Clinical Pharmacy Cough

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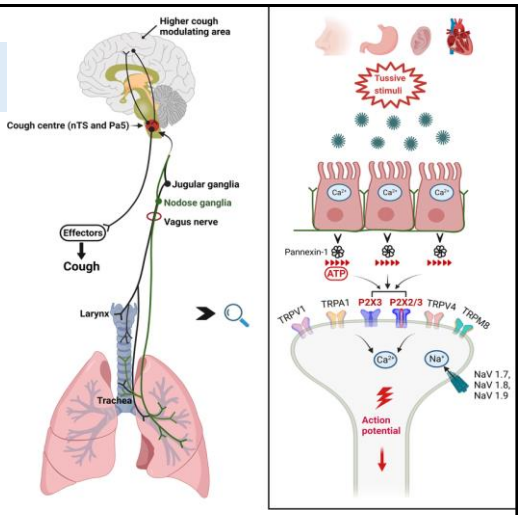
Lecture 3

Background

- Cough is a **reflex action** to remove secretions or foreign material from the airways.
- The **majority** of coughs presenting in the pharmacy will be caused by upper respiratory tract infections (URTIs).
- Cough is a symptom of many conditions, **most of which require referral** to a doctor for further investigation.
- It is the most **common symptom to seek medical care**.

Pathophysiology of Cough

- **Initiation of Cough**:
  - **Mechanical and chemical receptors are t**riggered by **chemical** and **mechanical** stimulation of **vagally** mediated sensory pathways in respiratory tract.



Current understanding of the neural processes in the cough reflex. Tussive stimuli from various sources can increase the calcium influx, leading to ATP release from the open pannexin-1 channel. This in turn activates the P2X3 and P2X2/3 receptors on sensory neurones within the airway mucosa. Other ion channels (TRPV1, TRPA1, TRPV4, TRPM8) on nociceptor terminals originating from jugular or nodose ganglia are activated by irritants or inflammatory reactions.

Pathophysiology of Cough

- **Mechanism** :
  - Cough starts with **deep inspiration**, followed by **glottis closure** and **forceful contraction of chest**, **abdominal**, and **diaphragmatic** muscles.
  - Thoracic pressure can reach up to **300 mm Hg**.
  - Upon glottis opening, air is expelled at **1115 m/s**, **clearing mucus and debris** from the respiratory tract.

Cough Duration and Classification:

Classification	Duration	Common Etiologies
Acute Cough	Less than 3 weeks	Viral URTI Pneumonia Acute Left Ventricular Failure Asthma Foreign Body Aspiration
Subacute Cough	3 to 8 weeks	Post infectious Cough Bacterial Sinusitis Asthma
Chronic Cough	More than 8 weeks	Asthma, GERD, COPD (chronic bronchitis), ACEIs, carcinoma, left ventricular failure, pharyngeal dysfunction

Types of cough

Productive (wet, chesty) cough:

Non-productive (dry) cough:

Chesty non-productive:

Where there is congestion on the chest but no mucus is produced, and this should be treated as a productive cough-rather than non productive.

Clinical Presentation of Cough

- **Types of Cough**:
  1. **Productive Cough** (wet or "chesty" cough):
     - Expels secretions from the lower respiratory tract.
     - Secretions, if retained, could impair ventilation and increase infection risk.
     - **Effective**: Secretions are easily expelled.
     - **Ineffective**: Secretions are present but difficult to expel.
     - **Appearance of Secretions**:
       - Clear in bronchitis.
       - Purulent in bacterial infections.
       - Malodor with anaerobic bacterial infections.
  2. **Non-productive Cough** (dry or "hacking" cough):
     - Associated with viral infections, atypical bacterial infections, GERD, cardiac diseases, and certain medications.
     - Serves no useful physiologic purpose.

Clinical Presentation of Cough

- **Common Complications of Cough**:
  - Exhaustion
  - Insomnia
  - Musculoskeletal pain
  - Hoarseness
  - Excessive perspiration
  - Urinary incontinence
- **Less Common Complications**:
  - Cardiac dysrhythmias
  - Syncope
  - Stroke
  - Rib fractures
- **Other Effects**:
  - Mechanical irritation leading to sore throat.
  - Prolonged absence from work or school.
  - Social withdrawal and anxiety about serious illnesses (e.g., cancer, tuberculosis).

