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Respiratory System

The primary function of the respiratory system is the gas exchange between the inspired air and the pulmonary artery blood. Because of the large surface area of the alveoli and exposure to the environment, this organ system is prone to antigen–allergy responses and infection.
The defenses of the respiratory system include *hypersecretion of mucus, *sneezing and coughing reflexes, *bronchoconstriction, and *macrophage activation and inflammation.
Pharmacology of the respiratory system centers around these defense mechanisms and can be simplified into seven categories:
(1) Elimination of excess secretions and membrane congestion.
(2) Bronchiole dilation when excessive constriction occurs.
(3) Cough suppression when it is nonproductive and detrimental to the animal.
(4) Control of infection and inflammation.
(5) Decrease pulmonary hypertension.
(6) Stimulate the peripheral chemoreceptors and the central respiratory center.

In this lecture we shall divide the drugs that effect on the respiratory system to categories and these are:-

1- Expectorants: the drugs that loosen and clear mucus and phlegm from the respiratory tract.
• Most of the expectorants act reflexively by irritating the gastric mucosa. This, in turn, stimulates secretions in the respiratory tract. Expectorants remove bronchial secretions which are purulent (containing pus), viscid (thick), or excessive. The loosened material is then moved toward the pharynx through ciliary motion and coughing. Like: Guaifenesin, ammonia salts, Ipecacaunna and senega.

2- Mucolytics*:* is any agent which dissolves thick mucus usually used to help relieve respiratory difficulties.

• Acetylcysteine:

- This drug reacts with mucus resulting in liquefaction of it.
- This is a mucolytic given by inhalation or nebulization. (Nebulization is treatment by spray).
- Mucomyst® solution is nebulized into a face mask or mouth piece because of
Acetylcysteine has an unpleasant (like rotten eggs) smell.
- Side effects associated with this agent include nausea and vomiting and broncho- spasms with higher concentrations.

• Bromohexine: (bisolvan®)

1.Bromhexine supports the body's own natural mechanisms for clearing mucus from the respiratory tract.

2.It is secretolytic: that is increases the production of serous mucus in the respiratory tract and makes the phlegm thinner and less sticky. This contributes to a secretomotoric effect: it helps the cilia - tiny hairs that line the respiratory tract - to transport the phlegm out of the lungs. For this reason it is often added to some antitussive (cough) syrups.

3- Drugs used to treat chronic obstructive pulmonary disease(COPD)

COPD is a chronic, irreversible obstruction of airflow that is usually progressive. Symptoms include cough, excess mucus production, chest tightness, breathlessness, difficulty sleeping, and fatigue. Although symptoms are similar to asthma, the characteristic **irreversible** airflow obstruction of COPD is one of the most significant differences between the diseases.

A. Bronchodilators

Inhaled bronchodilators, including the ß2 adrenergic agonists and anticholinergic agents (*ipratropium* and *tiotropium*, are the foundation of therapy for COPD. These drugs increase airflow, alleviate symptoms, and decrease exacerbation rates.

B. Corticosteroids

The addition of an ICS to a long-acting bronchodilator may improve symptoms, lung function and quality of life in COPD patients with FEV of less than 60% predicted. However, the use of an ICS is associated with an increased risk of pneumonia, and therefore, use should be restricted to these patients. Although often used for acute exacerbations, oral corticosteroids are not recommended for long-term treatment

4- Antitussives*:*

Agents that relieve or prevent coughing. Coughing is an important defense mechanism of the respiratory system to irritants and is a common reason for patients to seek medical care. A troublesome cough may represent several etiologies, such as the common cold, sinusitis, and/or an underlying chronic respiratory disease.
These agents, in general, act on the central nervous system to depress the cough reflex center in the medulla of the brain.
Antitussives are used to reduce respiratory irritation. Such reduction of respiratory irritation results in the patient's being able to rest better at night because he is not kept awake by his coughing.
Antitussives divided into:

- **A- Direct acting antitussives:** they act directly on the respiratory tract mucosa reducing their irritation like:
Demulucents(honey and syrup) .

- **B- Central acting antitussives:** this subdivision acts by depress the cough center in the medulla oblongata. example :-

- **Codeine**:

- Codeine is considered to be the most useful narcotic antitussive agent.
- Codeine aids in relieving the pain (that is, producing analgesia) associated with a hacking cough.
- The main side effects associated with codeine include drowsiness, nausea, vomiting, and constipation.

