Bronchodilators & Other Respiratory Agents

Drugs Affecting the Respiratory System

- Bronchodilators
  - Xanthine derivatives
  - Beta-adrenergic agonists
- Anticholinergics
- Antileukotriene agents
- Corticosteroids
- Mast cell stabilizers

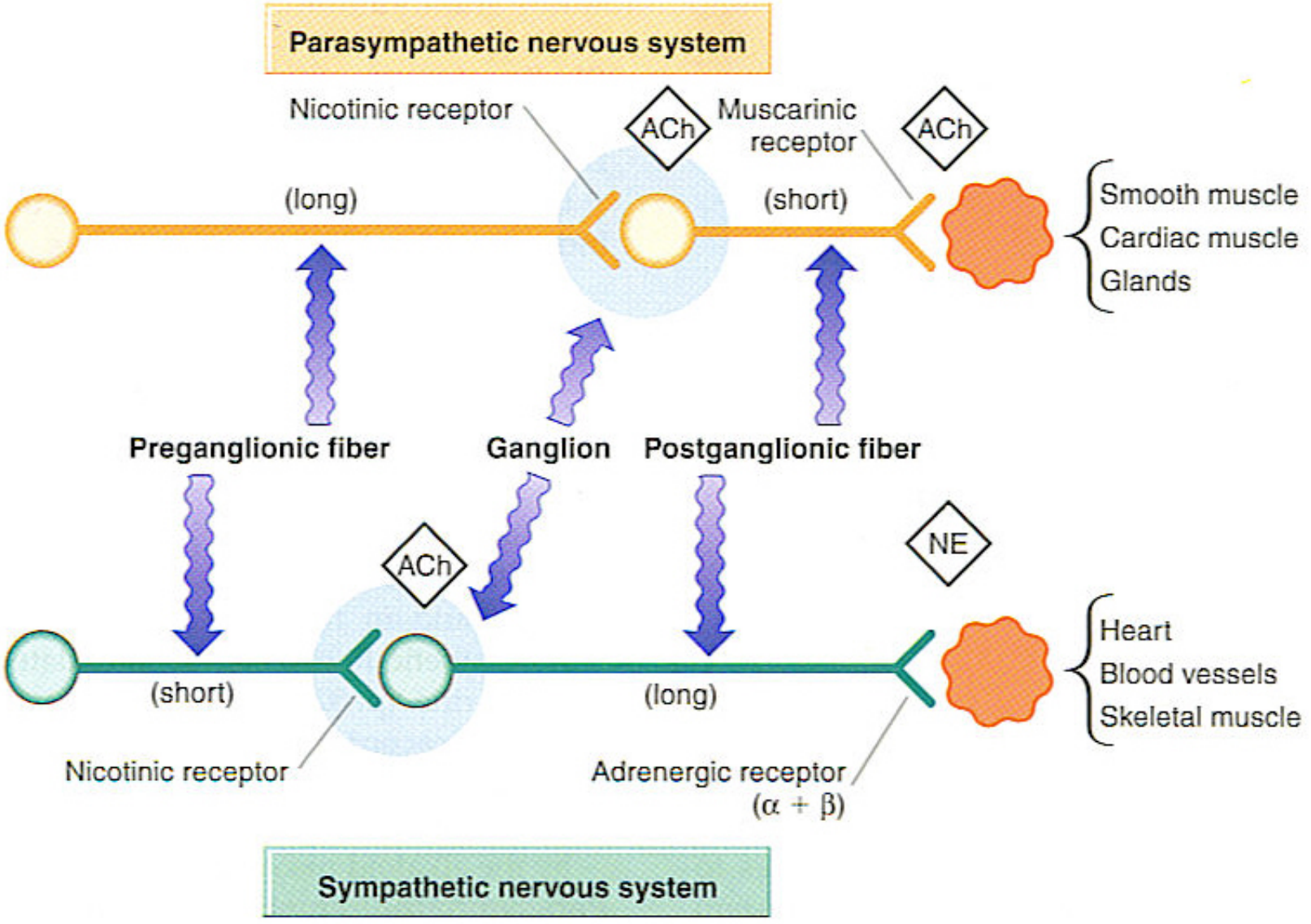
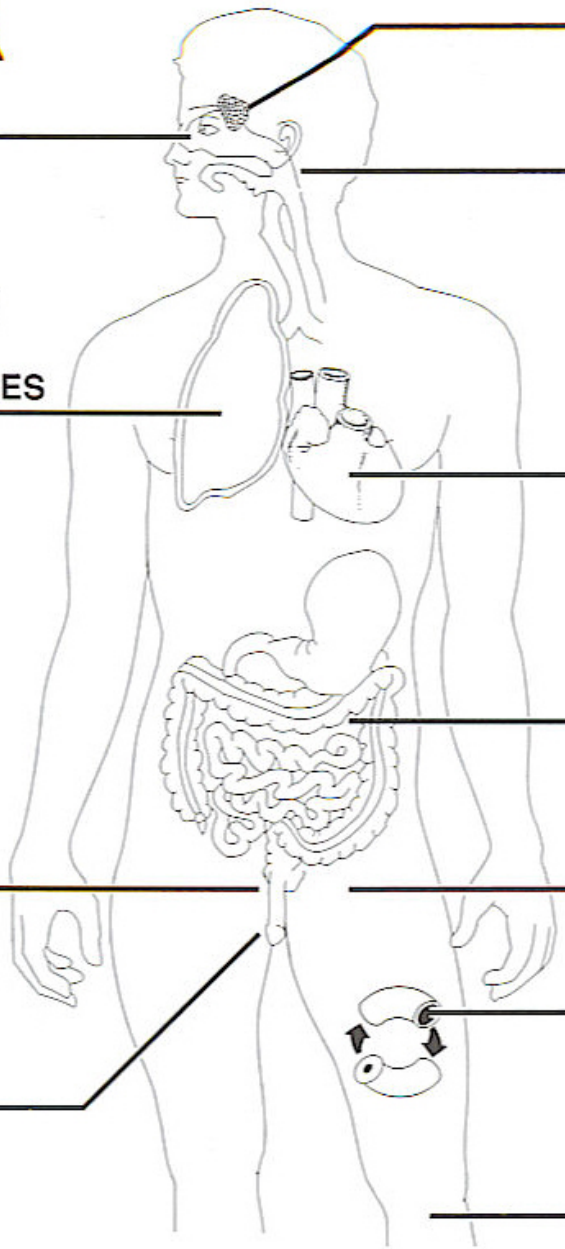