Patient Assessment of Cough

A. Duration:

- Most coughs are **self-limiting and resolve within a few days**, with or without treatment.

B. Nature of Cough:

- **Dry vs. Wet Cough**:
  - If the cough is **wet**, the color of the sputum should be assessed:
    - **Mucoid Sputum** (clear or whitish): Typically of little consequence, suggesting no infection.
    - **Coloured Sputum** (yellow, green, or brown): May indicate infection and requires **referral**.

Patient Assessment of Cough

C. Associated Symptoms:

1. **Tuberculosis (TB)**:
   - A **chronic cough** with haemoptysis (coughing up blood), along with chronic fever, weight loss, and night sweats, are classical symptoms of **TB**.
   - **Refer**: Any patient suspected of TB.
2. **Asthma**:
   - A **recurrent night-time cough**, especially in children, with or without wheezing, may indicate **asthma**.
   - **Refer**: if family history of eczema, asthma, or hay fever.

Patient Assessment of Cough

3. Heart Failure:

- **Symptoms**: Cough with **clear frothy sputum**, breathlessness (especially at night in bed), may indicate **heart failure**.
- **Refer**: A history of heart disease with a persistent cough.

4. Chest Pain, Shortness of Breath (SOB), Wheezing, Whooping:

- These symptoms require **referral** for further investigations.

Patient Assessment of Cough

5. Croup:

- **Population**: Typically occurs in **infants**.
- **Symptoms**: Harsh barking cough, difficulty breathing, and noisy breathing.
- **Refer**: Referral is necessary.

6. Gastroesophageal Reflux Disease (GERD):

- **Symptoms**: Coughing while **lying down**, with heartburn, may indicate **GERD**.
- **Management**: Symptoms may improve with **acid-lowering drugs**.
- **Refer**: patients for assessment.

Patient Assessment of Cough

8. Smoking:

- **Risks**: Smokers are prone to **chronic recurrent cough**, which may develop into **chronic bronchitis** or **emphysema**.
- **Referral**: A change in the nature of a smoker's cough (e.g., becoming more productive, frequent, or sounding different) may suggest **malignancy**, requiring further evaluation.

When to refer

1. Cough lasting 2 weeks or more and not improving
2. Sputum (yellow, green, rusty or bloodstained)
3. Chest pain
4. Shortness of breath
5. Wheezing
6. Whooping cough or croup
7. Recurrent nocturnal cough
8. Suspected adverse drug reaction
9. Failed medication

Drug-Induced Cough:

- **Angiotensin-Converting Enzyme (ACE) Inhibitors** (e.g., Lisinopril, Enalapril):
  - The cough may develop within **days, weeks, or even months** after starting treatment.
  - **Referral** is recommended, and a switch to **Angiotensin II receptor antagonists** (e.g., Valsartan, Losartan) may be suggested as an alternative.
- **Beta-adrenergic blockers** (systemic and ophthalmic) can induce cough in patients with obstructive airway diseases like asthma or COPD.

Treatment Timescale for Cough

- **Evaluation of Patient Outcomes:**
- **Treatment Duration**: Nonprescription therapy should **alleviate cough within 7 days**. If symptoms improve, continue until resolved.
- **Follow-Up**: Cough from viral upper respiratory tract infections usually resolves in 2 weeks; persistent post-viral coughs may last up to 3 weeks.
- Refer for further evaluation if cough worsens or persist within 2 weeks.

Treatment of Cough

- **Treatment Goals:**
- **Primary Goal**:
  - ✓**Reduce the number and severity of cough episodes**.
- **Secondary Goal**:
  - ✓**Prevent complications** associated with prolonged coughing.
- **Symptomatic Treatment**:
  - ✓Cough treatments focus on symptom relief, but **addressing the underlying cause** of the cough is essential to stop it completely.

General Treatment Approach for Cough

- **Medication Selection**:
  - The choice of medication depends on the **nature** and **cause** of the cough.
  - You should highlighting symptoms that require referal.

