



Section IV

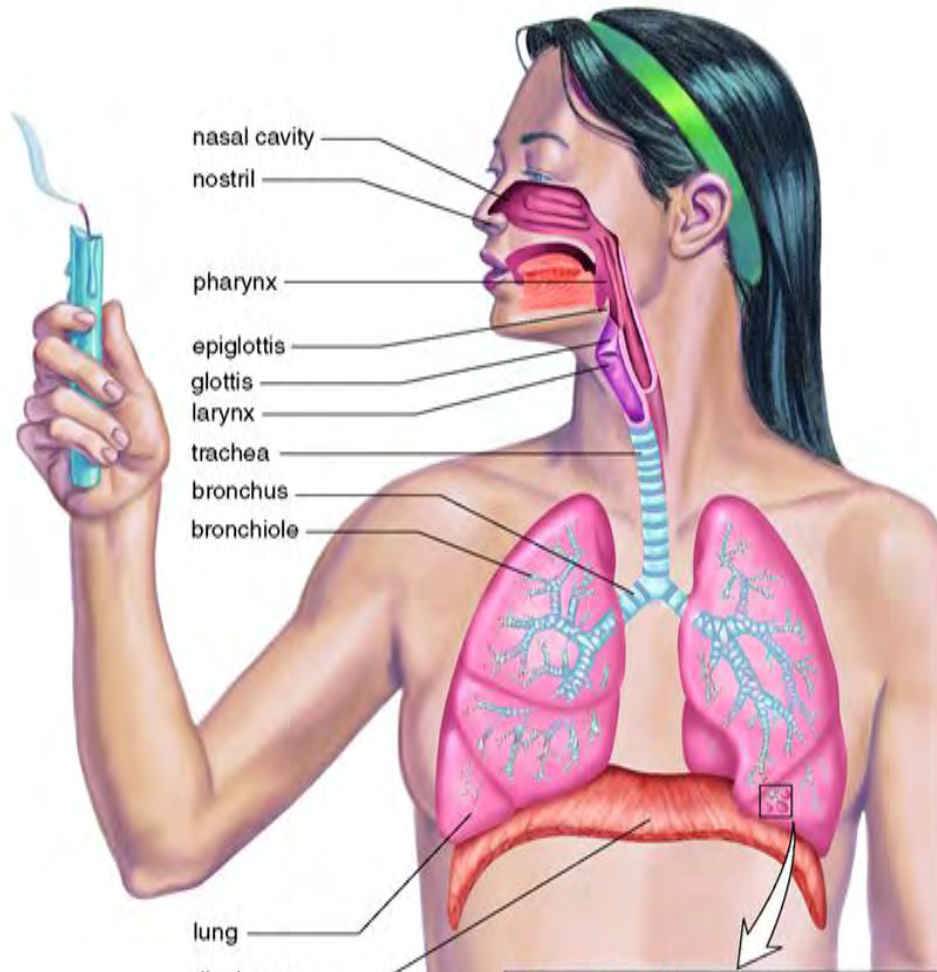
Respiratory systems

Chapter 6

Drugs for treatment of respiratory diseases



Antitussives
Expectorants
Antiasthmatic drugs



nasal cavity

nostril

pharynx

epiglottis

glottis

larynx

trachea

bronchus

bronchiole

lung

diaphragm

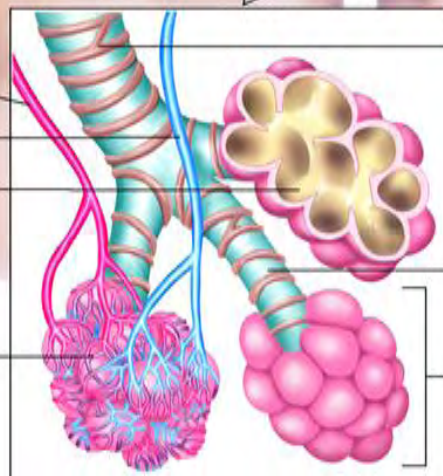
pulmonary venule

pulmonary arteriole

alveolus

capillary network

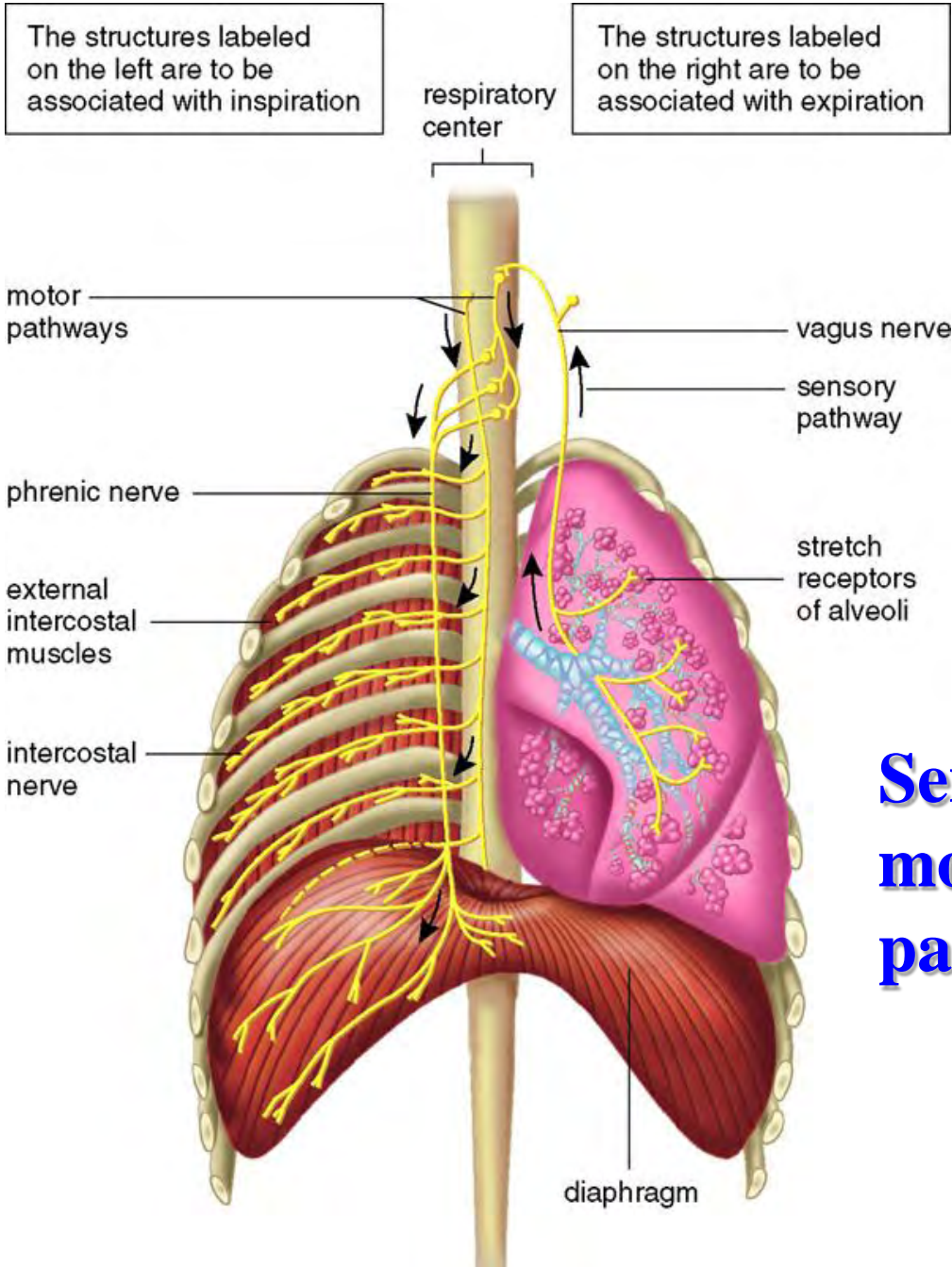
Normal structures of respiratory system



bronchiole

terminal bronchiole

alveolar sac



Sensory and motor nervous pathways

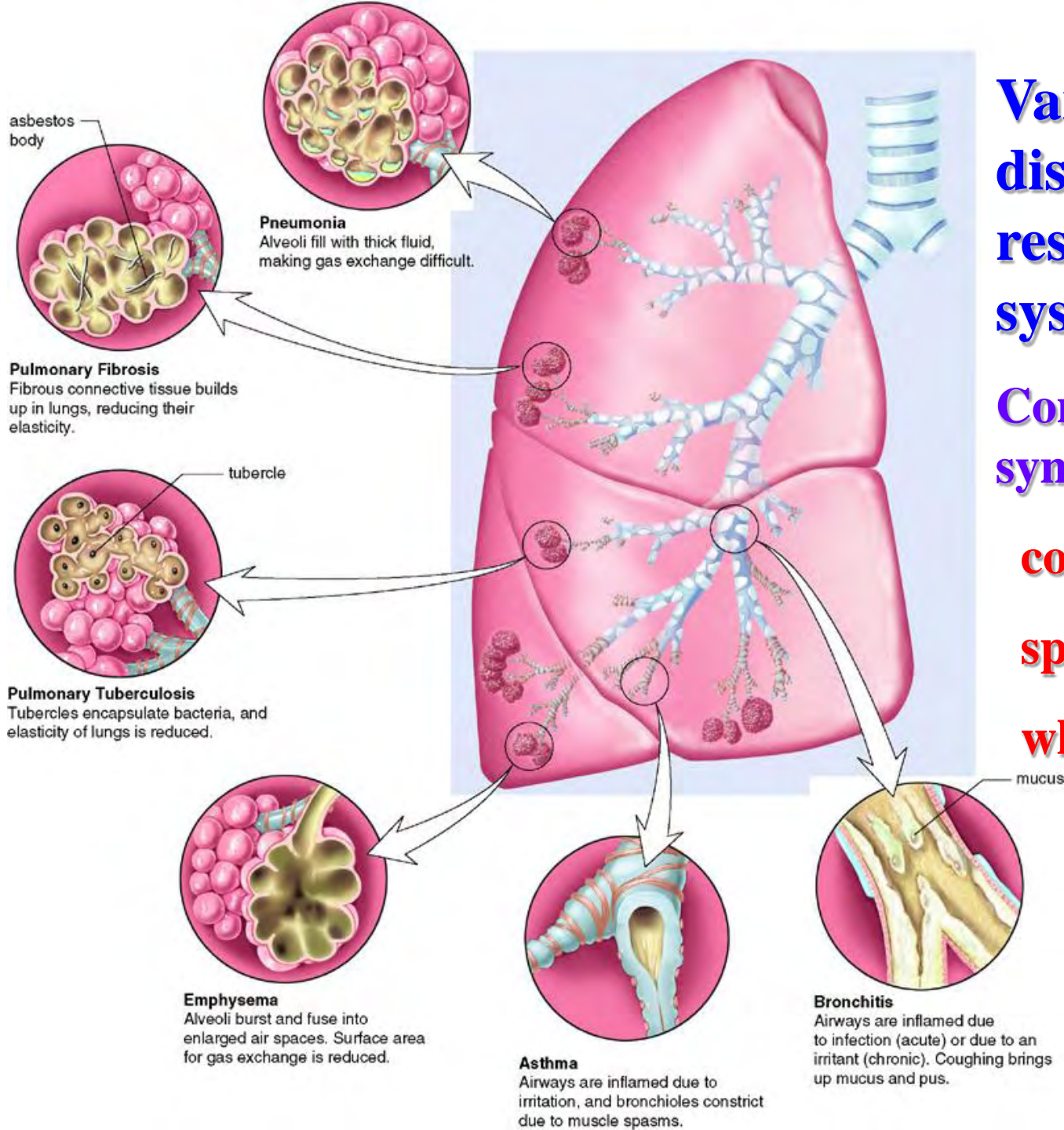
Various diseases of respiratory system

Common symptoms:

cough

sputum

wheezing



Drugs acting on respiratory system

- **Cough** **antitussive drugs**
- **centrally acting**
- **peripherally acting**
- **Sputum** **expectorant drugs**
- **sputum-diluting drugs**
- **mucolytic drugs**
- **Asthma** **antiasthmatic drugs**
- **bronchodilators**
- **β receptor agonists**
- **theophyllines**
