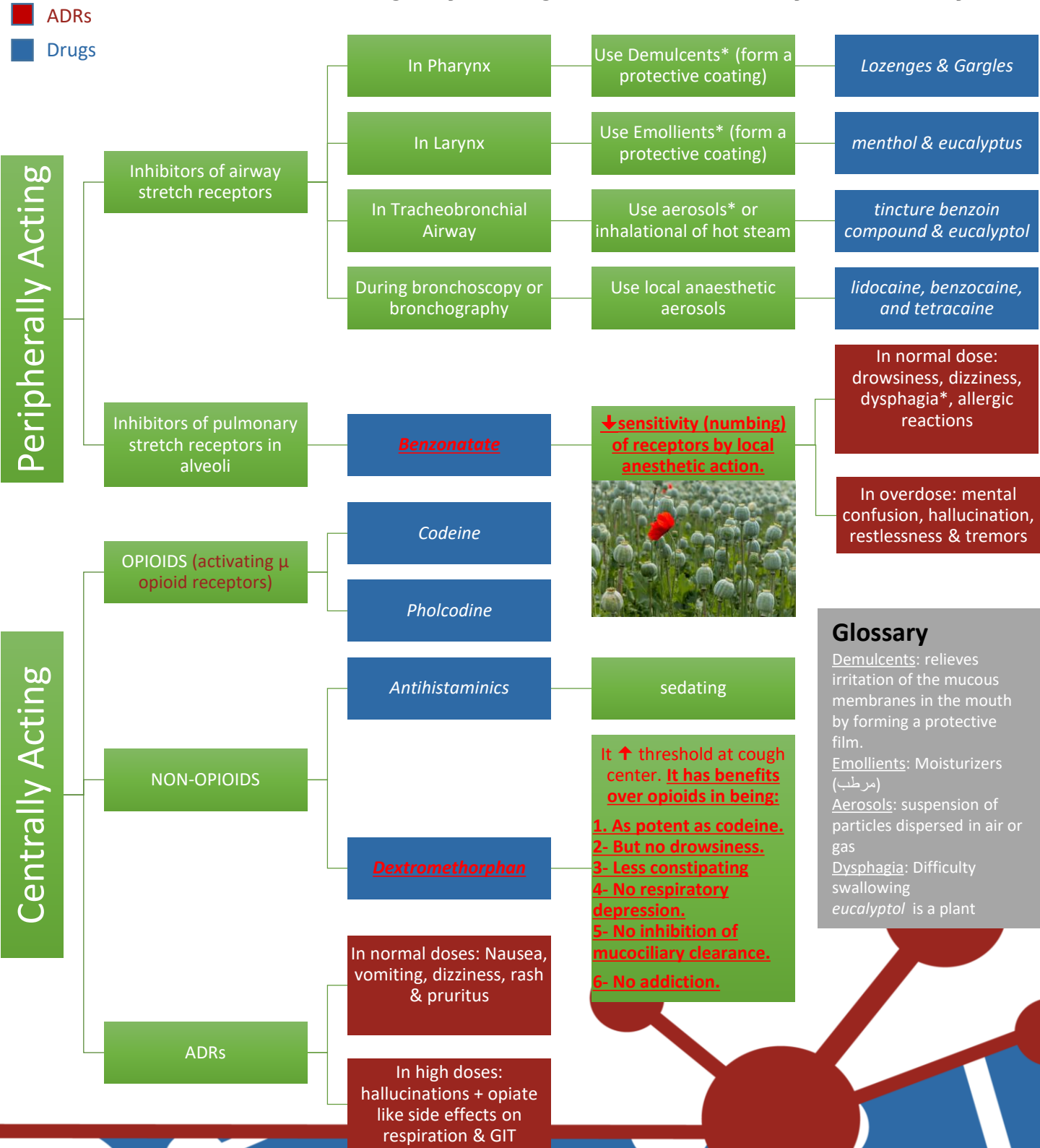
Stomatitis: inflammation of the mucous membrane of the mouth.

Rhinorrhea: runny nose

A recombinant* of human deoxyriboneuclease = rhDNA

Antitussive Agents

Stop or reduce cough by acting either peripherally or centrally



Glossary

Demulcents: relieves irritation of the mucous membranes in the mouth by forming a protective film.