1. **Antitussives (Cough Suppressants)**:
   - **Use**: Primarily for **non-productive coughs**.
   - **Caution**: Should not be used for **productive coughs**. Suppression of productive coughs can lead to retention of secretions, increasing the risk of airway obstruction and secondary bacterial infections.
2. **Protussives (Expectorants)**:
   - **Use**: Help change the consistency of mucus and increase the volume of sputum, making it easier to expel.
   - Beneficial for coughs with thick, tenacious secretions.

Cough Medications and Dosage Forms

- **Variety of Dosage Forms**:
  - **Cough medications** are available in various forms, including:
    1. Syrups
    2. Liquids and solutions
    3. Suspensions
    4. Tablets and capsules
    5. Lozenges
    6. Oral granules
    7. Topical ointments, creams, and patches
    8. Vaporizer solutions

Cough Medications and Dosage Forms

- **FDA-Compliant Combinations**:
  - The **FDA** allows combinations of various agents, including:
    - Antitussives (cough suppressants) or Protussives (expectorants) with
    - Analgesics
    - Decongestants
    - Antihistamines
  - **Caution**: Combining **antitussives** and **protussives** may be **counterproductive**, as suppressing a productive cough can hinder mucus clearance, while expectorants aim to promote it.

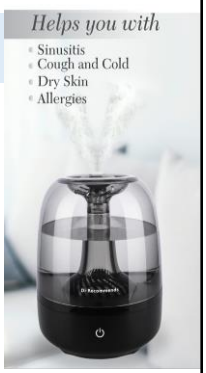
Nonpharmacologic Therapy for Cough

1. Non-medicated Lozenges (Demulcents) for Cough Relief

- **Ingredients**: **honey**, **lemon**, and **glycerol**.
- **Mechanism**:
  - These ingredients **coat the pharyngeal mucosa**, soothing inflammation and reducing irritation, making them useful for both **productive** and **non-productive coughs**.

- **Benefits**:
  - They are **harmless** and **cheap**.
  - Considered safe for **children** and **pregnant women** but should not be given to children **under three years** due to the **risk of choking**.
- **Administration**:
  - Can be taken **3-4 times daily** as recommended.

Nonpharmacologic Therapy for Cough



2. Humidification:

- **Humidifiers** increase moisture in inspired air, soothing irritated airways.
- High humidity may promote **mold**, **dustmites** and **microorganism** growth.

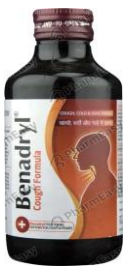
3. Vaporizers:

- Produce medicated vapor through a well or cup for **volatile inhalants**.
- Must be **cleaned daily** and **disinfected weekly** to prevent contamination.

Nonpharmacologic Therapy for Cough

4. **Nasal Drainage Promotion**:
   - **Babies and young children** (up to 2 years): Use a **rubber bulb nasal syringe** to clear nasal passages when postnasal drip causes coughing.
   - **Infants**: Propping them upright during sleep and raising the head of the bed promotes better nasal drainage.
5. **Hydration**:
   - Staying well-hydrated helps form less viscous, easier-to-expel secretions.
   - **Caution**: In conditions like **heart failure**, and **renal failure**, over hydration can worsen symptoms, so cautious hydration is advised.

Pharmacologic Therapy

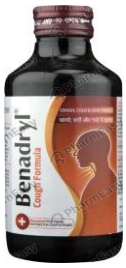


- **Oral Antitussives**

1. **Codeine (Robitussin, Cheratussin)**
   - Mechanism: Centrally suppresses the cough reflex.
2. **Dextromethorphan (Sedilar, Delsym)**
   - Mechanism: cough suppressant, works similarly to codeine.
3. **Diphenhydramine (Benadryl, Diphen Cough)**
   - Mechanism: Antihistamine with cough-suppressing effects.

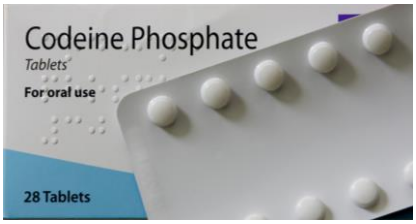
Pharmacologic Therapy

- Codeine, **pholcodine**, and **dextromethorphan** are effective in dry cough.
- **Dextromethorphan** and **pholcodine** have a **lower risk of causing constipation** and **dependence** compared to codeine.
- Additionally, both **pholcodine** and **codeine** can cause **sedation** in most individuals, whereas **dextromethorphan** is generally **non-sedating**.