- **muscarinic antagonists**
- **anti-inflammatory drugs**
- **glucocorticosteroids**
- **mediator release inhibitors**

A. *Antitussives*

- **Centrally acting**
- **Addictive drugs:**
- **codeine** 可待因
- **Non-addictive drugs:**
- **dextromethorphan** 右美沙芬
- **pentoxyverine** 喷托维林(咳必清)
- **Peripherally acting**
- **benzonatate** 苯佐那酯



The structures labeled on the left are to be associated with inspiration

The structures labeled on the right are to be associated with expiration

respiratory center

Respiratory center

Centrally acting antitussives

motor pathways

vagus nerve

sensory pathway

phrenic nerve

stretch receptors of alveoli

external intercostal muscles

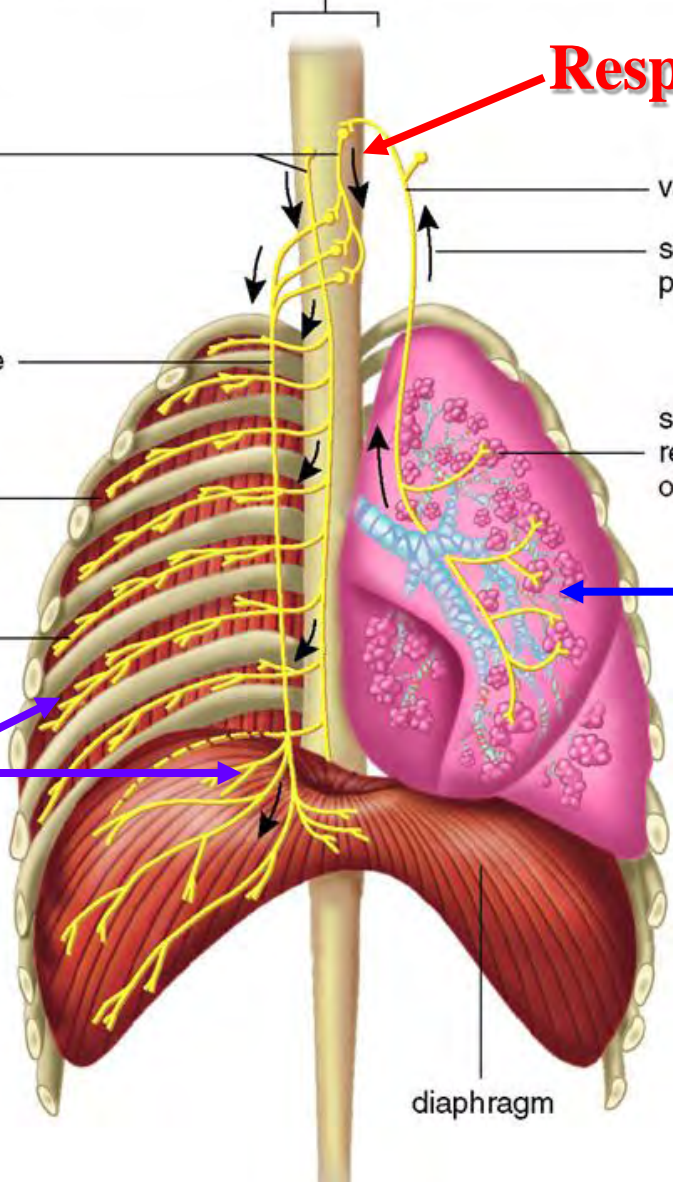
intercostal nerve

Sensory nerves

Peripherally acting antitussives

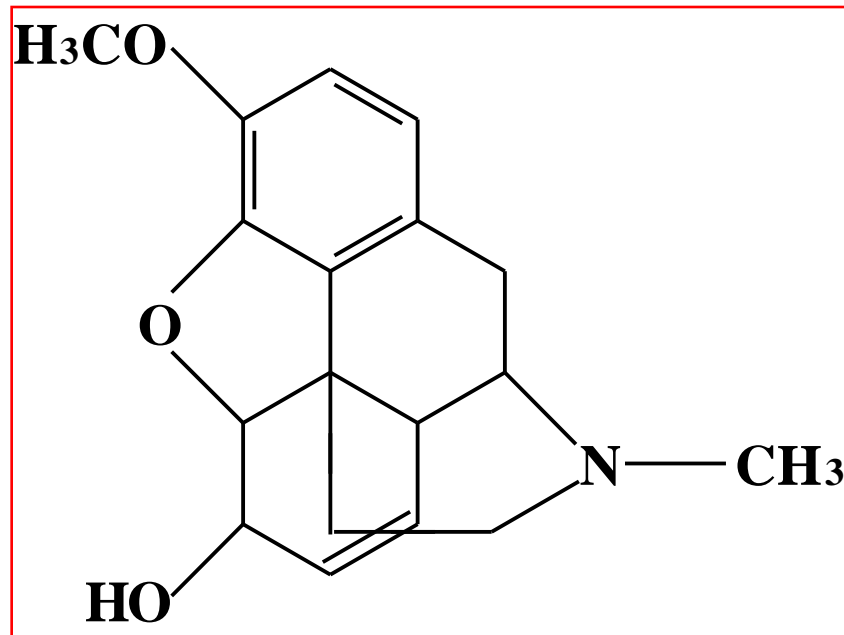
Motor nerves

diaphragm



A. *Antitussives*

Codeine 可待因



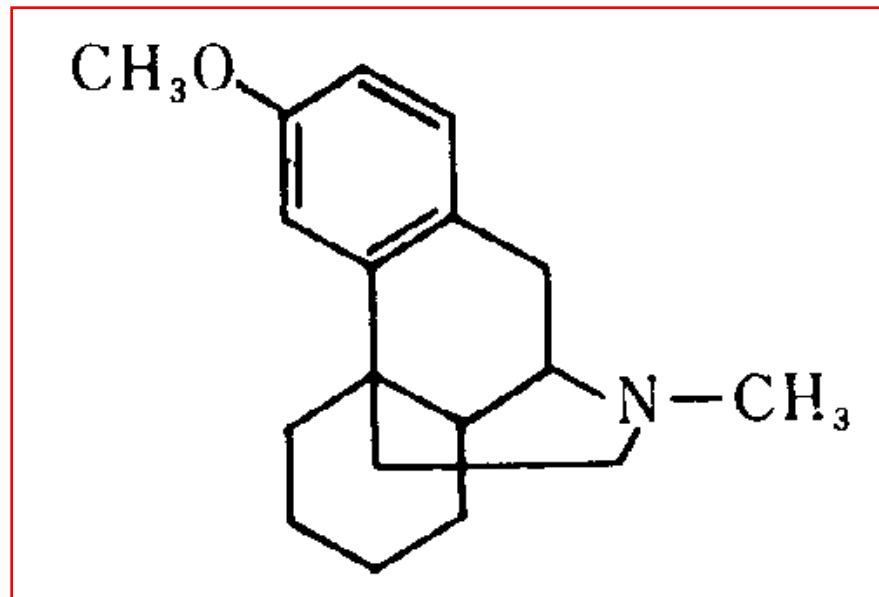
Other additive antitussives: Dihydrocodeine (双氢可待因); Drotebanol (羟蒂巴酚); Pholcodine (福尔可定)