FIG. 19-1 The parasympathetic and sympathetic nervous systems and their relationships to one another. *Ach,* Acetylcholine; *NE,* norepinephrine.

Bold type = sympathetic actions
Light type = parasympathetic actions



EYE

Contraction of iris radial muscle (pupil dilates)
Contraction of iris sphincter muscle (pupil contracts)
Contraction of ciliary muscle (lens accommodates for near vision)

TRACHEA AND BRONCHIOLES

Dilates
Constricts, increases secretions

URETERS AND BLADDER

Relaxes detrusor; contraction of trigone and sphincter
Contraction of detrusor; relaxation of trigone and sphincter

GENITALIA-MALE

Stimulates ejaculation
Stimulates erection

LACRIMAL GLANDS

Stimulates tears

SALIVARY GLANDS

Thick, viscid secretion
Copious, water secretion

HEART

Increased rate; increased contractility
Decreased rate, and contractility

GASTROINTESTINAL

Decrease in muscle motility and tone; contraction of sphincters
Increased muscle motility and tone

GENITALIA-FEMALE

Relaxation of uterus

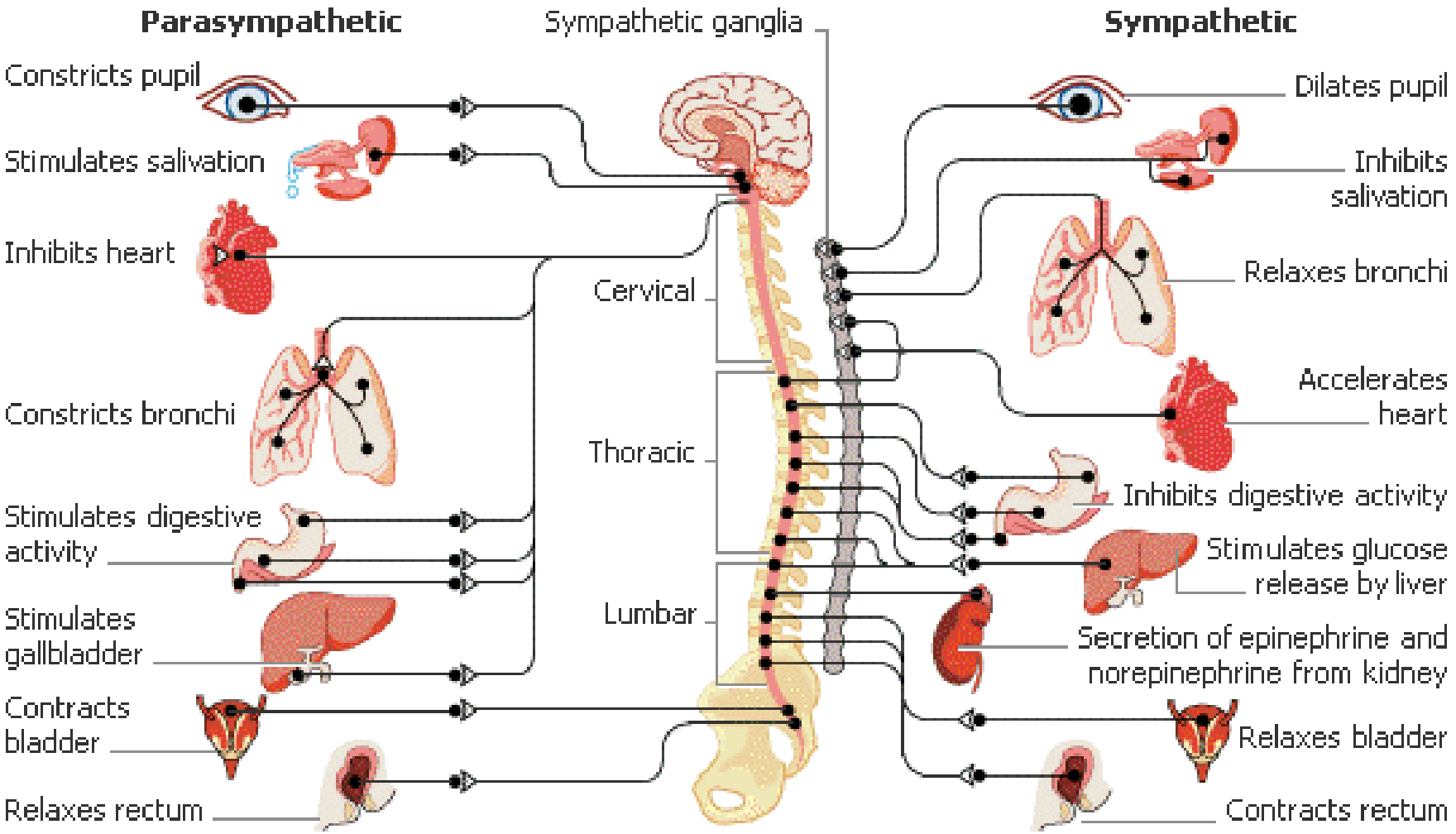
BLOOD VESSELS (skeletal muscle)