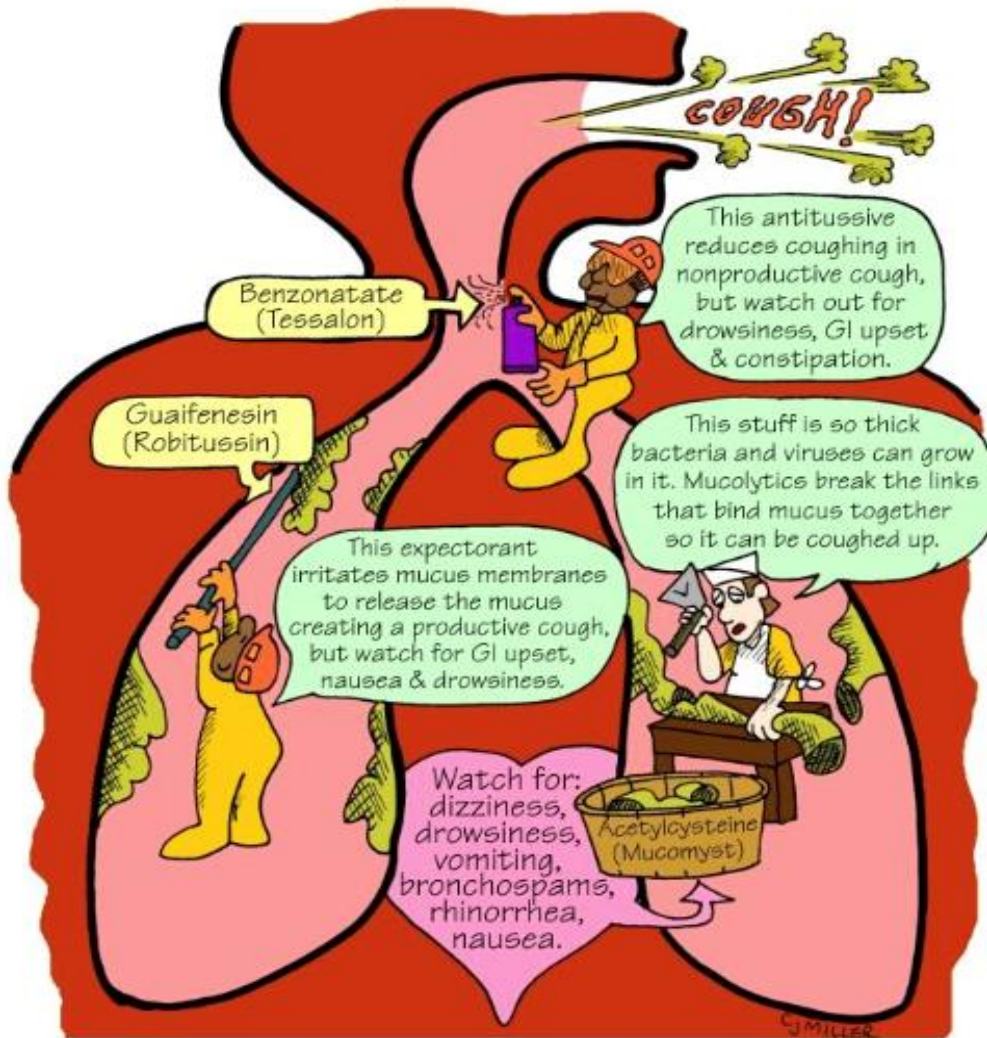
Emollients: Moisturizers (مرطب)

Aerosols: suspension of particles dispersed in air or gas


Dysphagia: Difficulty swallowing

eucalyptol is a plant

Antitussives, Expectorants, & Mucolytics



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 How do we cough?

 Mucolytics

A 39 male who work as driver came with runny nose and sneezing symptoms of seasonal. His past medical shows there is no allergy.

Q1: what is the drug can be given to him as anti histamine to relife the symptoms ?

2nd generation of H1 blocker such as cetirizine or loratadine

Q2: What is the mechanism of action ?

They are selective blocker for histamine receptors.

Q3: What is the best route of administration for this drug ?

Orally.

Q4:Which generation is contraindication in this case and why ?

1st generation such as chlorpheniramine due its sedative effects .

Q5: What are the ADRs effect when he took this drug with over dose ?

It has dangerous effects of acute poisoning are those on CNS such as hallucinations,excitement,ataxia and convulsions

Q1: what is the drug can be given for treatment of nasal stuffiness as decongested drugs?

α -Adrenergic agonists such as Naphazoline, Oxymetazoline, Xylometazoline

Q2: what is the drug can be given for treatment of vasomotor rhinitis ?

5-Anticholinergics such as Ipratropium can help to decrease the watery hyper secretion.

Q3:If the patient has wet cough due bacterial infection , what is the drug of choice as mucolytic ? What is its mechanism ?

Pulmozyme , act by Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum.

Quiz



| Boys | Girls |
|-------------------|----------------|
| عبدالرحمن ذكري | غادة المهنا |
| عبدالعزيز رضوان | اللولو الصليهم |
| مؤيد أحمد | روان القحطاني |
| فيصل العباد | امل القرني |
| فارس النفيسة | شروق الصومالي |
| خالد العيسى | سما الحربي |
| عبدالرحمن العريفي | انوار العجمي |
| عبدالرحمن الجريان | وتين الحمود |
| محمد خوجة | رنا باراسين |
| عمر التركستاني | |

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