A. *Antitussives*

- **1. *Pharmacological effects***
 - **suppression of cough** (1/4 of morphine)
 - **analgesia** (1/7~1/10 of morphine)
- **2. *Clinical uses***
 - **Cough without sputum**
- **3. *Adverse effects***
 - **Respiratory depression (at larger doses)**
 - **Addiction**
 - **Contraindicated in patients with thick sputum**

A. *Antitussives*

Dextromethorphan 右美沙芬



A. *Antitussives*

■ **Dextromethorphan** 右美沙芬

- **1. *Pharmacological effects***
 - **suppression of cough**
 - **muscarinic and NMDA receptor antagonism**
- **2. *Clinical uses***
 - **cough without sputum, upper respiratory infection, acute or chronic bronchitis**
- **3. *Adverse effects***
 - **Atropine-like side effects**

A. *Antitussives*

- **Pentoxifyverine** 喷托维林 (咳必清)

- **Suppression of cough**
- **Muscarinic antagonism and local anesthetic effects**
- **Uses and adverse effects are similar to dextromethorphan**

A. *Antitussives*

- **Benzonatate** 苯佐那酯 (退嗽)

- **Peripherally acting**

- **Blocking cough reflex**

- **Local anesthetic effects**

- **CNS depression**

- **Others:** Noscapine (那可汀); moguisteine (莫吉司坦)

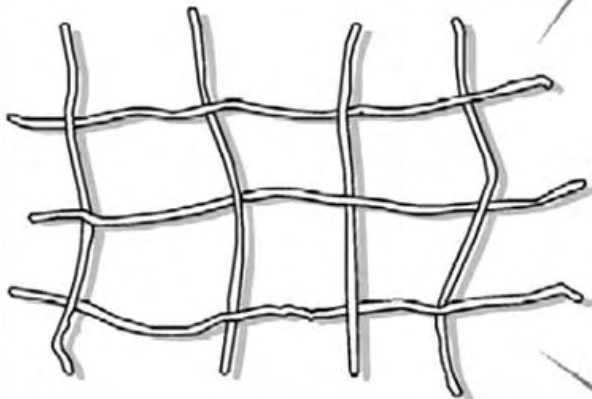
B. *Expectorants*

- **Sputum-diluting drugs**
- *Stimulating bronchial secretion*
- **Amonium chloride** 氯化铵
- **Potassium iodide** 碘化钾

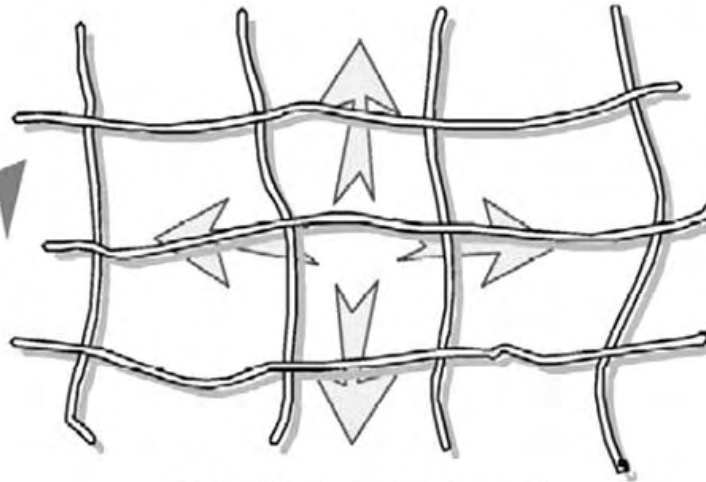
- **Mucolytic drugs**
- **Bromhexine** 溴己新
- **Ambroxol** 氨溴索
- **Acetylcysteine** 乙酰半胱氨酸
- **Methylcysteine** 美司坦
- **Carbocisteine** 羧甲司坦
- **Mesna** 美司钠

B. *Expectorants*

Schematic for Alteration of Mucous Glycoprotein Network by Hydration and/or Mucolysis



Before Treatment

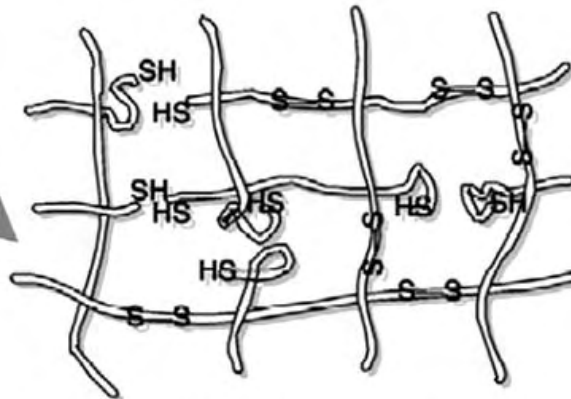


After Saline Treatment

Hydration:

Sputum
dilution

**Mucous glycoprotein
network**



After Mucolytic Treatment

Mucolysis

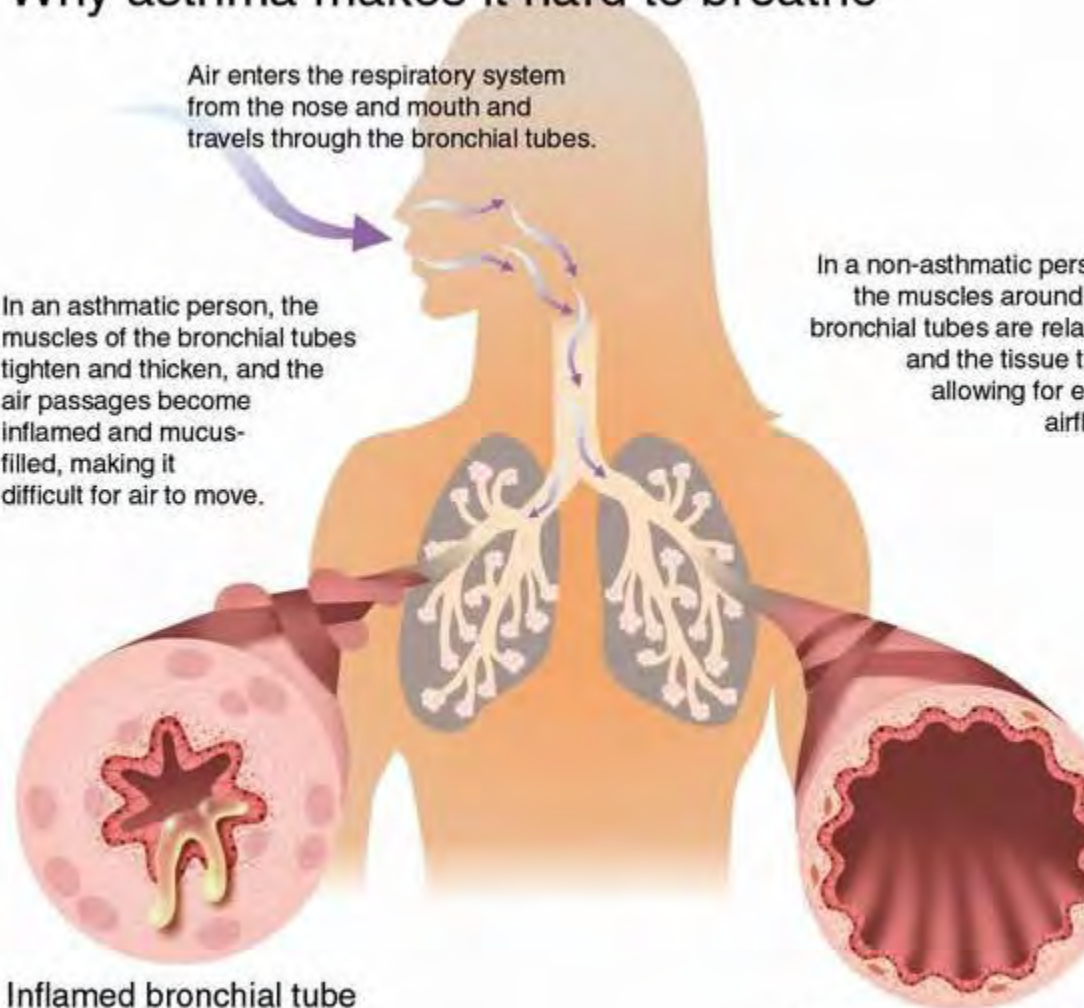
C. *Antiasthmatic drugs*

Why asthma makes it hard to breathe

Air enters the respiratory system from the nose and mouth and travels through the bronchial tubes.