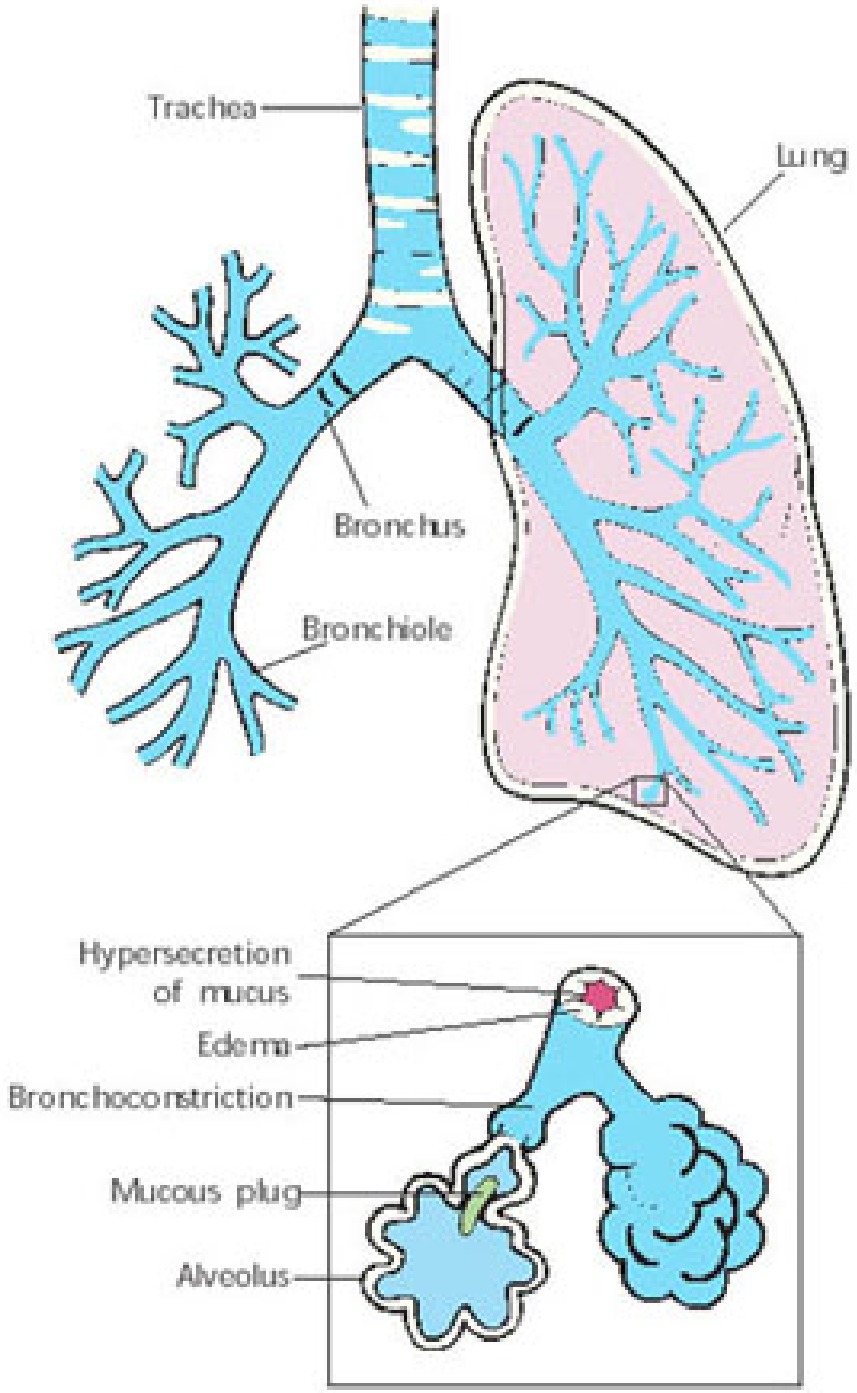
Dilatation

BLOOD VESSELS (skin, mucus membranes and splanchnic area)

Constriction

Autonomic Nervous System




Trachea
Lung
Bronchus
Bronchiole
Hypersecretion of mucus
Edema
Bronchoconstriction
Mucous plug
Alveolus

Bronchodilators

Xanthine Derivatives

- Plant alkaloids: caffeine, theobromine, and theophylline
  - Only theophylline is used as a bronchodilator
- Examples:
  - Aminophylline - IV
  - theophylline (Bronkodyl, Slo-bid, Theo-Dur, Uniphyl)

Bronchodilators
Xanthine Derivatives

- Mechanism of Action
  - Smooth muscle relaxation
  - Bronchodilation
  - Increased airflow

Bronchodilators

Xanthine Derivatives

- Drug Effects
  - Cause bronchodilation by relaxing smooth muscles of the airways.
    - Relief of bronchospasm and greater airflow into and out of the lungs.
  - Also causes CNS stimulation.
  - Also causes cardiovascular stimulation
    - Increased force of contraction and increased HR
      - Resulting in increased cardiac output and increased blood flow to the kidneys (diuretic effect)

Bronchodilators

Xanthine Derivatives

- Therapeutic uses
  - Dilation of airways in asthma, chronic bronchitis, & emphysema
  - Mild to moderate cases of asthma
  - Adjunct agent in the management of COPD
  - Adjunct therapy for the relief of pulmonary edema and paroxysmal nocturnal edema in left-sided heart failure

Bronchodilators

Xanthine Derivatives

- Side Effects
  - Nausea, vomiting, anorexia
  - Gastroesophageal reflux during sleep
  - *Sinus tachycardia, extrasystole, palpitations, ventricular dysrhythmias*
  - Transient increased urination

Bronchodilators

Beta-adrenergic Agonists

- Large group
- Aka sympathomimetics
- Used during acute phase of asthmatic attacks
- Quickly reduce airway constriction and restore normal airflow
- Stimulate $beta_2$ adrenergic receptors throughout the lungs

Bronchodilators
Beta-Agonists

Three types

- Nonselective adrenergics
  - Stimulate alpha$_1$, beta$_1$ (cardiac), and beta$_2$ (respiratory) receptors.

