بسم الله الرحمن الرحيم

PHARMACOLOGY

FINAL | Lecture 1

# Drug Treatment of Cough


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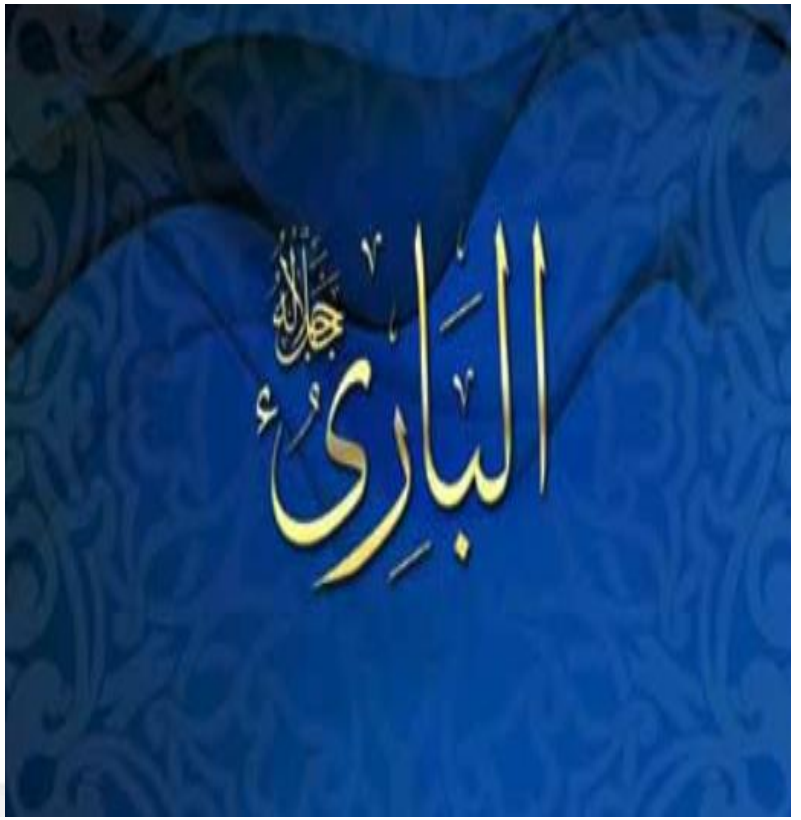
﴿وَلَقَدْ نَعْلَمُ أَنَّكَ يَضِيقُ صَدْرُكَ بِمَا يَقُولُونَ ﴿٩٧﴾ فَسَبِّحْ بِحَمْدِ رَبِّكَ وَكُن مِّنَ السَّاجِدِينَ﴾

سبحان الله وبحمده، سبحان الله العظيم

# وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا




**المعنى:** الموجد من العدم، والبرء هو التنفيذ وإبراز ما قدره وقرره إلى الوجود على صفة محددة.

**الورود:** ورد في القرآن (٣) مرات.

**الشاهد:** ﴿ هُوَ ٱللَّهُ ٱلْخَٰلِقُ ٱلْبَارِئُ ٱلْمُصَوِّرُ ﴾ [ الحشر:٢٤ ].

٧١

اضغط هنا لشرحٍ أكثر تفصيلًا

# Drug Treatment of Cough

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ابكِ، لا بأس، لكن اجعَل الجرح محرّكًا، خذ مع الجرح عهدًا، وابدأ عملًا، وغيّر فيك أمرًا ما كان !لا تقبل بأن تكون ردّات فعلك أحزان فقط ليتغيّر دون هذا الوجع، لا ترضى أن تكون ردّة فعلٍ مجرَّدة، بل خطوة مؤكّدة، أطلِق الفعل، وخذ موقعك، فلا تعلم علّه يكون الأخير لك

- The best treatment for cough is to treat the underlying cause. This means that cough is a symptom, not a disease, so management should focus on treating the cause. Until the underlying disease is treated, symptomatic treatment can be given using these drugs.