In an asthmatic person, the muscles of the bronchial tubes tighten and thicken, and the air passages become inflamed and mucus-filled, making it difficult for air to move.

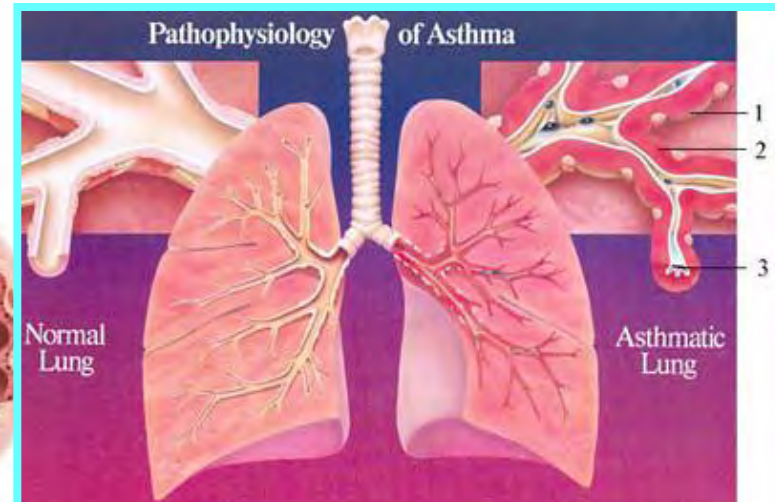
In a non-asthmatic person, the muscles around the bronchial tubes are relaxed and the tissue thin, allowing for easy airflow.



Inflamed bronchial tube of an asthmatic

Normal bronchial tube

Bronchial asthma:
inflammation;
bronchoconstriction;
airway hyperresponsiveness



C. *Antiasthmatic drugs*

Immunological and non-immunological stimuli

Airway inflammation → **bronchoconstriction**

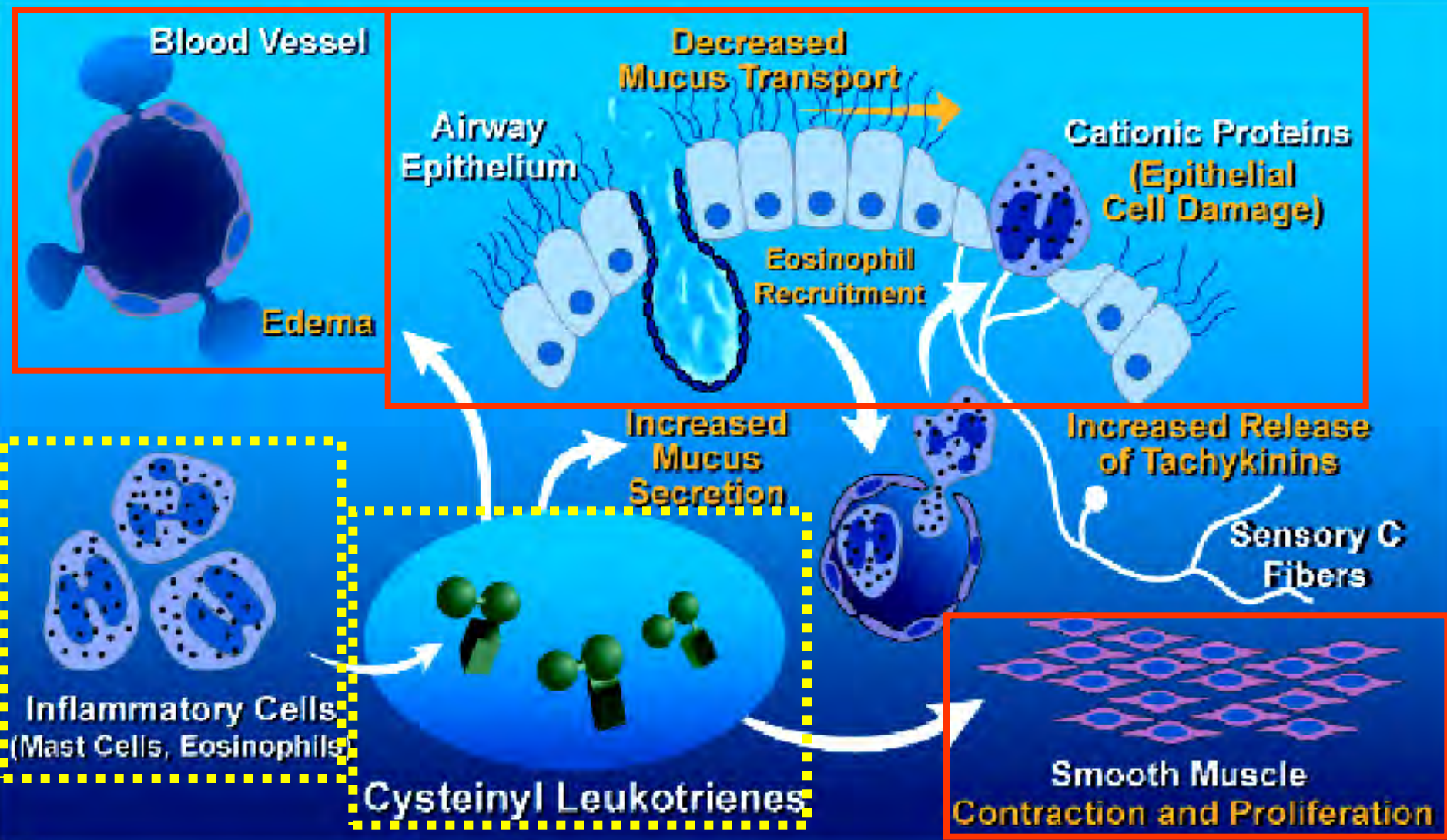
glucocorticosteroids
disodium cromoglycate
leukotriene modifiers

β_2 receptor agonists
theophylline
muscarinic antagonists

Airway hyperresponsiveness

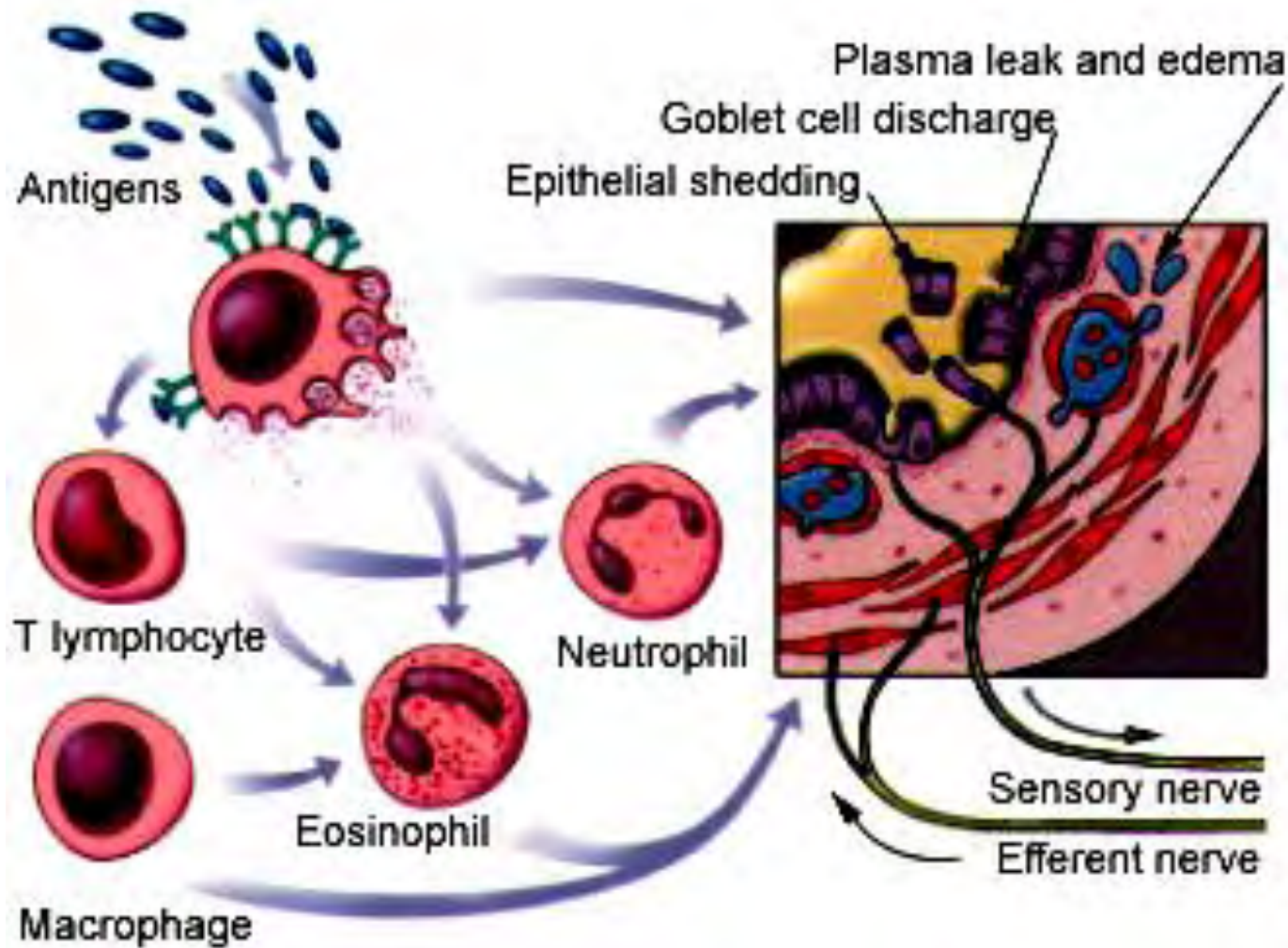
Wheezing (asthmatic symptoms)