    Example: epinephrine
- Nonselective beta-adrenergics
  - Stimulate both beta$_1$ and beta$_2$ receptors.

    Example: isoproterenol (Isuprel)
- Selective beta$_2$ drugs
  - Stimulate only beta$_2$ receptors.

    Example: albuterol

Bronchodilators

Beta-Agonists

VENTOLIN HFA

- Same as albuterol
  - Different manufacturer
- Built-in dose counter
- Does not contain flourocarbons (HFA label)
  - Safe for the environment

Bronchodilators

Beta-Agonists

Mechanism of Action

- Activation of $beta_2$ receptors activate cAMP
  - relaxes smooth muscles of the airway and
  - results in bronchial dilation and increased airflow

Bronchodilators

Beta-Agonists

Therapeutic Uses

- Relief of
  - Bronchospasm
  - Bronchial asthma
  - Bronchitis
  - Other pulmonary disease

Bronchodilators
Beta-Agonists

Side Effects:

Alpha-Beta (epinephrine)	**$Beta_1$ and $Beta_2$** (isoproterenol)	**$Beta_2$** (albuterol)
•**Insomnia** •**Restlessness** •**Anorexia** •**Cardiac stimulation** •**Hyperglycemia** •**Temor** •**Vascular headache**	•**Cardiac stimulation** •**Tremor** •**Anginal pain** •**Vascular headache**	•**Hypertension** •**Hypotension** •**Vascular headaches**

Respiratory Agents
General Nursing Implications

- Encourage preventative measures
  - Avoid exposure to conditions that precipitate bronchospasms (allergens, smoking, stress, air pollutants)
  - Adequate fluid intake
  - Compliance with medical treatment
  - Avoid excessive fatigue, heat, extremes in temperature, caffeine

Respiratory Agents
General Nursing Implications

- Encourage patients to get prompt treatment for flu or other illnesses
- Vaccination against pneumonia or flu
- Encourage patients to always check with their physician before taking any other medication
  - Including OTC

Respiratory Agents
General Nursing Implications

- Perform a thorough assessment before beginning therapy
  - Skin color
  - Baseline vital signs
  - Respirations (should be >12 or <24 breaths/min)
  - Respiratory assessment, including PO_2
  - Sputum production
  - Allergies
  - History of respiratory problems
  - Other medications

Respiratory Agents
General Nursing Implications

- Teach patients to take bronchodilators exactly as prescribed
- Teach how to use inhalers & MDIs
  - Have the patients demonstrate use of devices
- Monitor for side effects

Respiratory Agents
General Nursing Implications

- Monitor for therapeutic effects
  - Decreased dyspnea
  - Decreased wheezing, restlessness, and anxiety
  - Improved respiratory patterns with return to normal rate and quality
  - Improved activity tolerance

Bronchodilators
Nursing Implications

- Xanthine Derivatives
  - Contraindications
    - History of PUD or GI disorders
  - Cautious use
    - Cardiac disease
  - Timed-release preparations should not be crushed or chewed
    - Causes gastric irritation

Bronchodilators

Nursing Implications

Xanthine Derivatives

- Report to physician

Palpitations	Nausea	Vomiting
Weakness	Dizziness	Chest pain
Convulsions		

Bronchodilators
Nursing Implications

- Xanthine Derivatives
  - Be aware of drug interactions with:
    - Cimetidine
    - Oral contraceptives
    - Allopurinol
  - Large amounts of caffeine & nicotine can have deleterious effects

Bronchodilators
Nursing Implications

- Beta-Agonist Derivatives (Albuterol)
  - If used too frequently
    - Loses its $beta_2$-specific actions at larger doses
    - As a result, $beta_1$ receptors are stimulated
      - Causing nausea, increased anxiety, palpitations, tremors, and increased heart rate

Bronchodilators
Nursing Implications

- Beta-Agonist Derivatives
  - Patients should take medications exactly as prescribed, with no omissions or double doses
  - Patients should report insomnia, jitteriness, restlessness, palpitations, chest pain, or any change in symptoms

Anticholinergics Mechanism of Action

- Acetylcholine (ACh)
  - Causes bronchial constriction and narrowing of the airways
- Anticholinergics bind to the ACh receptors
  - Prevent ACh from binding
  - Result:
    - Bronchoconstriction is prevented
      - Airways dilate

Anticholinergics

- Ipratropium bromide (Atrovent)
  - Only short acting anticholinergic used for respiratory disease.
  - Slow and prolonged action
  - Used to <u>prevent</u> bronchoconstriction
  - NOT used for acute asthma exacerbations!