# Drug Treatment of Cough

- **Cough is a protective reflex mechanism.** It is an attempt to rid the respiratory system of abnormal substances, excessive sputum-mainly-, or foreign bodies.
- **It can be stimulated by irritation, inflammation or tumors of the respiratory tract.**

**Types of cough:**

1. **Useful cough (productive - produce secretions): serves a purpose and should not be suppressed. However, we may convert it to easy cough.**
2. **Useless cough (unproductive) :ناشفةis distressing and can exhaust the patient if severe, both physically and psychologically. Should either be made useful (by turning it into a productive cough that clears the respiratory tract) or suppressed.**

❖ **A patient goes to the pharmacy while coughing and feeling sick, and he is given a combination of cough medications. Giving medications in this way is wrong and may be harmful.**

# Drug Treatment of Cough

- **Drugs that suppress cough are called antitussives.**
- **Antitussives suppress cough without affecting the underlying cause. Therefore, they are only symptomatic treatment.** So its dangerous to treat cough alone without trearting the cause in order not to deteriorate the underlying cause.
- **They should not be used for the cough of bronchial asthma or that caused by suppurative lesions of the respiratory tract.( lesions that produce sputum or pus, such as pneumonia and lung abscess. In these cases, the secretions should be cleared because they are associated with infection and inflammation).**
- **The best antitussive treatment is treatment of the underlying cause. This means you terminate the cough by treating the cause. While you suppress the cough, the underlying cause will continue and become excessive later.**

# Antitussives Contraindications

- **Cough in asthma** is associated with airway obstruction and should not be suppressed, because it is a reflex mechanism that helps open obstructed bronchi and allows ventilation.

- **Cough in children** should not be suppressed under any circumstances, because it is almost always due to infection. Suppressing it can also be confusing for the patient and their family. If you ask the family whether the cough is productive, they will often say no, because children usually swallow the sputum, so you may not realize it is actually productive.

- In summary, antitussives are contraindicated in:

1- Bronchial asthma
2- Near suppurative lesions or diseases of the respiratory system (e.g., pneumonia, lung abscess)
3- Young children

# Drug Treatment of Cough

## Sites of Action of Antitussives:

I. On the peripheral sites (afferent side of the cough reflex): reduction of input of stimuli from throat, larynx, trachea and bronchial tree by relieving irritation - reduce inflammation as in infection -or producing a soothing effect. Soothing effect means creating a protective layer of thin mucus over irritated respiratory surfaces. This layer prevents the cough impulses from reaching the central respiratory center in the medulla, thereby reducing the cough reflex through.

## Demulcents:

**Agents that relieve irritation by forming a protective film on irritating surfaces.**

1. **Warm moist atmosphere (warm water vapor)التبخيرة : The best demulcent, promotes secretion of dilute mucous that provide protective coating of the inflamed mucous membrane.**

   **Used for cough arising *below the larynx*** ( from bronchial tree).

❖ Simply, place a pot of water on the stove and let it boil, then have the patient inhale the steam. You can add menthol, licorice, or chamomile for an additional soothing effect.

# Drug Treatment of Cough

## 2. Lozenges, syrup or linctus of licorice or methylcellulose:

- **Provides coating of mucous membranes for cough *arising above the larynx.***

**Menthol or Eucalyptus vapor or lozenges:**

- **They reduce irritation and thus tendency for cough,** due to their role in reducing impulses that reaching cough center.
- **They have local anesthetic effect.**
- **Can be combined with warm water vapor**

# Demulcents

❖**Lozenges** ملبس: These are tablets that the patient **sucks, not swallows**. They release substances that **coat and soothe the irritating surfaces above the larynx and throat.**

❖**Syrups** شراب: Taken **orally**, but they are **not very effective**. They may provide **temporary soothing** when passing through the throat, but their effect is short-lived.

❖**Linctus** لعوق: This is a type of **thick syrup** that you **put in the mouth, swish, and gargle**. It contains active substances, such as **menthol**, to relieve irritation. It can be combined with water vapor or used as lozenges.

Lozenges



Cough syrup

Extra images

# Mucolytics

- Another type of drugs are: Drugs acting on the **efferent side** act after the cough center has been stimulated. Normally, the cough center initiates **contraction** of the diaphragm and intercostal muscles to push air out of the lungs (cough). These drugs do not suppress the cough reflex; instead, they make secretions more easily removable.
- **Sputum** can adhere to the respiratory mucosa, so not all of it can be expelled. **These drugs break down and loosen the sticky sputum**, making it easier to remove. When sputum is cleared more effectively, cough impulses decrease until the next accumulation occurs. As a result, the **frequency of coughing is reduced**, while the **efficiency of cough increases**, because the sputum becomes less viscous.

