Chapter 7

Anticholinergic (Parasympatholytic) Bronchodilators
Clinical Indications for Use

- Indication for anticholinergic bronchodilator
  - COPD maintenance
- Indication for combined anticholinergic and β-agonist bronchodilators
  - COPD + airflow obstruction
- Anticholinergic nasal spray
  - Allergic and nonallergic perennial rhinitis + common cold
Specific Anticholinergic (Parasympatholytic) Agents

- Atropine sulfate
  - Not recommended for inhalation

- Ipratropium bromide
  - Available as MDI, nasal spray, and SVN solution
  - Quaternary ammonium derivative of atropine
  - Distribution limited to lung when inhaled
Specific Anticholinergic (Parasympatholytic) Agents

- Ipratropium + albuterol
  - Synergistic effect in COPD

- Glycopyrrolate
  - Used parenterally to reverse neuromuscular blockade
  - Not approved for inhalation

- Tiotropium bromide
  - Longer-acting (up to 24 hours) quaternary ammonium derivative of atropine
Clinical Pharmacology

- **Structure-activity relations**
  - Atropine and scopolamine
    - Tertiary ammonium compounds
    - Easily absorbed in bloodstream
  - Quaternary forms poorly absorbed in bloodstream (better for inhalation)
Pharmacological Effects

- Anticholinergic (antimuscarinic) agents
  - Tertiary ammonium compounds
    - Respiratory tract
    - CNS
    - Eyes
    - Cardiac
    - Gastrointestinal
    - Genitourinary
Pharmacological Effects

- Quaternary ammonium compounds
  - Respiratory tract
  - CNS
  - Eyes
  - Cardiac
  - Gastrointestinal
  - Genitourinary
Mode of Action

- Parasympathetic innervation causes basal level bronchomotor tone
- Parasympatholytic bronchodilators block this tone
- Degree of bronchodilation depends on amount of parasympathetic tone present
Mode of Action

- Vagally mediated reflex bronchoconstriction
  - Irritant aerosols, cold air, high flows, smoke, fumes, histamine release
  - Afferent impulse to CNS = reflex cholinergic efferent impulse = bronchospasm + cough + mucus
  - Can be blocked by competitive inhibitors of acetylcholine
Receptor Subtypes

- **Muscarinic**
  - $M_1$
    - Parasympathetic ganglia
    - Facilitate neurotransmission and bronchoconstriction
    - Cause secretion and rhinitis in nose
  - $M_2$
    - Inhibit continued use of acetylcholine
    - Blockade may enhance acetylcholine release, counteracting bronchodilation (tiotropium is selective for $M_1$ and $M_3$)
  - $M_3$
    - Smooth airway muscle
    - Cause bronchoconstriction
    - Cause secretion and rhinitis in nose
Adverse Effects

- Changes in BP, EKG, or HR not usually seen
- No worsening of ventilation-perfusion abnormalities
- No tolerance/loss of protection
- Side effects:
  - Dry mouth (most common)
  - Mydriasis (eyes should be protected)
  - SVN: also pharyngitis, dyspnea, flulike symptoms, bronchitis, upper respiratory infection
Clinical Application

- Use in COPD
  - More potent bronchodilators than β adrenergics in emphysema/bronchitis
  - FDA approved specifically for COPD
  - Tiotropium maintains higher PFT levels than ipratropium
Clinical Application

- **Use in asthma**
  - No label indication for asthma in United States
  - Antimuscarinics not clearly superior to β agonists in asthma
  - May be useful in:
    - Nocturnal asthma
    - Psychogenic asthma
    - Asthmatics being treated for another condition with β blockers
    - As an alternative to theophylline
    - In acute/severe episodes not responding to β agonist
Combination Therapy

- β-Adrenergic and anticholinergic agents in COPD
  - Additive effect of β agonists and anticholinergics
    - Mean peak increases:
      - 31 to 33% for combined drugs
      - 24 to 25% for ipratropium alone
      - 24 to 27% for albuterol alone
Administration

Sequence of administration

- No data to support either drug being administered first
- Not an issue when using Combivent
- β Agonist may be given first because
  - More rapid onset
  - Distributed in large and small airways
Respiratory Care Assessment

- **Anticholinergic bronchodilator therapy**
  - Assess effectiveness based on indication for use
  - Monitor flow rates
  - Perform respiratory assessment
  - Breath sounds, auscultation, respiratory rate (pre- and posttreatment)
  - Assess pulse
  - Subjective reaction
Respiratory Care Assessment

- Anticholinergic bronchodilator therapy (continued)
  - Arterial blood gases/SpO₂
  - Long term: PFTs
  - Instruct/verify correct use of delivery device
  - For long-acting drugs:
    - Ongoing lung function over time
    - Concomitant β-agonist use/nocturnal symptoms
    - Exacerbations/hospitalizations
    - Absences from work/school