Classifications

• Respiratory therapists administer several different class of drugs:
  – Sympathomimetics (adrenergic)
  – Parasympatholytics (anticholinergic)
  – Mucocactives (mucolytic)
  – Corticosteroids
  – Antiallergics (prophylactic)
  – Anti-infectives (antibiotic)
Sympathomimetics

• Agents
  – Albuterol (Ventolin, Proventil)
  – Bitolterol (Tornalate)
  – Formoterol (Foradil)
  – Levalbuterol (Xopenex)
  – Metaproterenol (Metaprel, Alupent)
  – Pirbuterol (Maxair)
  – Salmeterol (Serevent, Advair)
  – Terbutaline (Brethaire)

• General indication is relaxation of bronchial smooth muscle in the presence of reversible airflow obstruction associated with
  – acute and chronic asthma
  – bronchitis
  – emphysema
  – bronchiectasis
• Usually categorized as short-acting and long-acting

• stimulate
  – α-receptors → vasoconstriction
  – β1-receptors → cardiac stimulant
  – β2-receptors → relaxes bronchial smooth muscle
Sympathomimetics

• Short-acting agents
  – indicated for relief of acute episodes - termed "rescue drugs" in the National Asthma Education and Prevention Program Expert Panel II (NAEPP EPR II) guidelines
    • ultra-short-acting (<3 hours duration): epinephrine, isoproterenol, isoetharine
    • short-acting (4-6 hours duration): metaproterenol, terbutaline, albuterol, bitolterol, pirbuterol, levosalbuterol

• Long-acting agents
  – are indicated primarily for maintenance bronchodilation, control of bronchospasm and control of nocturnal symptoms; usually combined with an anti-inflammatory drug
    • long-acting (12 hours duration): salmeterol, formoterol
Common Respiratory Drugs

Sympathomimetics

- Anti-inflammatory actions
  - both short-acting and long-acting β-agonists show anti-inflammatory actions in vitro
    - salmeterol and formoterol inhibit human mast cell activation and degranulation
  - neither drug is considered to have an effect on airway inflammation sufficient to replace corticosteroids

Adverse side effects

tremor                 nausea
palpitations & tachycardia  tolerance to drug effects
headache                loss of bronchoprotection
insomnia                worsening of V/Q ratio
increased BP            hypokalemia
nervousness             bronchoconstrictor reaction
dizziness
Sympathomimetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Dose</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td>Pulmonary</td>
<td>4.5 mg/mL, 4.5 mg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasal</td>
<td>0.05 mg/mL, 0.1 mg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Otic</td>
<td>0.025 mg/mL, 0.05 mg/mL</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Topical</td>
<td>0.025 mg/mL, 0.05 mg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ophthalmic</td>
<td>0.025 mg/mL, 0.05 mg/mL</td>
<td></td>
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</tr>
</tbody>
</table>

Parasympatholytics

- Atropine
- Ipratropium bromide (Atrovent)
- Ipratropium bromide & albuterol (Combivent)
- Tiotropium bromide (Spiriva)
Parasympatholytics

- General indication is maintenance treatment in asthma and COPD, including chronic bronchitis and emphysema
- Combination products are indicated for patients with COPD on regular treatments who require additional bronchodilation relief of airflow obstruction

Parasympatholytics

- Atropine sulfate
  - a tertiary ammonium compound that is not fully ionized and is readily absorbed from the GI tract and respiratory mucosa
- Ipratropium bromide (Atrovent)
  - a quaternary ammonium derivative of atropine that is fully ionized and does not distribute well across lipid membranes, so its distribution is limited more to the lung when inhaled
### Parasympatholytics

- **Ipratropium bromide and albuterol (Combivent)**
  - A combination MDI product
  - Product has been shown to be more effective in stable COPD than either product alone
- **Tiotropium bromide (Spiriva)**
  - Developed as a long-acting bronchodilator
  - Structurally related to ipratropium and is poorly absorbed after inhalation
  - Appears to maintain a higher level of baseline bronchodilation than ipratropium

### Parasympatholytics

#### Adverse side effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>MDI &amp; SVN (common)</th>
<th>MDI (occasional)</th>
<th>SVN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>dry mouth</td>
<td>nervousness</td>
<td>pharyngitis</td>
</tr>
<tr>
<td></td>
<td>cough</td>
<td>irritation</td>
<td>dyspnea</td>
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<tr>
<td></td>
<td></td>
<td>dizziness</td>
<td>flu-like symptoms</td>
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<tr>
<td></td>
<td></td>
<td>headache</td>
<td>bronchitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>palpitation</td>
<td>upper respiratory infections</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rash</td>
<td>nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>occasional bronchoconstriction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>eye pain</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>urinary retention (&lt;3%)</td>
</tr>
</tbody>
</table>