# Drug Treatment of Cough

II. Measures acting on the efferent side of the cough reflex:

- To render secretions more easily removable.
- Reduce the amount of coughing by increasing its efficiency.

1. Mucolytics:

The most important ones, they are drugs which reduce viscosity of bronchial secretions -lyse mucus-, making them easily removable.

# Drug Treatment of Cough

❖Mucolytics examples :

**Bromehexine**

- **Causes depolymerization of the mucopolysaccharide fibers of mucous so that large, less viscous amounts can be expectorated** (to be expelled).

**Acetylcysteine, Carbocysteine, Mecysteine (methylcystine)**

- **Contain free sulfhydryl (-SH) groups, that can open disulfide bonds (-S-S-) of mucous, and thus, reducing its viscosity.**

❖Mucus contains disulfide bonds. Acetylcysteine breaks these bonds by replacing part of them, which reduces the size of mucus molecules, making the mucus less viscous. N-acetylcysteine breaks disulfide bonds in mucus glycoproteins, converting large mucus polymers into smaller, less viscous fragments, thereby facilitating expectoration.

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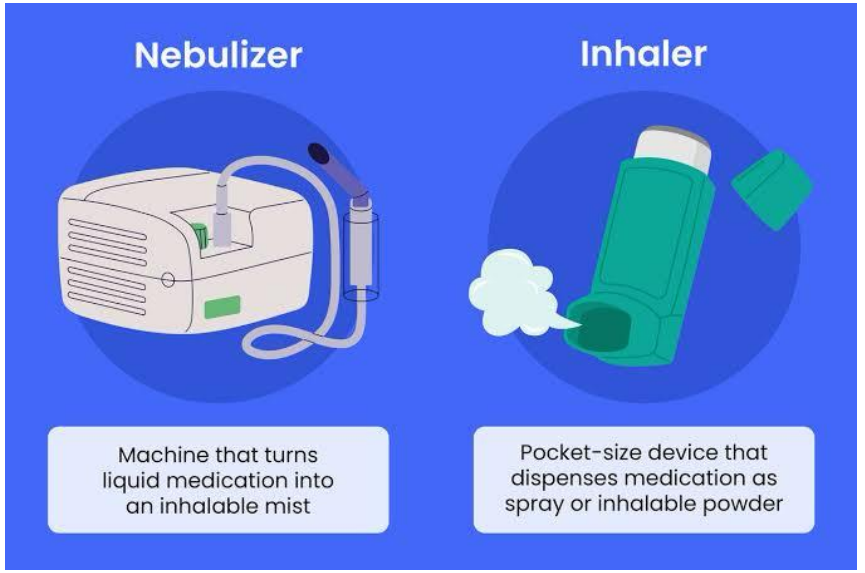
# Drug Treatment of Cough

- **Best results with mucolytics are achieved by inhalation or nebulization.**




- ➢ This is because the obstruction is usually located in the lungs due to infection or inflammation.
- ➢ The patient inhales the medication, allowing it to reach the site of action, namely the bronchial tree or the respiratory passages.
- ✓ ***Inhalation*** means that the drug is inhaled, which is why mucolytics are administered with nebulized water vapor.
- ✓ A ***nebulizer*** is a hospital device that is not very complex. It contains a reservoir in which water and active ingredients, such as menthol and bromhexine, are placed. The device is connected to oxygen—not supplemental oxygen, but at a normal concentration similar to atmospheric air (21%). It is then attached to either a mask or a nasal cannula, allowing the patient to breathe the medication along with air.

# Drug Treatment of Cough

- **Can also be given orally.**
  - ✓ However, they are **not as effective** as inhalation or nebulization.
  - ✓ Oral mucolytics can be used in certain types of **male infertility** associated with thick mucus, which hinders sperm movement. In such cases, mucolytics are used to **improve sperm motility**.
- **Can cause GI irritation and allergic reactions.**
  - ✓ **Allergic reactions** occur because these drugs are foreign substances.
  - ✓ **Gastrointestinal irritation** is a vague term that can refer to several symptoms, including nausea and vomiting, dyspepsia, diarrhoea, constipation, and abdominal pain caused by contractions of the GIT.
- **Water vapor inhalation or hydrating a dehydrated patient also reduce viscosity of bronchial secretions.**
  - ✓ This means that the water vapor has more than one action: it acts as a demulcent, mucolytic and expectorant (will be discussed).

