Drugs for Cough

There are two sorts of cough:
1. **Productive** (the useful) when it expels secretions or foreign material from the respiratory tract, this cough should be allowed to serve its purpose and suppressed only when it is exhausting the patient or is dangerous, e.g. after eye surgery.
2. **Unproductive** and persistent (the useless), should be stopped e.g. Asthma, rhinosinusitis, oesophageal reflux

**Mechanism of cough:**

Stimulation of mechano-or chemoreceptors (throat, respiratory passages or stretch receptors in lungs) → Afferent impulses to cough centre (medulla) → Efferent impulses via parasympathetic & motor nerves to diaphragm, intercostal muscles & lung → Increased contraction of diaphragmatic, abdominal & intercostal (ribs) muscles ⇒ noisy expiration (cough)

**SITES OF ACTION FOR TREATMENT:**

**Peripheral sites:**

On the afferent side of the cough reflex: by reducing input of stimuli from throat, larynx, trachea, a warm moist atmosphere has a demulcent effect on the pharynx.

On the efferent side of the cough reflex: to render secretions more easily removable (mucolytics)

**Central nervous system**

Agents may act on:
- The medullary paths of the cough reflex (opioids)
- The cerebral cortex
- The subcortical paths (opioids and sedatives in general).
The best antitussive of all is removal of the cause of the cough itself, e.g. treatment of underlying conditions such as:
- Asthma
- Postnasal drip
- Gastrooesophageal reflux.
In patients with hypertension or cardiac failure, a common cause of a dry cough is treatment with an ACE inhibitor.

COUGH SUPPRESSION:

Antitussives
1. Peripheral antitussives
2. Central antitussives

1. Peripheral antitussives
   1) Demulcients that soothingly coat the pharynx
   2) Linctus (mainly sugar-based syrup).
   3) Lozenges
   4) Inhalation
   5) Water aerosol inhalation
   6) Benzoin to give the inhalation a therapeutic smell (aromatic inhalation)
   7) Local anaesthetics block the mucosal cough receptors (modified stretch receptors) directly, nebulised lignocaine reduces coughing:
      - During some type of bronchoscopy
      - In the cough that accompany bronchial carcinoma.

2. Centrally acting Antitussives

The opioid analgesics are among the most effective drugs for the suppression of cough (medullary cough centre itself)
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- At doses below those necessary to produce analgesia. The receptors involved in the antitussive effect differ from those associated with the other actions of opioids. The opioid derivatives used as antitussives are **dextromethorphan, codeine, and noscapine**
- **Methadone or diamorphine** linctus preferred in patients with advanced bronchial carcinoma
- **Pholcodine**, (nonsedating and nonaddictive), is widely used.

**Dextromethorphan:**
- It is NMDA (N-methyl d-aspartate receptor) antagonist.
- Free of addictive properties and produces less constipation than codeine.
- The usual antitussive dose is 15-30 mg three or four times daily.

**Codeine:** has antitussive action at doses lower than those required for analgesia. Thus, 15 mg are usually sufficient to relieve cough.

**Antihistamines:** Sedation reduces the sensitivity of the cough reflex. Older sedating antihistamines, e.g. diphenhydramine often the doses needed causes drowsiness so that combination with other drugs, such as pholcodine and dextromethorphan,
- In children cough is nearly always useful and sedation at night is more effective than is codeine. A sedative antihistamine (e.g. promethazine), sputum thickening may be a disadvantage.

(3-5)
MUCOLYTICS AND EXPECTORANTS

Respiratory mucus consists largely of water and its slimy character is due to glycoproteins cross-linked together by disulphide bonds.

In pathological states much more mucus may be produced; an exudate of plasma proteins which bond with glycoproteins and form larger polymers results in the mucus becoming more viscous.

A mucolytic drug: is a drug that breaks down thick mucus, making it thinner and easier to cough out.

Carbocisteine and mecystine
- MOA: have free sulphhydryl groups that open disulphide bonds in mucus and reduce its viscosity.
- Orally administrated or by inhalation
- Uses: when viscous secretion is a problem (cystic fibrosis)
- Side effects: gastrointestinal irritation and allergic reaction.

Bromhexine:
- Thinning & fragmentation of mucopolysaccharide fibers
- ↑ volume & ↓ viscosity of sputum

Dornase alfa is phosphorylated glycosylated recombinant human deoxyribonuclease.
- MOA: hydrolyzes the DNA present in sputum/mucus of cystic fibrosis patients and reduces viscosity in the lungs
- It is given daily by inhalation

Expectorants:
- Encourage productive cough by increasing the volume of bronchial secretion.
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The group includes:
- Guaiphenesin
- Ipecacuanha
- Volatile oils

**Guaiphenesin**:
Expectorant drug usually taken by mouth, Available as single & also in combination
**MOA:** Increase the volume & reduce the viscosity of secretion in trachea & bronchi.

**Choice for drug therapy for cough:**
- Simple suppression of useless cough

Codeine, pholcodine, dextromethorphan and methadone.
In pertussis infection (whooping cough), codeine and atropine
- To increase bronchial secretion slightly and to liquefy what is there.

Water aerosol with or without menthol and benzoin inhalation, or menthol and eucalyptus inhalation may provide comfort harmlessly.
Carbocysteine or another mucolytic orally may occasionally be useful.
- Cough originating in the pharyngeal region lozenges or demulcents are used.