- MDI: 3-4 puffs per day
- SVN: 1-2 puffs per day

### Parasympatholytics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dose</th>
<th>Onset</th>
<th>Peak Time</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium bromide</td>
<td>MDI</td>
<td>100 μg/act</td>
<td>15 min</td>
<td>0.5-1.5 hr</td>
<td>4-6 hr</td>
</tr>
<tr>
<td></td>
<td>SVN</td>
<td>100 μg/act</td>
<td>15 min</td>
<td>1-4 hr</td>
<td></td>
</tr>
<tr>
<td>Ipratropium and albuterol (Combivent)</td>
<td>MDI</td>
<td>2 puff/act</td>
<td>15 min</td>
<td>2-6 hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SVN</td>
<td>2 puff/act</td>
<td>15 min</td>
<td>2-6 hr</td>
<td></td>
</tr>
<tr>
<td>Tiotropium bromide</td>
<td>MDI</td>
<td>18 μg/act</td>
<td>15 min</td>
<td>0.5-1.5 hr</td>
<td>4-6 hr</td>
</tr>
<tr>
<td></td>
<td>SVN</td>
<td>18 μg/act</td>
<td>15 min</td>
<td>1-4 hr</td>
<td></td>
</tr>
</tbody>
</table>
Mucoactive Agents

- Agents
  - Acetylcysteine (Mucomyst)
  - Dornase alpha (Pulmozyme)

- Acetylcysteine has been used to treat conditions associated with viscous secretions (aerosol, direct instillation)
  - A use is an antidote (antioxidant) to reduce hepatic injury with acetaminophen overdose (oral)
- Dornase alpha is indicated in the management of cystic fibrosis to reduce the frequency of respiratory infections requiring parenteral antibiotics and to improve or preserve pulmonary function in these patients
Mucoactive Agents

• Modes of action
  – acetylcysteine disrupts the structure of mucus by substituting free thiol (sulfhydryl) groups for the disulfide bonds in the mucus
  – dornase alpha reduces the viscosity and adhesivity of infected respiratory secretions when given by aerosol
    • this action is associated with a decrease in the size of the DNA in the sputum
    • the change in sputum viscosity is dose dependent – greater reduction occurs at higher concentrations of the drug

Mucoactive Agents

• Adverse effects
  – Acetylcysteine
    • most serious potential problem is bronchospasm
      – more likely with hyperreactive airways
      – more common with the 20% solution
      – occurrence can be lessened with concomitant use of a bronchodilator, which can be mixed with the acetylcysteine, or given before administration of the acetylcysteine – should use a bronchodilator with rapid onset and peak effect

Mucoactive Agents

• Adverse effects
  – Acetylcysteine
    • other possible complications include
      – stomatitis
      – rhinorrhea
      – airway obstruction due to liquefied secretions
      – nausea and vomiting from odor/taste
Mucoactive Agents

• Adverse effects
  – Dornase alpha
    • common
      – voice alteration
      – pharyngitis
      – laryngitis
      – rash
      – chest pain
      – conjunctivitis

• Adverse effects
  – Dornase alpha
    • less common
      – respiratory
        • cough
        • dyspnea
        • pneumothorax
        • hemoptysis
        • rhinolalia
      – flu-like symptoms
      – malaise
      – GI obstruction
      – hypoxia
      – weight loss

• Dosage and administration
  – acetylcysteine is used in solution for aerosol or for direct instillation into the tracheobronchial tree
    • aerosol – 3-5 ml of the 20% solution tid or qid
    • aerosol – 6-10 ml of the 10% solution tid or qid
    • direct instillation – 1-2 ml of either the 10% or 20% solution
Mucoactive Agents

- Dosage and administration
  - Dornase alpha is available as a unit dose ampoule containing 2.5 mg in 2.5 ml of solution; the solution should be refrigerated and protected from light.
  - The usual dose of dornase alpha is 2.5 mg daily by aerosol, delivered through one of the approved nebulizers:
    - Hudson T Updraft II
    - Marquest Acorn II with a Pulmo-Aide compressor
    - Pari LC Jet Plus with the Pari Inhaler compressor
  - Other nebulizers may work, but delivery of aerosol dornase alpha requires a system capable of appropriate aerosol particle size and quantity.

Corticosteroids

- Indications
  - Asthma – recommended for maintenance and control therapy of chronic asthma, identified in the NAEPP EPR-II as Step 2 asthma (greater than 2 days/week of symptoms, greater than 2 nights/month with symptoms, FEV1 or PEF 80% ± 20% or greater)
  - COPD – not currently recommended by the American Thoracic Society for other than acute exacerbations; however, many COPD patients report lessened symptoms when taking aerosol corticosteroids
  - Active interstitial lung disease
  - Neonatal respiratory distress syndrome
  - ARDS
  - Aspiration pneumonitis
Corticosteroids

• Beclomethasone Dipropionate
  – brand names: Beclovent, Vanceril, Vanceril 84µg
  – dosage
  • MDI (42 µg): adults: 2 inhalations tid or qid; children: 1-2 inhalations tid or qid
  • MDI (84 µg): adults and children > 6 yrs: 2 inhalations bid

