Bronchial Asthma

- **CLINICAL CASE**
- **Ms. Hoda is a 30 years-old woman was suffering from an acute attack of bronchial asthma. She had also a mild hypertension with figures of 140/100 mmHg for her blood pressure.**

Bronchial Asthma

- **1) One of the following drugs was prescribed to relieve her acute attack of asthma:**
- **A- Atropine**
- **B- Morphine**
- **C- Cromolyn sodium**
- **D- Salbutamol**

Bronchial Asthma

- **Your answer to the previous question was based on that this drug acts on One of the following mechanisms:**
- **A- Stimulation of alpha$_1$ and alpha$_2$ adrenoceptors.**
- **B- Selective stimulation of alpha$_2$ adrenoceptors.**
- **C- Selective stimulation of beta$_2$ adrenoceptors.**
- **D- Selective inhibition of beta$_1$ adrenoceptors.**

BRONCHIAL ASTHMA

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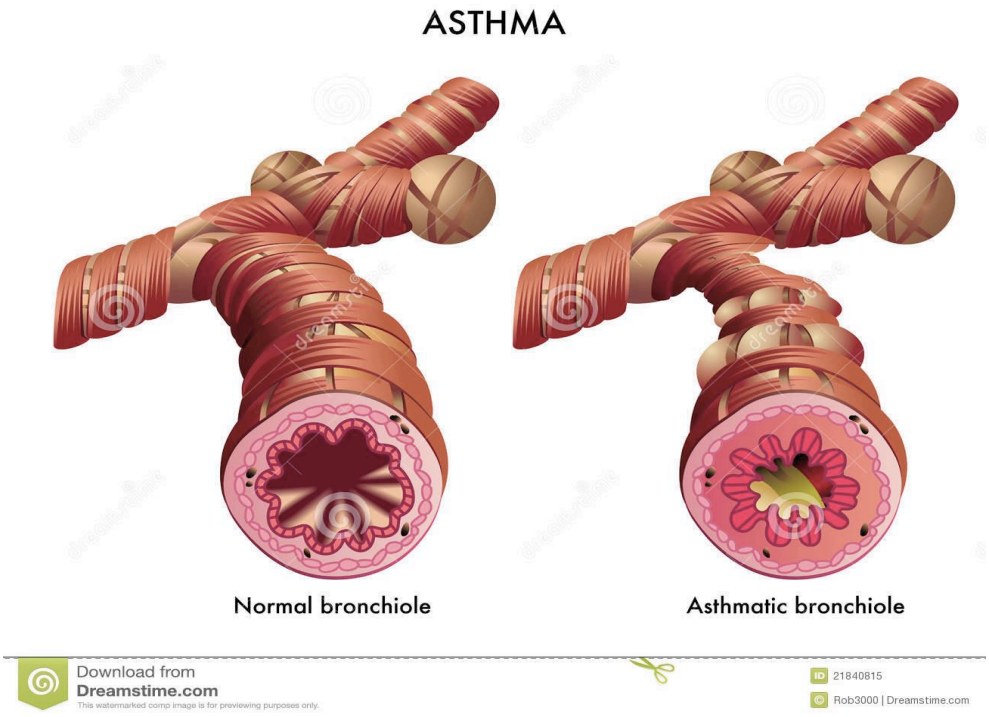
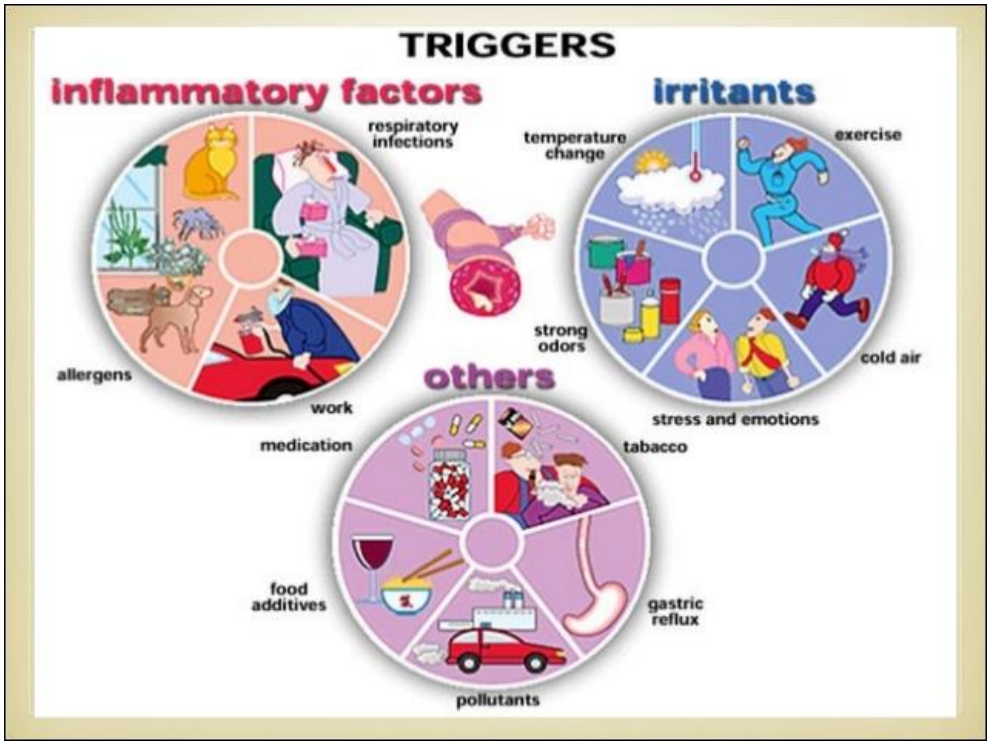