Anticholinergics

- ipratropium bromide/albuterol sulfate (Combivent)
  - Combination product
    - Adrenergic and anticholinergic properties
  - Inhalation canister
    - Needs to be shaken for 10 seconds prior to each inhalation

Anticholinergics
Side Effects

- Dry mouth or throat
- Gastrointestinal distress
- Headache
- Coughing
- Anxiety

No known drug interactions

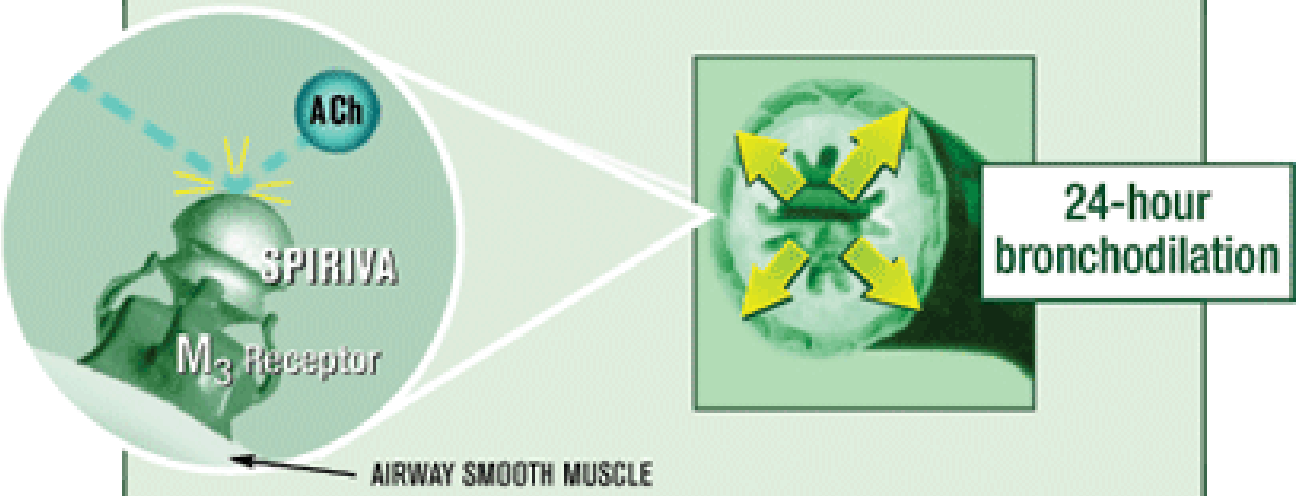
Anticholinergics
(tiotropium bromide)

- Spiriva
  - Long acting
  - Once daily maintenance therapy
  - Not indicated for rescue therapy