C. *Antiasthmatic drugs*



Airway pathological changes in pathogenesis of bronchial asthma

C. *Antiasthmatic drugs*



Airway pathological changes in pathogenesis of bronchial asthma

C. *Antiasthmatic drugs*

■ **Bronchodilators**

■ **β Receptor agonists**

■ **Non-selective:** adrenaline, isoprenaline

■ **β_2 -selective: moderate-acting:** salbutamol, terbutaline

■ **long-acting:** salmeterol, formoterol

■ **Theophyllines:** aminophylline

■ **Muscarinic antagonists:** ipratropine

■ **Anti-inflammatory drugs**

■ **Glucocorticosteroids:**

■ **Systemic:** hydrocortisone, dexamethasone

■ **Inhalation:** beclomethasone, budesonide

■ **Inhibitors of mediator release:** cromolyn sodium, nedocromil

Drugs used in the treatment of asthma

- Classification in Grash Course: Respiratory system (2nd Edition) -

■ **Relievers - *Bronchodilators***

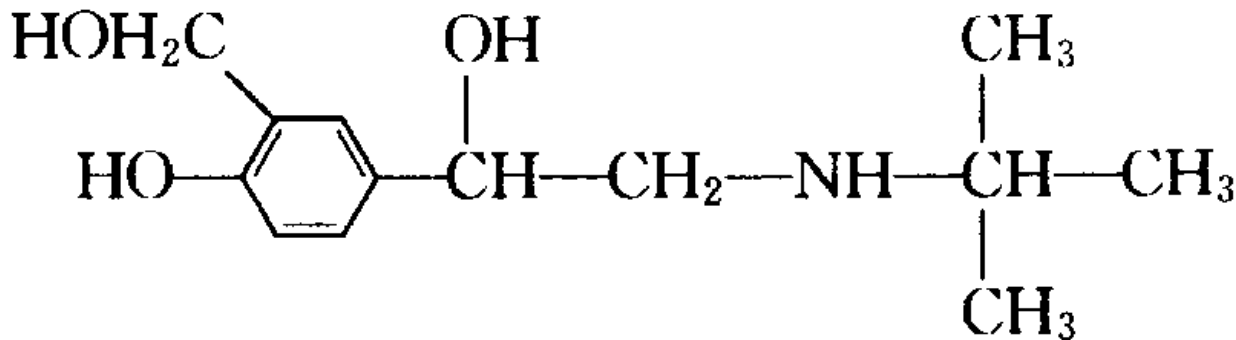
- **β_2 agonists**
 - **short-acting:** salbutamol, terbutaline
 - **long-acting:** salmeterol, formoterol
- **Anticholinergics (muscarinic antagonists):** ipratropine
- **Xantines (theophyllines):** aminophylline

■ **Preventers - *Anti-inflammatory drugs***

- **Glucocorticosteroids:**
 - **Inhaled steroids:** beclomethasone, budesonide, fluticasone
 - **oral steroids:** hydrocortisone, prednisone, *dexamethasone*
- **Leukotriene (LT) receptor antagonists (leukotriene modifiers):**
 - **LT antagonists:** montelukast (孟鲁司特), zafirlukast (扎鲁司特)
 - **5-lipoxygenase inhibitors:** zileuton (齐留通)
- **Inhibitors of mediator release:** cromolyn sodium, nedocromil