Clinical picture

Clinically bronchial asthma is characterized by **recurrent attacks** of:

- ✓ Shortness of breath (dyspnea).
- ✓Chest tightness.
- ✓Wheezing.
- ✓Cough.

Classification of drugs

➢ **BRONCHODILATORS**

- **Selective β_2 agonists**:

- Short & long acting.

- **Methyl-xanthines**:

- Theophylline & Aminophylline.

- **Anti-cholinergics**:

- Ipratropium bromide & Tiotrpium bromide.

☙ **ANTI-INFLAMMATORY**

- **Corticosteroids**:

- Prednisone & Methyl-prednisolone.

- **Mast cell stabilizers**:

- Cromolyn sodium.

- **Anti-Leukotrienes**:

- Leukotriene receptor antagonists & 5-lipoxygenase inhibitor.

ANTI-ASTHMATIC DRUGS

- **Bronchodilators**
- β2-adrenergic agonists
- Methylxanthines
- Anticholinergic drugs
- **Antiinflammatory drugs** :
- Corticosteroids
- Cromolyn sodium
- Leukotriene antagonists
- **Anti-IgE therapy**

Selective β2- agonists

(main stay treatment of bronchial asthma)

- **Short acting**: e.g. Salbutamol (albuterol) and terbutaline

-They have **rapid onset** and **short duration** of action (3-6 hours)

-Used in treating **acute attacks**

- **Long acting:** e.g. salmeterol, formoterol, levalbuterol

- **slow onset** and **longer duration** of action (up to 12 hours).
- Used as a **prophylactic** treatment

Side effects:

- ❖Tremors
- ❖Tachycardia
- ❖Tolerance (down regulation)

Mechanism of action: selective stimulation of β_2 adrenoceptors leading to relaxation of bronchial smooth muscles causing bronchodilatation**.**

Route of administration:

- ❖Inhalation
- ❖Parenteral
- ❖Oral

Anticholinergic drugs

Ipratropium, Tiotropium

In Bronchial asthma

- It reverses vagally (cholinergic) mediated bronchospasm in asthmatic patients where the parasympathetic tone is high.
- It also decreases mucous gland hypersecretion seen in asthma.

Therapeutic uses:

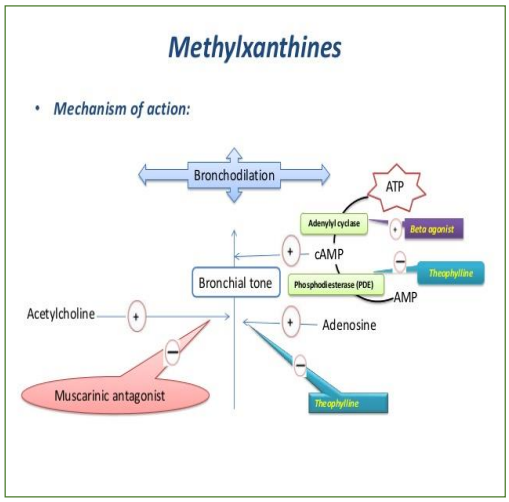
- They are **less effective** as bronchodilators than the selective β_2 agonists, therefore their use is only as **adjunct therapy** with selective β_2 agonists to **enhance their bronchodilator action.**
- Tiotropium has longer duration of action (24 hours).
- **GIVEN BY INHALATION**.