Codeine

- **Schedule Classification and Regulation**:
  - At antitussive dosages, codeine is a **Schedule V narcotic**.
- **Pharmacodynamics**:
  - Codeine acts centrally on the **medulla** to increase the cough threshold. It is **metabolite morphine** may contribute to its antitussive effect.



Codeine

- **Indications**:
  - Codeine is used for **non-productive cough**
- **Dose and Dosage Forms**:
  - 1 mg/kg/day in **4 equal divided dosages** (adult 70 kg, 20mg QID, Max 120mg)
  - Available as **oral solutions, liquids, suspensions, and syrups**, often in combination.
- **Adverse Effects**:
  - Common side effects include **nausea, vomiting, sedation, dizziness, and constipation** and at high doses might cause **respiratory depression**.

Codeine

- **Cautions and Contraindications**:
  1. Used cautiously in Asthma, COPD
  2. Those using **CNS depressants** (e.g., Sedatives, alcohol) due to additive CNS depression effects.
  3. It is contraindicated in patients with **codeine hypersensitivity**
  4. During labor if **premature birth** is expected.

Dextromethorphan

- **Non-opioid antitussive** with lower risk of sedation, respiratory depression, or addiction at normal therapeutic doses.
- **Abuse Potential**:
  - Dextromethorphan is known for its **abuse potential**, particularly for its **euphoric effects** at high doses.

Dextromethorphan

- **Pharmacodynamics**:
  - Dextromethorphan acts centrally in the **medulla** to increase the cough threshold, much like codeine.
- **Indications**:
  - Dextromethorphan is indicated for the suppression of **non-productive cough** due to respiratory tract irritation. Like codeine, its **efficacy in children** is not well-established.

Dextromethorphan

- **Dose and Dosage Forms**:
  - **Adult:** 30 mg every 6-8 hours (120 mg)
  - **Children:** 15 mg every 6-8 hours (60 mg)
  - **Children:** (2-6y) 7.5 mg every 6-8 hours (30 mg)
- It is available in a variety of forms: **syrups, liquids, solutions, extended-release suspensions, gel caps, tablets, capsules, powders, and lozenges**.

Dextromethorphan

- **Adverse Effects**:
  - **Usual doses** of dextromethorphan have a **wide margin of safety**, with **side effects** being uncommon but potentially including **drowsiness, nausea, vomiting, stomach discomfort, and constipation**.
  - **Overdose** can lead to symptoms such as **confusion, excitation, restlessness, drowsiness**, and severe **nausea and vomiting**. At very high doses, it can cause **respiratory depression**.

Dextromethorphan

- **Cautions and Contraindications**:
  - **Additive CNS depression** may occur when taken with **antihistamines**, or **psychotropic medications**.
  - **Serotonin syndrome** can occur if taken with **monoamine oxidase inhibitors (MAOIs)**, causing symptoms such as **hypertension, hyperpyrexia, arrhythmias, and myoclonus**.
  - Patients should avoid taking dextromethorphan for **14 days** after discontinuing an MAOI.

Diphenhydramine

- **Pharmacodynamics**:
  - Diphenhydramine is sedating **antihistamine**. It acts centrally in the **medulla** to increase the **cough threshold**, making it effective as an **antitussive**.
- **Indications**:
  - Diphenhydramine is used for the suppression of **non-productive cough** due to **chemical or mechanical respiratory tract irritation**. It is a common ingredient in **cold and allergy** medications.

Diphenhydramine

- **Dose and Dosage Forms**:
  - **Adult**: 25 mg every 4 hours.
  - **Children**: 12.5 mg every 4 hours
  - **Children** (2-6y): 6.25 mg every 4 hours
  - Available in multiple formulations: **syrups (including alcohol-free formulations), liquids, tablets, capsules**, and as a combination in **cold and allergy products**.

