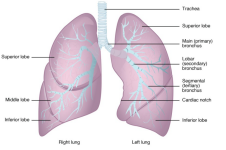




Interactions in respiratory system pathologies.

They are the main reason for first consultations in primary medicine.

Third leading cause of death in Europe.



Cough

reflex action with a protective function

Productive: there is expectoration (without treatment).
Non-productive or dry: there is no expectoration (requires treatment).

Can be acute or **chronic** (>10 days).

is initiated by **irritant** stimuli carried by the **vagus** nerve (neumogastric)

vagal sensory fibers: **fast** adapting receptors, **capsaicin**-sensitive and bronchopulmonary afferent **C-fibers** (cough reflex)

integration in the **cough center** in the **medulla oblongata** (independent of the respiratory centre)



cough centre efferent pathways → muscle response → **act of coughing:** inhalation, ↑intrathoracic pressure and then expulsion.

Antitussive Drugs

opioid antitussives

Codeine

Depresses the medullary **cough centre**, inhibits the production of **tachykinins**, the main neurotransmitters of the **C-fibers** of this center.

Oral, with or without food, **syrups**? directly or **dissolved** in another liquid.

Not in COPD, severe asthma. Causes **respiratory depression**.

Not in pregnancy → neonatal asstinence syndrome (**FDA category C**).

May give **nausea**, vomiting, constipation. Interacts with **alcohol** ↑effect.

Dextromethorphan

Codeine **analog**. Depresses the medullary **cough centre**, inhibits **tachykinins** (**C-fiber** neurotransmitters).

Rapidly absorbed **orally**, with or without food. **avoid grapefruit juice** or bitter oranges.

Not in asthma or COPD, children and lactation.

May give **dizziness**, drowsiness, **nausea**, vomiting, intestinal discomfort, fatigue.

Lacks narcotic effects. **Alcohol** and **grapefruit juice** ↑effect.

Noscapine

Depresses the medullary **cough centre**, inhibits **tachykinins** (**C-fiber** neurotransmitters).

Oral or suppositories, preferably after meals.

Not respiratory depressant, not mucociliary clearance, not bronchial secretions, **bronchodilator**.

Yes in children from 2 years old, not in pregnancy/lactation.

It causes **nausea**, headache and drowsiness. Interacts with **alcohol** ↑effect.

non-opioid antitussives

Cloperastine

possible depression of the **cough centre** + **bronchodilation** and local **anesthesia** in the bronchi

syrup, oral suspension → shake before use, can be taken **with or without food**

Does **not** result in **dependence** or nervous depression like opioids

Yes in **children** from 2 years of age

They have **anticholinergic** effects (be careful in children as they are more sensitive).

Levodropropizine

Interference in the release of sensory neuropeptides in the respiratory tract (inhibits **capsaicin**-induced cough).

Oral, 3 **fasting** doses → at least 6 hours apart.

Greater effects than cloperastine if cough is induced by **peripheral** stimuli.

10x **less effective** than codeine in cough of **central** origin.

May cause **nausea**, vomiting, **diarrhea**, abdominal pain, gastric hyperacidity, dyspepsia, somnolence, headache, vertigo, palpitations.

other antitussives

Mepiromide

Xanthine. Nonspecific **H1 antihistamine**, produces slight bronchodilator effect.

Oral with food

Not in porphyria

May cause **nausea**, vomiting, constipation, diarrhea, epigastric pain, anorexia, dry mouth (symptoms **decrease** if taken **with food**).

With **alcohol** there is drowsiness

Ipratropium bromide

bronchodilator and anticholinergic + cough reflex impulse blocker.

Inhaled

may cause **nausea**, dry mouth and dyspepsia.

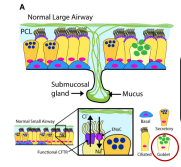
Diphenhydramine

Central cough suppressant and H1 antihistamine.

with sufficient **liquid**, with or without **food**, before going to **bed**.

May cause **dry** mucous membranes and **thickening** of mucus.

With **alcohol** produces drowsiness



Produced by **goblet cells** (MUC5AC) and **submucosal gland cells** (MUC5B)

purpose: to **protect** the tracheal mucosa

mature **glycoproteins** or mucins, high molecular weight: **gel-like mucus**.

increased mucus viscosity due to the presence of high amounts of **DNA**

Mucous **drainage:** ciliary activity and coughing

Drugs

Expectorants

eucalyptus and menthol

Essential oils of the terpenes group

Iodides (potassium iodide)

increase the **aqueous secretion** of the **submucosal glands** by direct action or by activation of the **gastropulmonary vagal reflex**.

potassium iodide: **gastrointestinal** discomfort, rhinorrhea, iodism and thyroid alterations.

Guaifenesin

guaiaacetyl glyceryl ether. Stimulates the production of **bronchial** secretions by reflex mechanism of irritation of the gastric mucosa

Oral, syrup directly and then a **glass of water**, with or without food.

Not in **porphyria**, not in children <2 years.

Adverse effects: **nausea**, vomiting, diarrhea, dizziness, headache.