Methylxanthines

Theophylline

Mechanism of action:

- **Inhibition** of **phosphodiesterase enzyme** leading to **blocking** of the **breakdown** of both cAMP and cGMP.
- **Competitive inhibition** of **adenosine receptors** (adenosine in asthmatics can cause bronchoconstriction).



Methylxanthines

Pharmacological actions:

- **CVS:** **2 antagonistic effects**

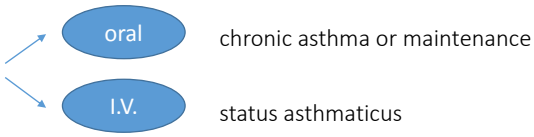
Central	Peripheral
▪ stimulation of vagal & vasomotor centers.	▪ Direct myocardial stimulation and direct peripheral vasodilatation.

- **In high doses, the peripheral effects predominates.**

(tachycardia, palpitation & extrasystoles)

(transient fall in blood pressure)

Therapeutic uses



- **Bronchial asthma**

The use of Methyl-xanthines in treatment of bronchial asthma has receeded to the 3rd or 4th line after β_2 agonists, corticosteroids & cromolyn

1- narrow margin of safety

2- difficult to design safe therapeutic regimen

3- clearance is influenced by genetic and environmental factors.

4- drug interactions (CYP3A4 substrate)

- inhibitors ---- cimetidine, erythromycin
- inducers ---- rifampin, phenytoin

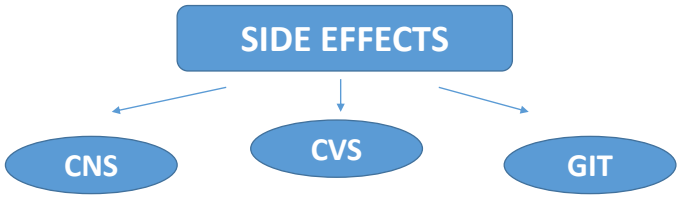
Therapeutic uses

- **Apnea in premature infants**

- Given oral or I.V. to stimulate respiratory center.
- Doxapram is added in refractory cases.

- **Headache & Migraine**

- Caffeine is added to aspirin to relief headache.
- Theophylline increases absorption and plasma levels of ergotamine.



Side effects

- ***In therapeutic dose***: gastro-intestinal discomforts, insomnia, tachycardia and palpitation.

- ***higher doses:*** seizures and arrhythmia that may be fatal especially if the drug in given I.V. in a rapid way.

So, theophylline I.V. administration **should be given slowly.**

What drugs can trigger asthma?

- **Medicines Can Trigger Asthma**
- Aspirin.
- Non-steroidal anti-inflammatory drugs, like ibuprofen and naproxen
- Non-selective Beta-blockers, which are usually used for heart conditions, high blood pressure and migraines like propranolol, nadolol.
- Cholinomimetic drugs like bethanechol.

Bronchial Asthma

•3) This drug also provides one of the following advantages:

•A- It effectively lowers her blood pressure in addition to its bronchodilator activity.

•B- Its bronchodilator activity is associated with an increase in the force of myocardial contractility.

•C- Its bronchodilator activity is associated with a cough sedative action.

•D- Its bronchodilator activity is associated with an effective diuretic action.

Bronchial Asthma

CASE 1

•4) One of the following appeared as a major side-effect of the drug you selected :

•A- Severe tachycardia.

•B- Orthostatic hypotension.

•C- Frequent tremors.

•D- Dry mouth.

Bronchial Asthma

CASE 1

•5) The side-effect you selected in the last question appeared due to one of the following:

•A- Stimulation of beta$_2$ receptors in skeletal muscle.

•B- Stimulation of beta$_2$ receptors in smooth muscles.

•C- Stimulation of beta$_2$ receptors in adrenal medulla.

•D- None of the above.