Pharmacological effects of SPIRIVA

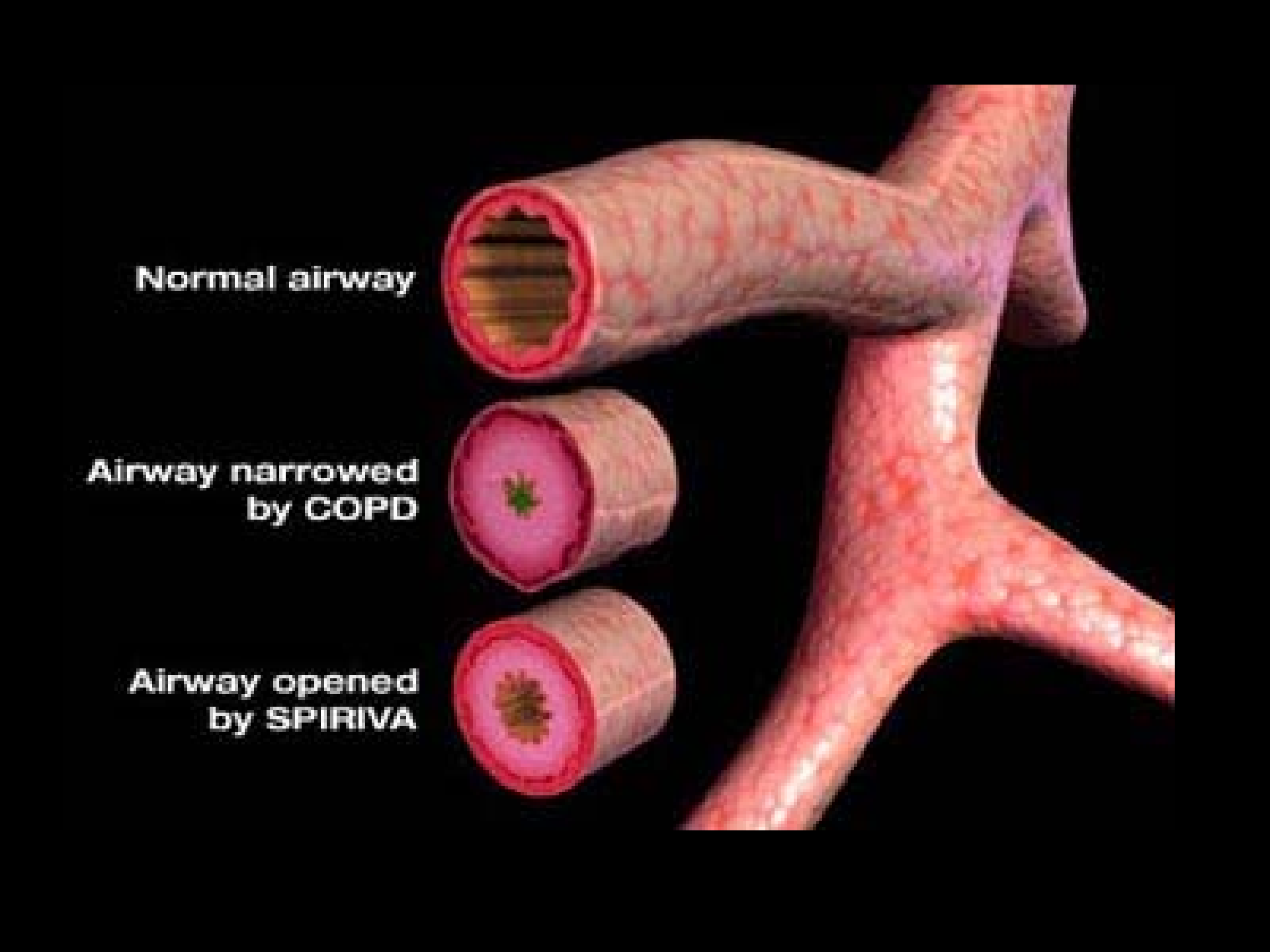
1. SPIRIVA has similar affinity to the subtypes of muscarinic receptors, M_1 to M_5

2. In the airways, SPIRIVA exhibits pharmacological effects through inhibition of M_3-receptors at the smooth muscle leading to bronchodilation



3. Prevents receptor binding by **acetylcholine (ACh)**, the principal neurotransmitter of the parasympathetic nervous system; this blocks receptor stimulation and airway smooth muscle contraction[6,7]

4. In preclinical *in vitro* and *in vivo* studies, prevention of methacholine-induced bronchoconstriction effects were dose-dependent and lasted longer than 24 hours. The bronchodilation following inhalation of SPIRIVA is predominantly a site-specific effect


Normal airway
Airway narrowed by COPD
Airway opened by SPIRIVA

Antileukotrienes

- Also called leukotriene receptor antagonists (LRTAs)
- New class of asthma medications
- Three subcategories of agents

Antileukotrienes

Currently available agents:

- montelukast (Singulair)
- zafirlukast (Accolate)
- zileuton (Zyflo)

Antileukotrienes
Mechanism of Action

- Leukotrienes
  - Substances released when a trigger (i.e., cat hair or dust) starts a series of chemical reactions in the body
  - Cause inflammation, bronchoconstriction, and mucus production
  - Result:
    - Coughing, wheezing, shortness of breath

Antileukotrienes

Mechanism of Action

- Prevent leukotrienes from attaching to receptors on cells in the lungs and in circulation.
- Inflammation in the lungs is blocked
  - Asthma symptoms are relieved