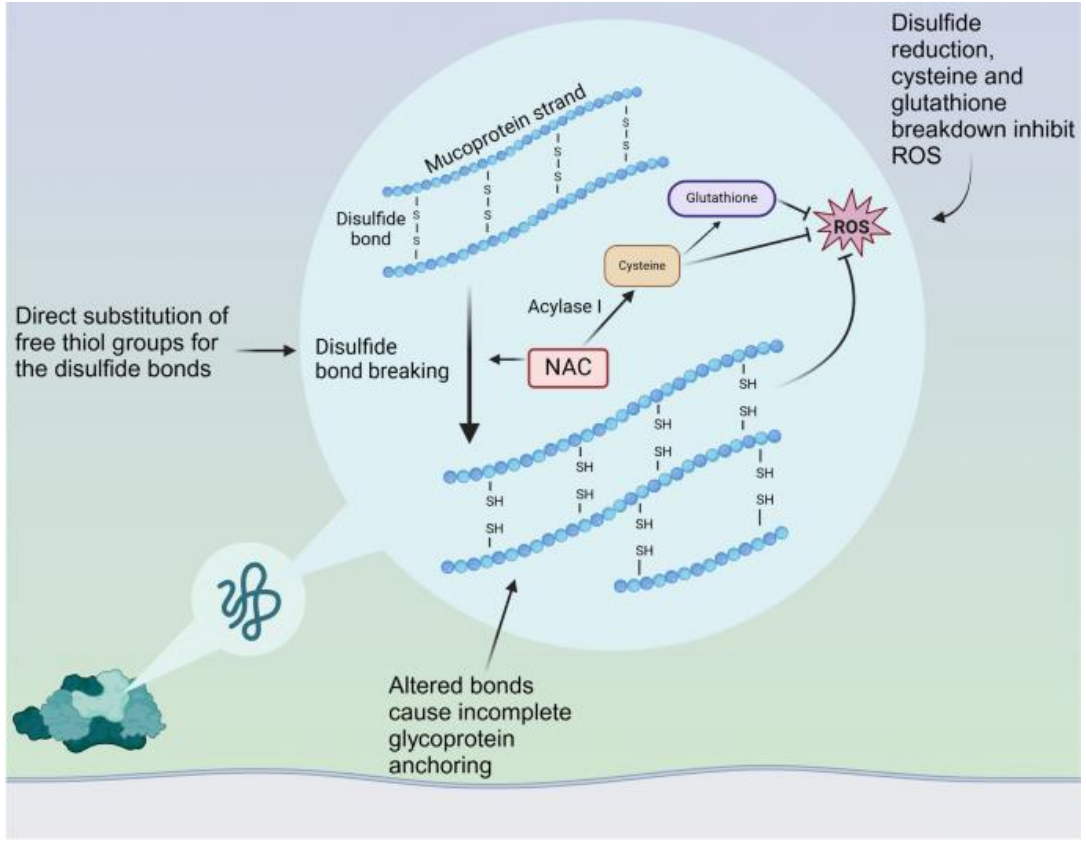
# Drug Treatment of Cough

❖ **Dornase alfa (Specific treatment)**

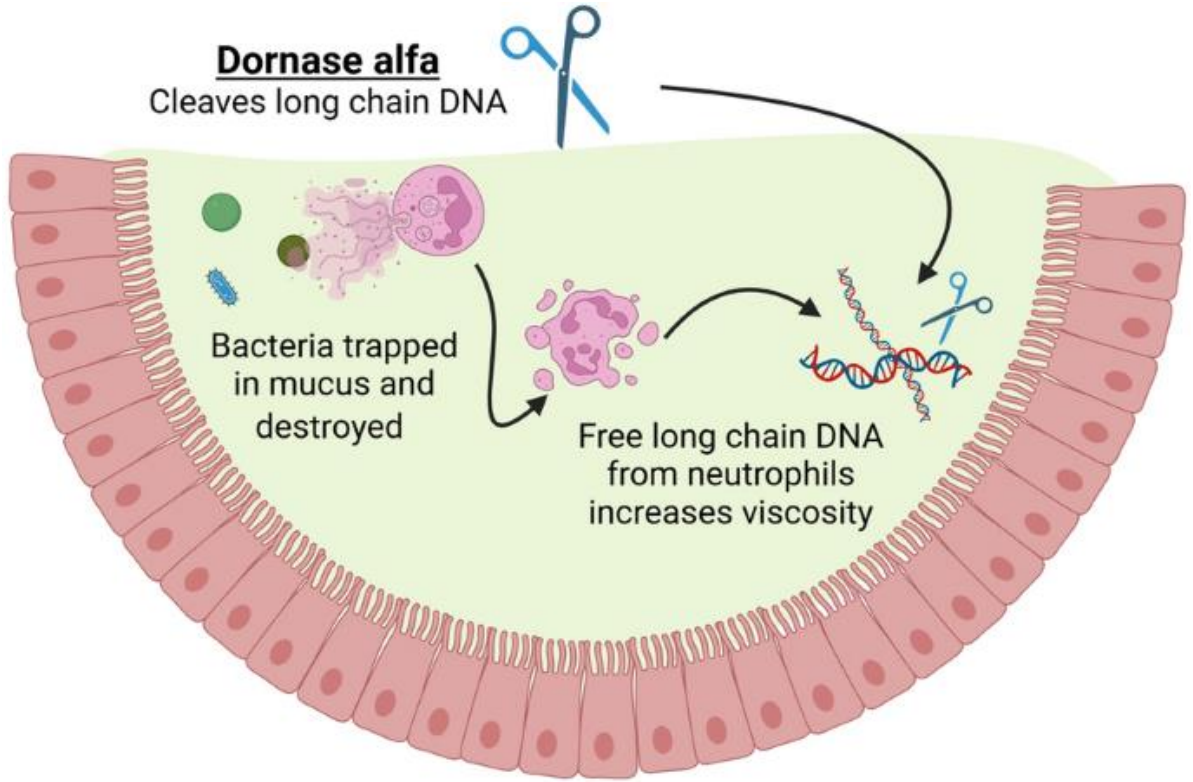
- **It is a phosphorylated glycosylated recombinant human deoxyribonuclease (enzyme).**
- **Given by inhalation or nebulization to patients with cystic fibrosis, where there is a genetic defect in $Cl^-$ transport leading to viscous sputum.**
- **The blocked airways , sputum and the thick mucus trap pathogens, inflammatory cells and microbes ,which when lysed produce substantial amounts of free and very viscous DNA.**

✓ DNA makes this sputum more viscous because the DNA itself is viscous.

# Extra figures for Mechanisms of Action




Acetylcysteine




Dornase alfa

# Drug Treatment of Cough

## 2. Expectorants:

- **Agents which increase the amount of, and liquefy bronchial secretions without lysing the mucus.**

**Mentholyated water vapor**

### ❖ Guaifenesin:

- **It reduces adhesiveness of sputum to the bronchial mucosa and reduces surface tension which facilitates removal of mucus and soothes dry, irritated membranes.**
- **It is of questionable clinical value.**

✓ Critics argue that the drug's efficacy is attributed to a **placebo effect**. Regardless, it is stocked in pharmacies within the mixed cough preparations often combined with other active ingredients such as vasoconstrictors.

See the next slide for more clarification

# Mixed Cough preparations

- ✓ As vasoconstriction reduces blood flow and therefore sputum output but does not remove existing sputum, it makes it thick and adherent to the mucosa.
- ✓ While these vasoconstrictors decrease the production of new sputum by reducing blood flow, they fail to eliminate the secretions already present. Consequently, the existing sputum becomes dehydrated, thicker, and more adherent to the respiratory mucosa, making it significantly harder to expectorate.
- ✓ Some argue that **cough mixtures are merely placebos**. Therefore, we should identify the **specific cause** of the cough—whether it is due to sputum or simple irritation—rather than prescribing a general mixture. This includes considering rare causes such as cancer and metastasis, which, although rare compared to common respiratory infections, require a specific diagnostic approach. You should carefully read the ingredients to ensure they are suitable for your particular patient's cough, as the condition can be caused by various factors, as they cannot be treated effectively until a specific therapeutic target is identified.