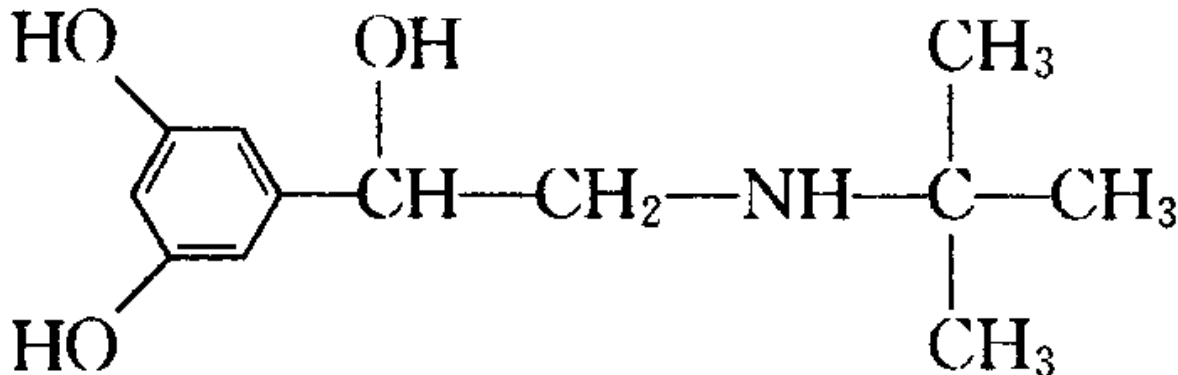
C. *Antiasthmatic drugs*

- **Bronchial dilators**
- **β_2 receptor selective agonists**



Salbuterol

沙丁胺醇



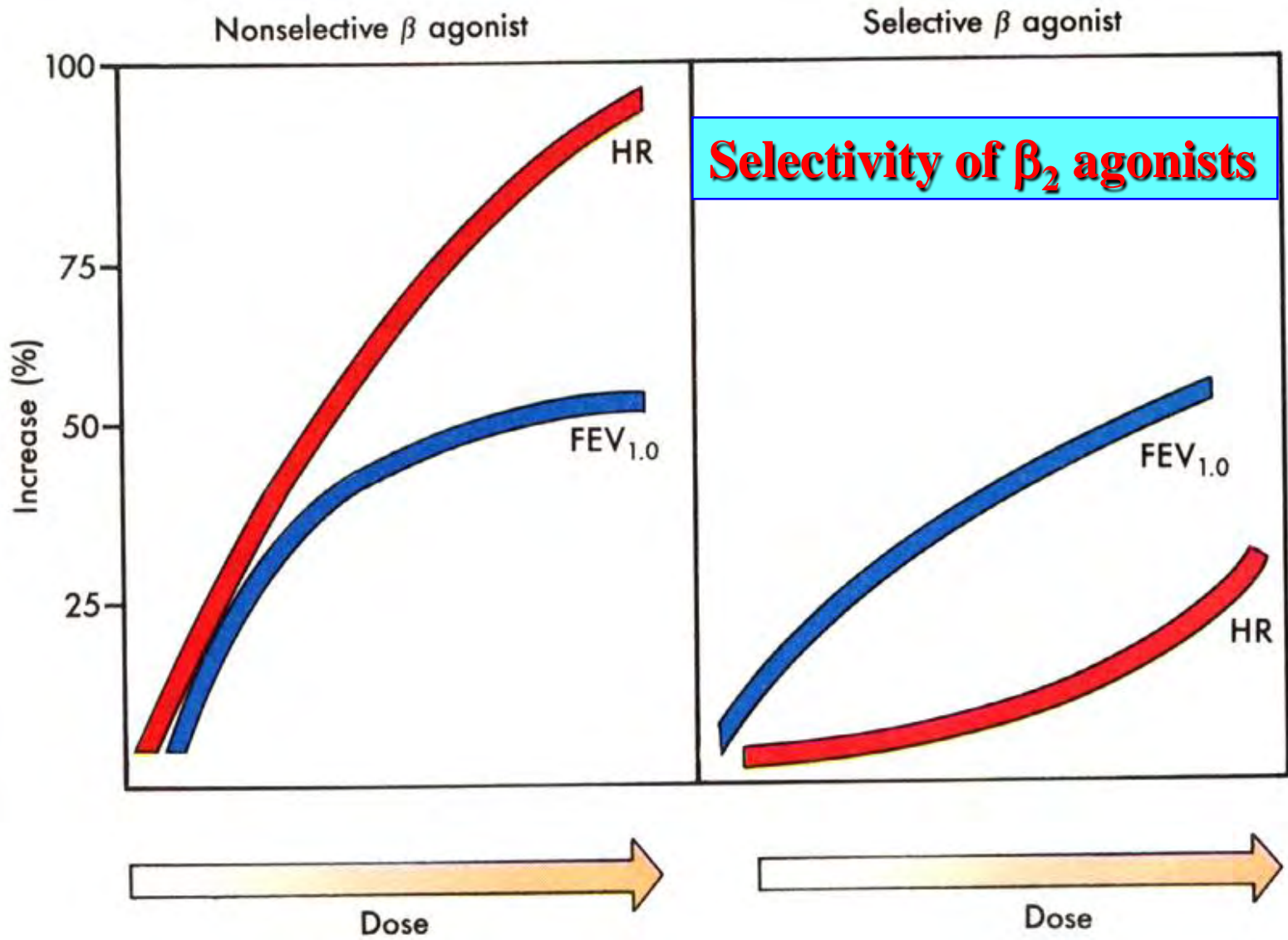
Terbutaline

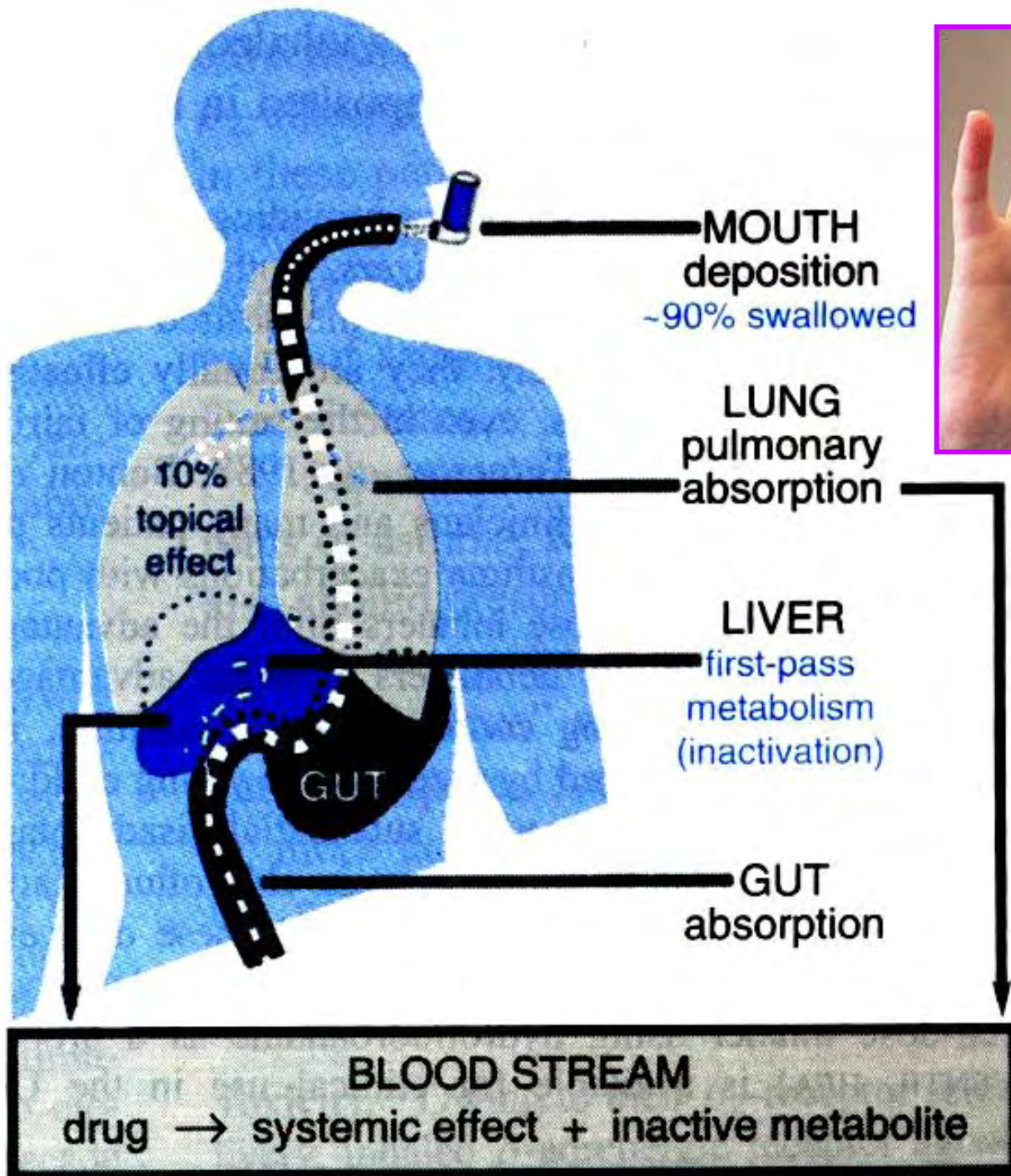
特布他林

C. *Antiasthmatic drugs*

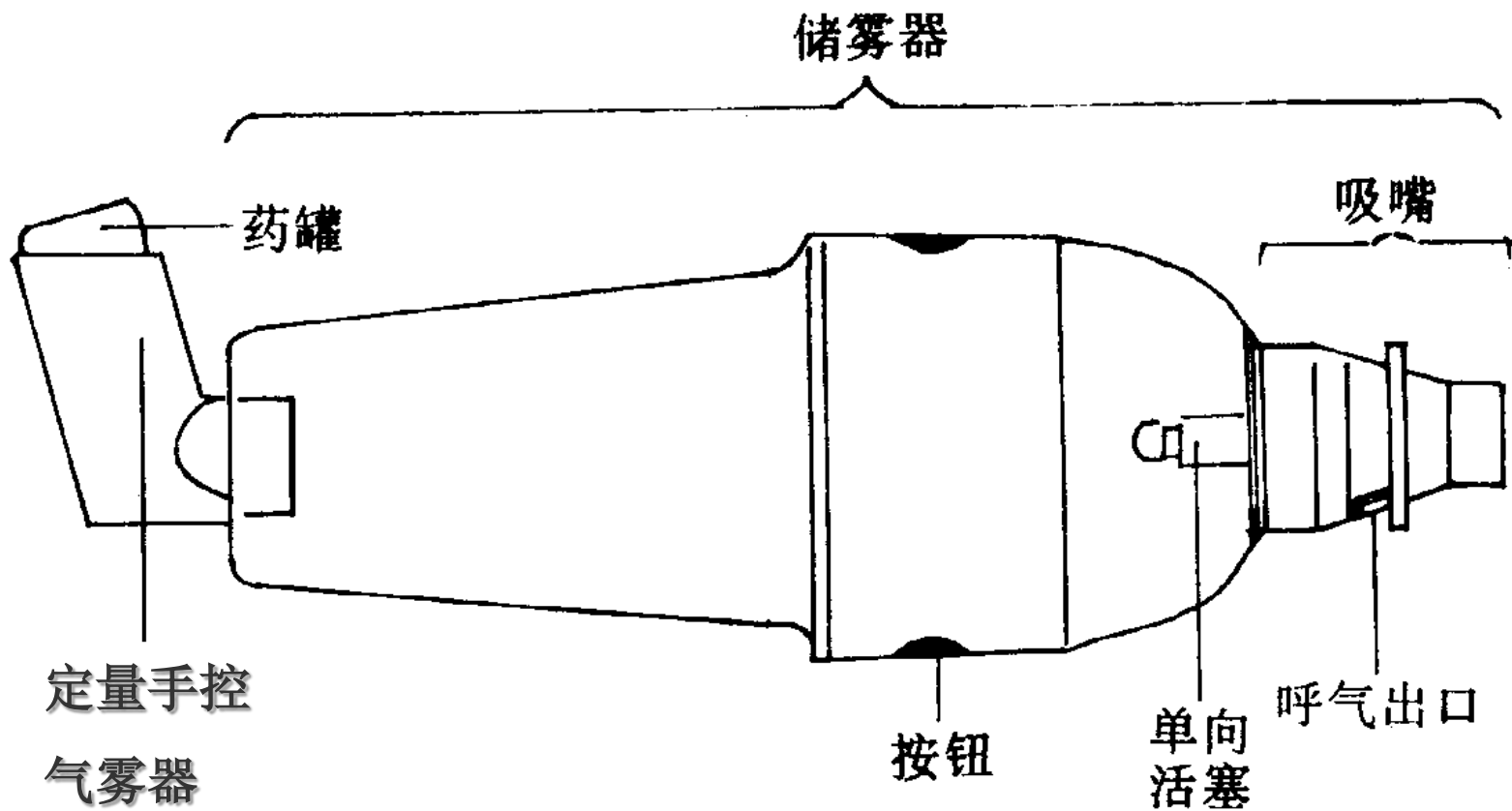
Salbuterol 沙丁胺醇

- **1. *Pharmacological effects***
 - **Relaxing bronchial smooth muscles**
- **2. *Clinical uses***
 - **Controlling asthmatic symptoms**
 - **Given by **inhalation**, oral or injection**
- **3. *Adverse effects***
 - **Skeletal muscle tremor**
 - **Cardiac stimulation (larger doses)**
 - **Dysfunction of metabolism (hypokalemia, *etc.*)**

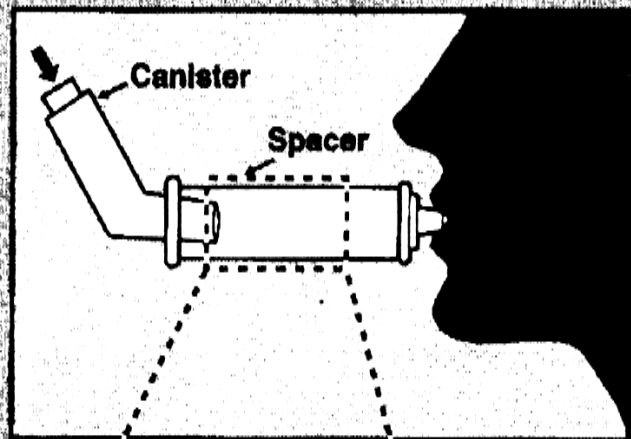




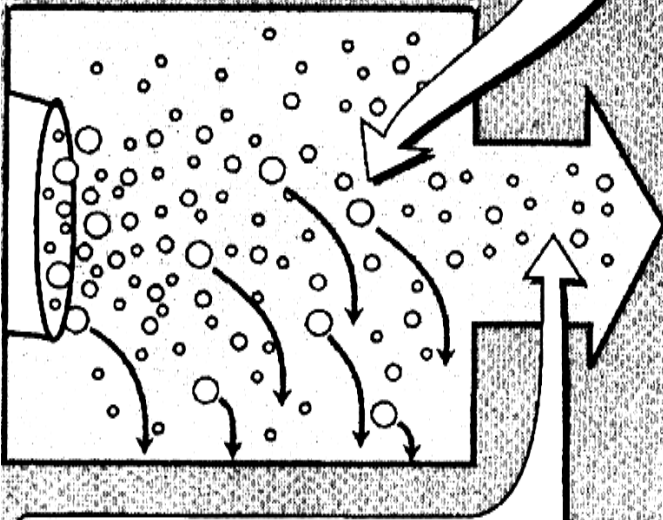
**Aerosol
inhalation**



Spacer used for aerosol inhalation



Large particles of aerosol are deposited in chamber before patient inhales.