Mucolytics

Thiol derivatives

Acetylcysteine

They **break disulfide bridges**, reducing mucus viscosity. maximum effect at pH 7-9.

Oral, best with food, best in the **morning**

Reduces mucus hyperviscosity in common cold and flu

Not in hypersensitivity, caution in children.

May cause **nausea**, vomiting, diarrhea and gastric hyperacidity

Carbocysteine

increases the **synthesis of sialomucins**, thus re-establishing the normal composition of mucus secretion, **normalizing mucus viscoelasticity**.

Oral, maximum dose 600mg once a day, **glass of water after each dose**, plenty of water during the day.

Not in **peptic ulcer** (aggravation), not in <2 years.

May give **nausea**, vomiting, dyspepsia and abdominal pain.

Vasidin derivatives

Bromhexidine

activation of **sialyl-transferase**, responsible for synthesizing **sialomucins**

normalization of mucus composition. Activation of **lysozyme** which induces the **breakdown of mucopolysaccharides**.

Oral, inhalation or injectable, **glass of water after each dose**, plenty of water during the day.

Reduces mucus hyperviscosity in common cold and flu. Not in hypersensitivity, caution in children

May cause **nausea**, vomiting, diarrhea and abdominal pain.

Ambroxol

increased synthesis of **sialomucins** → **normalizes** mucus composition.

Mucous glands of the bronchial epithelium increasing **lysozyme** → **breakdown** mucopolysaccharides and stimulation of mucociliary activity.

Oral

Reduces mucus hyperviscosity in common cold and flu

Not in children <2 years. May cause **nausea**, dysgeusia and hypoesthesia.

Enzymes

Dornase Alpha

Degradation of **DNA** molecules from **neutrophil lysis** (the cause of mucus hyperviscosity).

Inhalation

For **cystic fibrosis** (treatment >5 years). Not in hypersensitivity.

May cause **hoarseness** and **pharyngitis**, rash with urticaria and conjunctivitis, possible chest pain.

Streptodornase

deoxyribonuclease that produces an **enzymatic degradation** of suppurative and viscous exudates.

Nebulisation

Indicated in **very specific cases** and only for a few days.

Can cause **bronchospasm** and **hypersensitivity** reactions of varying severity.

Highly **variable efficacy** and low yield.

Drugs

Bronchodilators

for immediate phase response

B2-adrenergic agonists

Salbutamol (ventolin) and **Terbutalin** → short action
Salmeterol, **Formoterol**, **vilanterol**, **indacaterol** → long action

Taken by inhalation

short-acting, on demand, 3-5 hours of action. **Long-acting**, twice daily, 12 hours of action.

For asthma and COPD, give mild **tremor**, tachycardia or **hypokalaemia** after high doses.

Caution in hyperthyroidism, **cardiovascular disease** or arrhythmias.

Anticholinergics

Ipratropium bromide → short action
Tiotropium → long action

They **block muscarinic receptors**, (M3), which respond to **parasympathetic** bronchoconstrictor tone

Inhaled

Not in glaucoma, prostatic hypertrophy and pregnancy.

may cause dry mouth. Systemic effects are rare.

Xanthines

Thiophylline

inhibits **phosphodiesterase** by increasing **cAMP** levels → smooth muscle relaxation and **bronchodilation**

also anti-inflammatory

Oral

Not in heart disease, may cause **digestive problems**, nausea, vomiting, tremor, **insomnia** and tachycardia

interacts with **tobacco**, lowering the effect of thiophylline.

Anti-inflammatories

for late phase response

Leukotriene receptor antagonists

Montelukast

inhibit the effect of endogenous **leukotrienes** and produce **bronchodilation**.

Oral

may cause **inflammation** of blood vessels, **nausea**, vomiting, abdominal pain and **diarrhoea**.

interacts with **orange juice** lowering its **bioavailability** and **efficacy**.

Glucocorticoids

Budesonide, **beclomethasone**, **dipropionate**, **fluticasone propionate**

reduce mucosal inflammatory response → **reduce** bronchial **hyperresponsiveness**.

inhaler. oral or intravenous is reserved for severe chronic asthma

more potent and effective treatment, may give oral or pharyngeal candida, cough, pharyngitis

Interacts with **grapefruit juice** ↑effect, **alcohol** (ulcers), **Ca** (must be supplemented), **echinacea** (↑effect), **liquorice** (↑effect), **tobacco** (↑effect).

Chronic inflammatory disease with bronchial **hyperresponsiveness** and variable airflow **obstruction**.

Goal of approach:
- To achieve and maintain **control** of the pathology.
- **Prevention** of future risk (exacerbations)

Prevalence: increasing ↑12.6% from 1990 to 2015, more in **middle age** and **women**.

Many **risk factors:** host, perinatal, environmental, and medication.

Exaggerated contraction of bronchial smooth muscle (**hyperresponsiveness**) to allergens causing mast cell degranulation.

Inflammatory mediators → inflammatory reaction in bronchi (damage and further hyperresponsiveness).