- **Adverse effects: Nausea, vomiting, headache.**

اللهم إن عمر عطية عبدك وابن عبدك وابن أمتك كان يشهد أن لا إله إلا أنت ، وأن محمداً عبدك ورسولك ، وأنت أعلم به ، اللهم إن كان محسناً فزد في إحسانه، وإن كان مسيئاً فتجاوز عن سيئاته.

# Drug Treatment of Cough

## Drugs that act on the CNS:

- Act by suppressing the medullary cough center.

1. Opioids and related drugs:

- Lower doses are needed to suppress cough than those needed to produce analgesia.

✓ Opioids are centrally acting analgesics, not NSAIDs. They work by inhibiting the reception of pain impulses.

✓ They are controlled substances and their use is restricted; you will not find them in community pharmacies, but only in hospitals. Every dose is strictly accounted for, whether in the form of injection ampoules or tablets.

- Antitussive effect is not blocked by the opiate antagonist, Naloxone.

More details will be discussed in CNS

# Drug Treatment of Cough

## ❖ Codeine (Methylmorphine): = don't use it, at all. ☺

- **Antitussive dose 15 mg (analgesic dose is 60 mg).**
- **It has less addictive and less respiratory depression than other opiates.**

✓ The doctor opposes this view because **codeine** is metabolized to **morphine** via O-demethylation by the **CYP2D6** enzyme, a member of the cytochrome P450 family, which confers a potential for **dependence and abuse.** Although antitussive doses are relatively low and therefore less addictive than analgesic doses, **the risk of abuse still exists.**

✓ Some patients, particularly those with obsessive tendencies, may begin to overuse the medication once symptoms improve, such as taking doses pre-emptively in anticipation of coughing or becoming excessively focused on the timing of cough episodes to schedule the treatment, those are more prone to dependence and addiction.

- **Part of the antitussive effect is due to sedation.**

✓ Sedation maintains the mucus secretions and causes retention of mucus (Disadvantage) as it reduces the impulses towards the cough center. The cough is less severe during sleeping.

# Drug Treatment of Cough

- **Adverse effects:**

1. **Inhibition of ciliary activity in bronchioles** (Cilia move the foreign bodies out of the respiratory tract, including sputum, as it is normally not present there) **and dryness of secretions lead to reduced clearance of thick sputum and sputum retention,** making mucus expulsion more difficult which might cause obstruction, single bacterial infection may become polymicrobial or superimposed by fungal infection in immunocompromised patients.

2. **Constipation.**

# Drug Treatment of Cough

❖ **Dextromethorphan** = use it. ☺

- **It was thought that its an opioid-related drug, however, it is totally different one.**
- **Non-narcotic, non-analgesic, non-addictive, non-constipating and does NOT inhibit mucociliary clearance.**
- **Antitussive action is equal to codeine.**
- **Adverse effects are minor at therapeutic doses.**
- This is the antitussive **drug of choice** to suppress the cough centers in the medulla.

# Drug Treatment of Cough

## ❖ $H_1$-histamine Receptor Blockers (Diphenhydramine):

= It's also bad, but less than codeine. ☺

- **Can suppress cough with substantial sedation** as they possess a central anticholinergic action.

✓ **Sedative action:** reduces cough by retaining the secretions.

✓ **Anticholinergic action:** dries the secretions.

- **Can be used in children only at night.** However, the doctor is not a fan of it.
- **Usually, cough in children is almost always useful and should NOT be suppressed.**

✓ The sedative action of this drug is often **misused by families**; they may administer the cough syrup to a restless child simply to induce sleep and quiet them down.

# Mixed Cough preparations

- Cough mixtures often contain active ingredients like Diphenhydramine or similar drugs. A single mixture might combine bromhexine, an antihistamine, and a vasoconstrictor to address multiple symptoms simultaneously. However, this approach is **INCORRECT** as it can lead to antagonistic effects; treatment must be specific to the underlying cause.

❖ Specific Treatment Examples:

✓ **Allergic cough:** Should be treated with an antihistamine.

✓ **Retention of secretions:** Requires agents that make secretions easily removed.

✓ **Mucus accumulation:** Requires medications that enhance the removal of mucus.

✓ **Dry cough due to cancer:** May require Dextromethorphan, which might be combined with an antihistamine or Bromhexine.