• Beclomethasone Dipropionate HFA
  – brand name: QVAR
  – dosage form
  – dosage
  • adults ≥ 12 yr.: 40-80 µg bid*, 40-160 µg bid**
    – * recommended starting dose if on bronchodilators alone
    – ** recommended starting dose if on inhaled corticosteroids previously

• Flunisolide
  – brand names: AeroBid, AeroBid-M
  – dosage form
  • MDI: 250 µg/actuation
  – dosage
  • adults and children ≥ 6 yrs.: 2 inhalations bid (am and pm)
Corticosteroids

- Fluticasone Propionate
  - brand names: Flovent, Flovent Rotadisk, Advair
  - dosage form
    - MDI: 44, 110 or 220 µg/actuation
    - DPI (Rotadisk): 50, 100, 250 µg/inhalation
    - DPI (Advair): 100, 250 or 500 µg/inhalation (with 50 µg salmeterol)

Corticosteroids

- Fluticasone Propionate
  - dosage
    - (Rotadisk): adults 100 µg bid*, 100-250 µg bid**, 1000 µg bid***, children 4-11 yr.: 50 µg bid
    - (Advair): adults and children ≤ 12 yr.: one inhalation 100 µg q 12h (starting dose if not currently on inhaled corticosteroids)
      - * recommended starting dose if on bronchodilators alone
      - ** recommended starting dose if on inhaled corticosteroids previously
      - *** recommended starting dose if on oral corticosteroids previously

Corticosteroids

- Triamcinolone Acetonide
  - brand names: Azmacort
  - dosage form
    - MDI: 100 µg/actuation
  - dosage
    - adults: 2 inhalations tid or qid
    - children: 1-2 inhalations tid or qid
Corticosteroids

- **Budesonide**
  - brand names: Pulmicort Turbuhaler (DPI), Pulmicort Respules (nebulizer solution)
    - DPI: 200 µg/actuation
    - SVN: 0.25 mg/2ml; 0.5 mg/2ml unit dose respules

- **Dosage**
  - SVN: adults: 1 respule daily, children 6-12 yrs.: 0.5 mg or 1 mg once daily or twice daily in divided doses
    - * recommended starting dose if on bronchodilators alone
    - ** recommended starting dose if on inhaled corticosteroids previously
    - *** recommended starting dose if on oral corticosteroids previously

Corticosteroids

- **Adverse reactions (aerosol administration)**
  - local - throat irritation, hoarseness, dry mouth, coughing, oropharyngeal fungal infection (Candida albicans or Aspergillus niger); rinsing and gargling after administration may prevent this infection
  - systemic - suppression of HPA mechanism
  - other - bronchospasm, rashes
Nonsteroidal Antiasthmatics

• Agents
  – Cromolyn sodium (Intal)
  – Nedocromil sodium (Tilade)

• Cromolyn sodium
  – Indications
    • to decrease the frequency and intensity of asthma attacks in both allergic and nonallergic asthma
    • prevention of exercise induced asthma
    • treatment and prevention of allergic rhinitis and allergic conjunctivitis
Nonsteroidal Antiasthmatics

- **Cromolyn sodium**
  - **Mode of action**
    - inhibits the degranulation of mast cells by directly blocking the influx of calcium ions entering the mast cell, preventing the release of chemical mediators of inflammation
    - action is prophylactic and pretreatment is required
    - effective in blocking the late-phase reaction in asthma (more severe airway obstruction 6-8 hours after initial bronchoconstriction)

- **Adverse reactions**
  - CNS: dizziness, headache
  - pulmonary: bronchospasm, wheezing, cough, laryngeal edema
  - miscellaneous: dermatitis, joint swelling, abdominal pain, sneezing, nasal congestion, epistaxis, urinary frequency, throat irritation or dryness
  - allergic: urticaria, rash, angioedema, anaphylaxis

- **Clinical application**
  - complete prophylactic activity may require 4-6 weeks

- **Dosage forms**
  - nebulizer solution: 20 mg/2 ml liquid ampule
  - MDI: 800 µg/actuation

- **Dosage**
  - nebulizer solution: adults and children ≥ 2 yrs.: 1 liquid ampule by SVN qid at regular intervals
  - MDI: adults and children ≥ 5 yrs.: 2 inhalations qid at regular intervals
Nonsteroidal Antiasthmatics

- **Nedocromil sodium**
  - **Indications**
    - to decrease the frequency and intensity of asthma attacks in both allergic and nonallergic asthma
  - **Mode of action**
    - inhibits mediator release from mast cells
    - inhibits eosinophil chemotaxis
    - does not have bronchodilator properties
    - optimum control of asthma symptoms depends on regular use, even if symptoms are not present

- **Adverse reactions**
  - CNS: headache, dizziness
  - GI: unpleasant taste, nausea, vomiting
  - Cardiopulmonary: chest pain, cough, pharyngitis, rhinitis, bronchospasm, dyspnea, upper resp. tract infections

- **Dosage form**
  - MDI: 1.75 mg/actuation

- **Dosage**
  - MDI: 2 inhalations qid