• Benzonatate (Tessalon®).

- Benzonatate is a nonnarcotic antitussive that produces its effect through a CNS depressant effect similar to codeine.

- Furthermore, it produces a local anesthetic effect on the stretch receptors in the lower respiratory tract, which control coughing.
- This drug has few side effects except that it will numb the mouth, tongue, and pharynx if the capsules are chewed (this is because of its topical anesthetic effect).

• Dextromethorphan (Pertussin CS®).
- Dextromethorphan is another non-narcotic antitussive.
- It is found alone or in combination--usually with expectorants.
- The most common side effect associated with this drug is gastrointestinal (G.I.) upset.

C- Miscellaneous drugs: this item of antitussive drugs includes:

I- Histamine receptor blockers: this group acts by blocking H1receptor in order to get rid from the cough which arises from histamine release. Example promethazine and diphenhydramine.

II- Corticosteroids: they are effective in treating of chronic cough. Example: Prednisolone.

5- Anti-asthmatic agents:

***Asthma*:** a condition usually caused by allergic reactions to substances in the environment, affects many people. The allergic reactions cause the bronchioles to spasm. Hence, the flow of air

into and out of the lungs becomes impaired. Characterized by episodes of acute bronchoconstriction causing shortness of breath, cough, chest tightness, wheezing, and rapid respiration.

Drugs used for treatment of asthma:

• **Bronchodilators:** Sympathomimetic bronchodilators act by relaxing contractions of the smooth muscle of the bronchioles. and they are according to their mechanism of action to:

1- β receptor agonists:

- These drugs have a β2 agonist effect so that they cause bronchodilation, like: albuterol and salmetrol.

- Other β receptor agonists act without selectivity (also they act with different mechanisms) like, epinephrine, ephedrine, metaproterenol and Isoproterenol.

2- Xanthines:

- They have long duration of action. The mechanisms which explain how the xanthiens work induce production of high amount of cAMP and consequently which increase norepinephrine release, and production of bronchodilation.

- The main adverse effect of the xanthines is the narrow margin of safety.

- Example: Aminophylline and Theophilline.

3- Anticholinergic agents:

- They are very useful in case of exercise- induced asthma.
- The most predominant drug for this purpose is Ipratropium.
• **Anti-inflammatory agents:** agents or drugs which prevent or minimize the inflammatory reaction in the bronchi.

1- Corticosteroids:

- Inhibit all arachidonic acid derivatives (specially: Prostaglandins and Leukotrienes).which act as inflammatory mediators.

- Corticosteroids are very useful in the treatment of asthma and prevention of recurrent attacks.

- Corticosteroids have many serious side effects Include: Primary insufficiency (Addison's disease) upon withdrawal, Osteoporosis, cataracts, growth retardation in children, Diabetes, Hypokalemia, Cushing's Syndrome, behavioral affects and Susceptibility to infections.

- Example: dexamethasone, betamethasone, and prednisolone.

2- Cromolyn (Intal®).

• Cromolyn is a unique product that works by inhibiting the release of histamine and other spasm-causing compounds from mast cells located in the lungs and prevents bronchoconstriction.

• It is used mainly for the treatment or prevention of mild bronchospasms associated with asthma.

• It is available as an inhalation aerosol and nebulization solution.

3- Anti-leukotrienes:

• These drugs decrease inflammatory reaction in the bronchi by decrease production of leukotrienes and the capability of them to bind to their receptors in the lung.

• Example: Zileuton and Zafirlukast.

6- Respiratory stimulants*:* the agents which used to treat respiratory failure. They are divide to:-

• Physiological stimulants:

I- CO_2:- a direct and potent respiratory stimulant

• CO_2 works in two ways; those are :

a- Directly, by stimulation of respiratory center.

b- Indirectly, by reflex and stimulation of carotid and aortic sinuses.

• CO2 used to treat respiratory failure in small animals.

II- O2:-

- O2 used by inhalation and it's mixed with 5% CO2.
- The mechanism of stimulation depends on the sensation of CO2.

• **Analeptics (CNS stimulants):** they act indirectly by stimulating respiratory center in the medulla oblongata. Examples: Leptazole, Nickthamide, Bemigride, Doxapram Ethamivan, Amiphenazole, Picrotoxin and Camphor.

• **Local irritants:** act by reflex stimulation of respiratory and vasomotor center to improve respiration and ventilation. Like Ammonia.