- Consequently, these cough mixtures are not always useful and can even be dangerous. It is essential to examine the ingredients carefully to understand their interactions and potential effects on one another.

# Drugs Summary

| Category | Drug / Type | MOA (Mechanism) | Use / Indication | Notes / Pearls | Adverse Effects |
|---|---|---|---|---|---|
| **Cough type** | Productive | Clears mucus | Usually do NOT suppress | Enhance secretion removal | N/A |
| | Dry (Unproductive) | Symptomatic | Suppress if distressing | Treat underlying cause | Suppression risk if infection present |
| **Demulcents** | Steam, Licorice, Menthol | Coat & soothe mucosa | Mild cough | Acts peripherally | Temporary relief |
| **Mucolytics** | Bromhexine, N-acetylcysteine, Carbocysteine | Break mucus polymer bonds | Thick sputum | Nebulization more effective | GI irritation, allergic reactions |
| | Dornase alfa | DNAse enzyme | Cystic fibrosis | Inhalation only | Rare hypersensitivity |
| **Expectorants** | Guaifenesin | ↑ sputum volume & ↓ viscosity | Facilitate productive cough | Symptomatic only | Minimal |
| **Antitussives – Central** | Codeine | Opioid, medullary suppression | Severe dry cough | Use low dose, hospital if possible | Sedation, constipation, risk of sputum retention |
| | Dextromethorphan | NMDA receptor + sigma receptor | Dry cough | No addiction, less side effects | Mild GI, dizziness |
| **Antihistamines (H1)** | Diphenhydramine | Sedative + anticholinergic | Allergic cough | Mainly night use | Sedation, drying secretions |
| **Key principles** | — | — | Treat cause first | Avoid suppressing productive cough | Avoid irrational mixtures, read ingredients |

# PHARMACOLOGY QUIZ

## LECTURE 1

# External Resources

# رسالة من الفريق العلمي

Additional sources:

1. Dr Fouda (عم الفارما)

اللهم إن عمر عطية في ذمتك وحبل جوارك، فقِه من فتنة القبر وعذاب النار،
أنت أهل الوفاء والحق، فاغفر له و لموتى المسلمين وارحمهم إنك أنت الغفور الرحيم

قال رسول الله :ﷺ

»المؤمن القوي خيرٌ وأحبُّ إلى الله من المؤمن الضعيف، وفي كلٍّ خير .احرص على ما ينفعك، واستعن بالله ولا تعجز، وإن أصابك شيء فلا تقل :لو أنّي فعلتُ كان كذا وكذا، ولكن قل :
قدرُ الله وما شاء فعل، فإنَّ لو تفتح عمل الشيطان«


اللهم لا تُرِهم منا ما ..اللهم نجِّ إخواننا المنكوبين في بلاد الإسلام واستعملنا في نصرتهم
اللهم انتقم من كل مَن يشارك في تضييق الخناق عليهم وإسلامهم لعدونا ..يسوؤُهم ويحزنهم
اللهم انصر عبادك ووفّقهم لطاعتك لتجعلَ مكر أعدائهم لصالِحهم اللهم ارحم ..وعدوهم
ضعفهم وتولَّ أمرهم وأحسن خلاصَهم واجعل لهم من لدنك وليًّا واجعل لهم من لدنك نصيرًا
اللهُمَّ احفظ عبادك على خطّ الخطرِ أينما حلَّت خُطاهم .وأعِنَّا على نصرتهم يا أرحم الراحمين
فأنتَ خيرُ الحافظين، نسألك اللهُمَّ بنورِ وجهك الذي ملأ أركان عرشِك، وبعزّك الذي لا
يُرام، وبمُلكك الذي لا يُضام، يا ذا الجلال والإكرام، أن تنصُرهم نصرًا عزيزًا مُؤزرًا وتُثبِّت
أقدامهم على الثُّغور، وتُسدِّد رميهم، وتأوي طريدهم، وتداوي جريحَهم، اللهُمَّ إنّا نستودعكَ
.إيّاهُم يا مَن لا تضيع عنده الودائع، فاحفظهم بعينِك التي لا تنام

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| Versions | Slide # and Place of Error | Before Correction | After Correction |
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| V0 → V1 | | | |
| V1 → V2 | | | |