Diphenhydramine

- **Adverse Effects**:
  - Common side effects include **drowsiness, disturbed coordination, respiratory depression, blurred vision, urinary retention, dry mouth, and dry respiratory secretions**.
  - **Uncommon side effects**: **oculogyric crisis** (rotation of eyeballs)
- **Cautions and Contraindications**:
  - Use with **caution** in patients with conditions exacerbated by **anticholinergic activity** (e.g., **narrow-angle glaucoma, BPH, asthma**, and **cardiovascular disease**).

Protussives (Expectorants)

- **Guaifenesin** is an **FDA-approved expectorant** and is available **over-the-counter (OTC)**.
- **Pharmacodynamics**:
  - Guaifenesin works by **loosening and thinning mucus in the lower respiratory tract**, which helps make a **minimally productive cough more effective**.
- **Indications**:
  - It is indicated for the **symptomatic relief of acute, ineffective productive cough**.

Guaifenesin

- **Dose and Dosage Forms**:
  - Adult: 200-400 mg every 4 hours (2.4 g)
  - Children : 100-200 mg every 4 hours (1.2 g)
  - Children (2-6y): 50-100 mg every 4 hours (600 mg)
  - Guaifenesin is available in various formulations, including **oral liquids, syrups, caplets, granules, immediate-release, and extended-release tablets**.

Guaifenesin

- **Adverse Effects**:
  - Guaifenesin is generally well tolerated, but common side effects include **nausea, vomiting, dizziness, headache, rash, diarrhea, drowsiness**, and **stomach pain**.
  - **Large doses** have been associated with **renal calculi** (kidney stones).
- **Cautions and Contraindications**:
  - **Hypersensitivity** to the drug.
  - **Overuse** might cause overdose symptoms.

Bromhexine

- Bromhexine is a mucolytic used in the treatment of respiratory disorders associated with productive cough.
- It is usually given orally in a dose of 8-16 mg three times daily.

Guidelines by ACCP (American College of Chest Physicians):

1. Central cough suppressants like codeine and dextromethorphan are **ineffective** for coughs associated with the **common cold**.
2. A **first-generation antihistamine** combined with a **decongestant** is recommended to treat **virus-induced postnasal drip**, which often causes cough.
3. **Naproxen**, an anti-inflammatory, may reduce cough associated with **viral infections** by decreasing upper airway nerve sensitivity.
4. For **chronic upper airway cough syndrome**, a first-generation **antihistamine/decongestant** combination is recommended when the cause is unclear.
5. **Codeine or dextromethorphan** is suggested for **short-term relief of acute and chronic bronchitis** and **post-infectious subacute cough**.

Special Populations and Dosage Guidelines for Cough and Cold Medications:

- **FDA Public Health Advisory**:
  - In 2008, FDA advised **against using nonprescription cough and cold medications** for **infants and children under 2 years** due to serious and potentially life-threatening side effects.

- **Codeine** (Pregnancy Category C):
  - **Pregnancy**: Use only if benefits outweigh risks due to risks like **neonatal respiratory depression** and withdrawal.
  - **Breastfeeding**: Excreted in breast milk, can cause **drowsiness** in infants.
  - **Elderly**: More prone to **sedation**; start with the lower end of dosage range and titrate cautiously.

Special Populations and Dosage Guidelines for Cough and Cold Medications:

- **Dextromethorphan** (Pregnancy Category C):
  - **Pregnancy**: Considered **causiously**.
  - **Breastfeeding**: Unknown if excreted in breast milk.
  - **Elderly**: More susceptible to **sedating effects**; start at a lower dose with careful monitoring.
- **Diphenhydramine** (Pregnancy Category B):
  - **Pregnancy/Breastfeeding**: Excreted in breast milk, may cause **irritability** or decrease milk flow.
  - **Elderly**: Identifies diphenhydramine as potentially inappropriate for older adults.
  - Both **children and elderly** may experience **paradoxical excitation**.
- **Guaifenesin** (Pregnancy Category C):
  - **Pregnancy/Breastfeeding**: No controlled data available.
  - **Elderly**: No special considerations needed.

Patient Counselling for Cough

Administration:

- **Lozenges**: Dissolve slowly in the mouth; do not chew.
- **Tablets/Capsules**: Swallow whole; do not crush or chew.
- **Follow Dosage Guidelines**: Adhere strictly to recommended dosages.
- **Storage**: Store medications as recommended; do not use expired drugs.