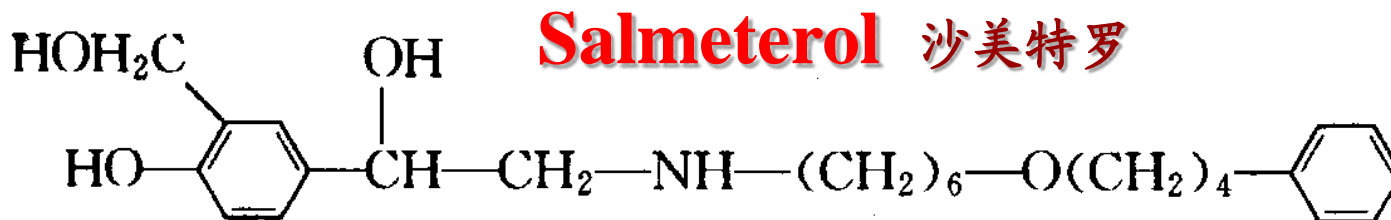
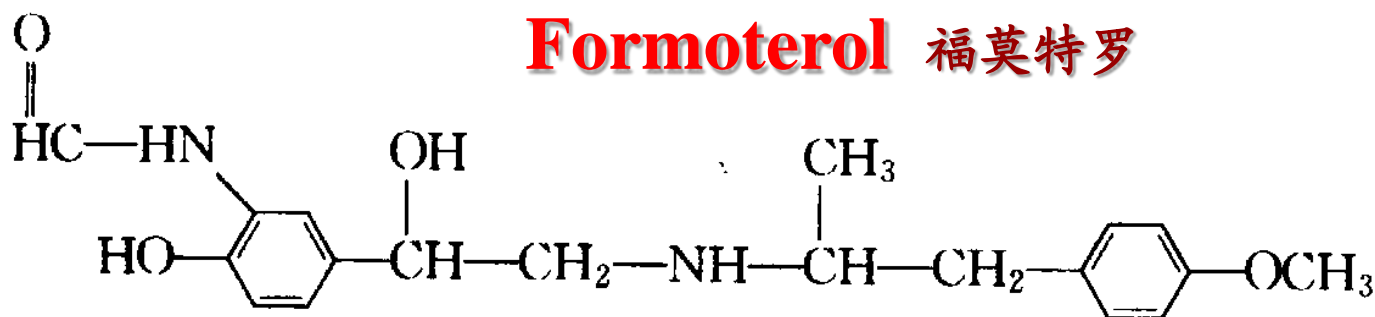
Inhaled aerosol is enriched in small particles which more readily travel to small airways.

Spacer will aid patients to inhale the aerosolized drugs easier

C. *Antiasthmatic drugs*

β_2 receptor selective agonists:

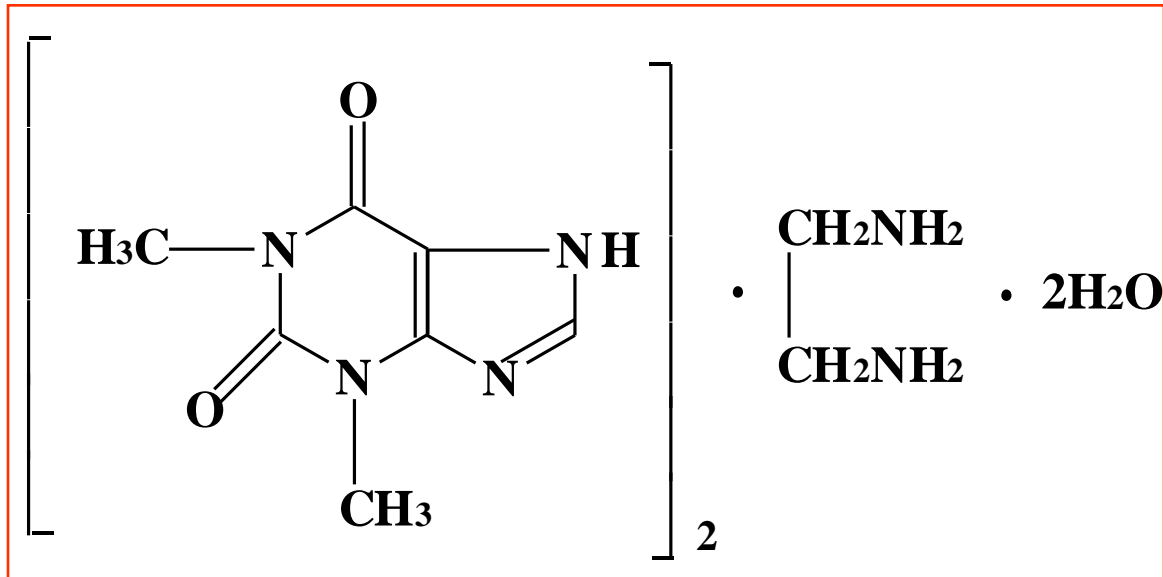
long-acting



C. *Antiasthmatic drugs*

■ Theophyllines

Aminophylline 氨茶碱



Theophyllines:

One type of xanthine derivatives (甲基黄嘌呤类衍生物)

C. *Antiasthmatic drugs*

- **1. *Pharmacological effects***
- **Inhibiting phosphodiesterase;**
- **Blocking adenosine receptors;**
- **Increasing catecholamine release;**
- **Immunomodulation;**
- **Increasing respiratory muscle contractility;**
- **CNS stimulation, diuretic, gastric acid secretion, *etc.***

C. *Antiasthmatic drugs*

■ *2. Clinical uses*

- **Bronchial asthma (*p.o.*, *i.v.*)**
- **Others: acute pulmonary edema, *etc.***

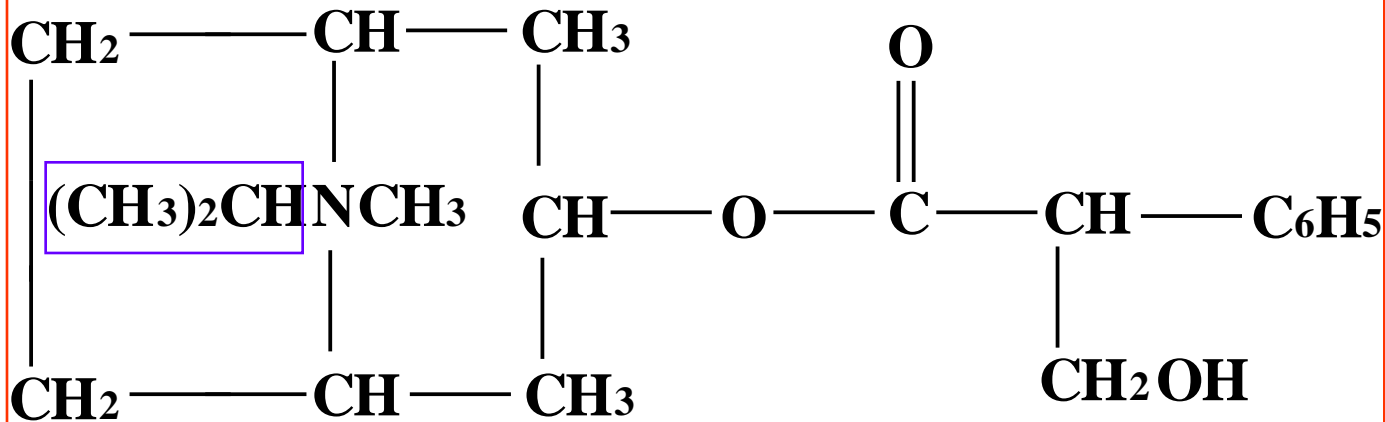
■ *3. Adverse effects*

- **GI reactions**
- **CNS stimulation**
- **CVS reactions**
- **Acute intoxication (*i.v.* injection too rapidly)**