Antileukotrienes
Drug Effects

- Prevent smooth muscle contraction of the bronchial airways
- Decrease mucus secretion
- Prevent vascular permeability
- Decrease neutrophil and leukocyte infiltration to the lungs
  - Prevent inflammation

Antileukotrienes

Therapeutic Uses

- Prophylaxis and chronic treatment of asthma in adults and children over age 12
- NOT meant for management of acute asthmatic attacks!
- Montelukast (Singulair) is approved for use in children age 2 and older

Antileukotrienes

Side Effects

Zileuton (Zyflo)	zafirlukast (Accolate)
Headache	Headache
Dyspepsia	Nausea
Nausea	Diarrhea
Dizziness	Liver dysfunction
Insomnia	
Liver dysfunction	

*montelukast has fewer side effects

Antileukotrienes

Nursing Implications

- Ensure that the drug is being used for chronic management of asthma
  - Not acute asthma!
- Teach the patient purpose of the therapy
- Improvement should be seen in about one week

Antileukotrienes

Nursing Implications

- Check with physician before taking any OTC or prescribed medications
  - Many drug interactions
- Assess liver function before beginning therapy
- Medications should be taken every night on a continuous schedule
  - Even if symptoms improve

Corticosteroids

- Anti-inflammatory drugs
- Used for CHRONIC asthma
- Does not relieve symptoms of acute asthmatic attacks
- Oral or inhaled forms
- Inhaled forms reduce systemic effects
- May take several weeks before full effects are seen

Corticosteroids

Mechanism of Action

- Stabilize membranes of cells that release harmful bronchoconstricting substances
  - Cells include leukocytes, or white blood cells
- Increase responsiveness of bronchial smooth muscle to beta-adrenergic stimulation

Inhaled Corticosteroids

Examples

- beclomethasone dipropionate (Beclovent, Vanceril)
- budesonide (Pulmicort)
- triamcinolone acetonide (Azmacort)
- fluticasone (Flovent)
- dexamethasone sodium phosphate (Decadron Phosphate Respihaler)
- flunisolide (AeroBid)

Inhaled Corticosteroids Therapeutic Uses

- Treatment of bronchospastic disorders
  - Not controlled by conventional bronchodilators
- NOT considered first-line agents for management of acute asthmatic attacks or status asthmaticus

Inhaled Corticosteroids

Side Effects

- Pharyngeal irritation
- Coughing
- Dry mouth
- Oral fungal infections

**Systemic effects are rare because of the low doses used for inhalation therapy*

Inhaled Corticosteroids

Nursing Implications

- May be contraindicated in patients with suppressed immune systems
  - Fungal infections, AIDS, TB, etc
- Cautious use in patients with diabetes, glaucoma, osteoporosis, PUD, renal disease, CHF
- Teach patients to gargle and rinse the mouth with water afterward to prevent the development of oral fungal infections

Inhaled Corticosteroids

Nursing Implications

- Abruptly discontinuing these medications can lead to serious problems.
- Should be weaned for a period of 1 to 2 weeks if discontinued
  - Only if recommended by physician
- REPORT
  - Weight gain of more than 5 pounds a week
  - Occurrence of chest pain.

Mast Cell Stabilizers

- Stabilize the cell membranes of inflammatory cells
  - Mast cells
  - Monocytes
  - Macrophages
- Prevent release of harmful cellular contents
- No direct bronchodilator activity
- Used prophylactically

Mast Cell Stabilizers

- Examples
  - cromolyn (Nasalcrom, Intal)
  - nedocromil (Tilade)

Mast Cell Stabilizers

Therapeutic Uses

- Adjuncts to the overall management of COPD
- Used solely for prophylaxis
  - NOT for acute asthma attacks
- Prevention of exercise-induced bronchospasm
- Prevention of bronchospasm associated with exposure to known precipitating factors
  - Cold, dry air or allergens

Mast Cell Stabilizers

Side Effects

Coughing

Sore throat

Rhinitis

Bronchospasm

Taste changes

Dizziness

Headache

Mast Cell Stabilizers

Nursing Implications

- For prophylactic use only
- Contraindicated for acute exacerbations
- Not recommended for children under age five
- Therapeutic effects may not be seen for up to 4 weeks
- Teach patients to gargle and rinse the mouth with water afterward to minimize irritation to the throat and oral mucosa