C. *Antiasthmatic drugs*

■ Muscarinic antagonists

Ipratropine 异丙托溴铵, 异丙托品



C. *Antiasthmatic drugs*

■ **Glucocorticosteroids**

■ **Systemic:**

■ **hydrocortisone** 氢化可的松

■ **prednisone** 泼尼松

■ **dexamethasone** 地塞米松

■ **Inhaled:**

■ **beclomethasone dipropionate** 二丙酸倍氯米松

■ **budesonide** 布地奈德

■ **triamcinolone acetonide** 曲安奈德

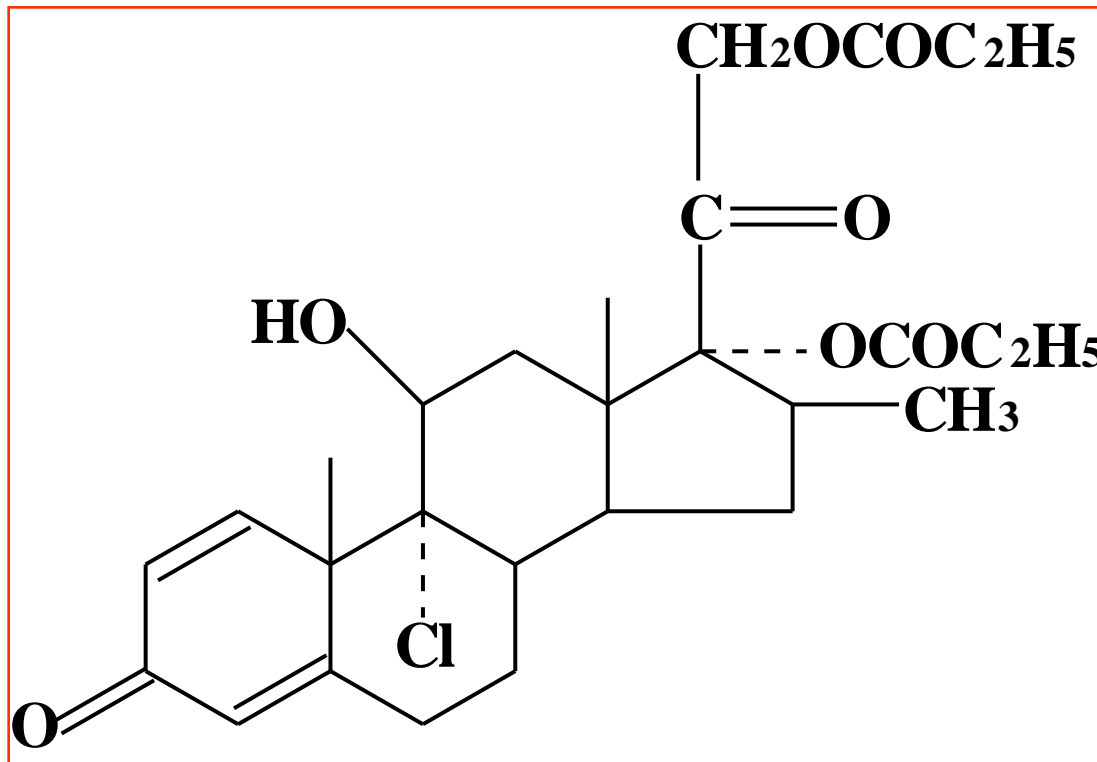
■ **fluticasone propionate** 丙酸氟替卡松

■ **flunisolide** 氟尼缩松

C. *Antiasthmatic drugs*

Beclomethasone dipropionate

二丙酸倍氯米松



C. *Antiasthmatic drugs*

- **1. *Pharmacological effects***
 - **Antiinflammation:** inhibiting inflammatory cell activities, antibody production, mediator release
- **2. *Clinical uses***
 - **As first-line drugs, currently**
 - **Controlling chronic symptoms**
 - **Ineffective for acute symptoms**
- **3. *Adverse effects***
 - **Local:** oropharyngeal candidiasis — **using spacer**
 - **Systemic effects**

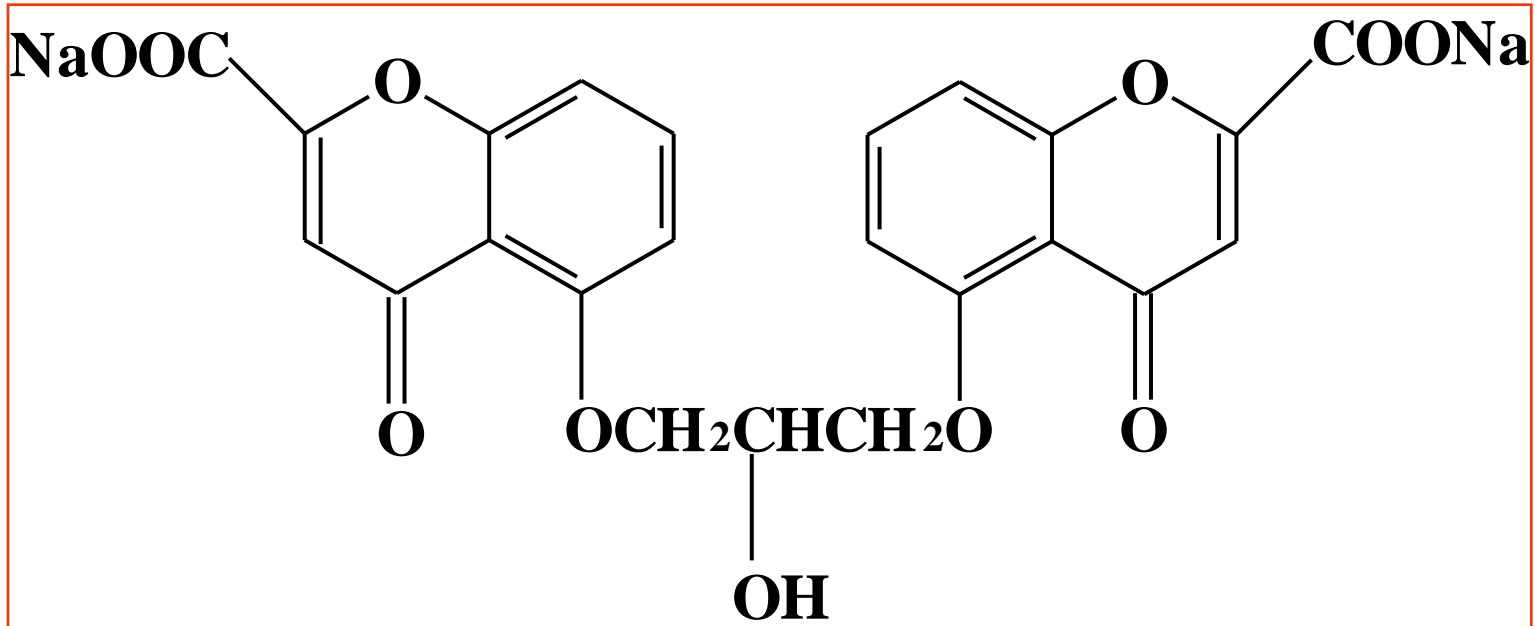
C. *Antiasthmatic drugs*

- **Inhibitors of mediator release**

Disodium cromoglycate

色甘酸二钠

(*cromolyn*) (色甘酸钠)

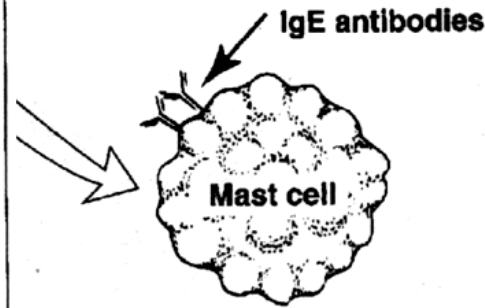


C. *Antiasthmatic drugs*

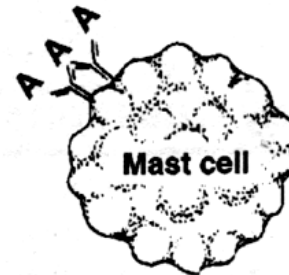
- **1. *Pharmacological effects***
 - **Inhibiting mediator release from mast or other cells**
 - **Inhibiting sensory neuropeptide release**
- **2. *Clinical uses***
 - **Prevention of allergic asthma**
 - **Acting slowly (2-4 weeks)**
- **3. *Adverse effects***
 - **Oropharyngeal irritation**

1 MAST CELL SENSITIZATION

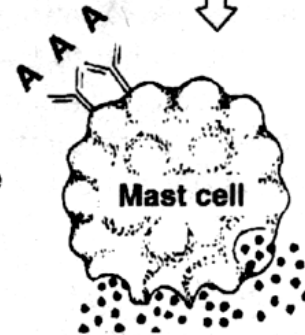
First exposure to antigen causes the production of specific IgE antibodies, which attach to the surface of tissue mast cells and blood basophils.



Exposure to antigen (A)



Mast cell degranulation



Allergic response

2 MAST CELL DEGRANULATION

Subsequent exposure to antigen results in binding to surface-bound IgE molecules. The sensitized mast cells are stimulated to release granules containing histamine, leukotrienes, prostaglandins, and other potent chemical mediators.

Cromolyn Inhibits mediator release from mast cells

C. *Antiasthmatic drugs*

- **Other inhibitors of mediator release**
- **Nedocromil sodium** 奈多罗米钠
- **Tranilast** 曲尼司特
- **Ketotifen** 酮替芬 (H_1 receptor antagonist)