Chapter 32

Airway Pharmacology
Learning Objectives

- Analyze three phases that constitute the course of drug action from dose to effect.
- Describe classes of drugs that are delivered via aerosol route.
- Compare mode of action, indications, duration of action, adverse effects, and contraindications that characterize each major class of aerosolized drug.
Learning Objectives (cont.)

- Compare available aerosol formulations, brand names, and dosages for each specific drug class.
- Select the appropriate drug class for a given patient or clinical situation.
- Assess the outcomes for each class of aerosol drug therapy.
DRUG NAMES

Example: ipratropium bromide (Atrovent™)

Chemical
8-azoniabicyclo(3.2.1.)-octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl1-8-(1-methyl-ethyl)-, bromide

Code
SCH 1000

Generic
ipratropium

Official
ipratropium

Brand (trade, or proprietary)
Atrovent™ (Boehringer-Ingelheim)
**THE PRESCRIPTION**

1. Name ____________ Date ________
   Address _______________________

2. Rx

3. Albuterol 4 mg tabs
   No. 120

4. [Directions on preparing]

5. Sig: Take 1 p.o. QID
   A. Gleason MD

6. □ Generic substitute permitted
Principles of Pharmacology

- Drug administration phase
  - Method by which drug is made available to body
  - Aerosol therapy is most common route for drug administration to pulmonary patient
  - Most common devices used to administer inhaled aerosols are:
    - metered-dose inhaler (MDI)
    - small-volume nebulizer (SVN)
    - dry-powder inhaler (DPI).
Principles of Pharmacology (cont.)

- Drug administration phase (cont.)
  - Advantages of inhaled aerosols:
    - Can use smaller doses as compared to systemic route
    - Onset of drug is rapid
    - Delivery is to specific organ needing treatment
    - Less systemic side effects
Principles of Pharmacology (cont.)

- Pharmacokinetic phase
  - Describes time course & disposition of drug in body based on its absorption, distribution, metabolism, & elimination
  - Fully ionized aerosol drug has little or no systemic side effects (e.g., ipratropium)
  - Non-ionized aerosol drug is lipid soluble & diffuses across cell membranes & into bloodstream, producing systemic side effects (e.g., atropine)
  - Lung availability/total systemic availability ratio (L/T ratio) quantifies efficiency of aerosol delivery to lung
    - L/T ratio = lung availability/(Lung + GI Availability)
Interpreting the L/T Ratio

- **L/T = 0**: (very ineffective aerosol device)
  - worst;
  - lung = 0 / (lung = 0 + GI = 100)
  - all body exposure from GI, no lung delivery

- **L/T = 1**: (very effective aerosol device)
  - best;
  - lung = 1 / (lung = 1 + GI = 0)
  - all body exposure from lung delivery only
Principles of Pharmacology (cont.)
PHASES OF DRUG ACTION: Dose to Effect

Drug Administration - DOSE

↓

Dosage form
Route of administration

↓

Pharmacokinetic Phase

↓

Absorption
Distribution
Metabolism
Elimination

\{\}

Pharmacodynamic Phase

↓

Drug + Receptor

↓

EFFECT

(stimulation, inhibition, etc.)

↓

Clearance

\↓

Metabolism, Elimination
Principles of Pharmacology (cont.)

● Pharmacodynamic phase
  ➢ Describes mechanisms of drug action by which drug molecule causes its effects in body
  ➢ Drug effects are caused by combination of drug with matching receptor
    • https://youtu.be/4YOwEqGyKDM
  ➢ Drug signaling mechanisms include:
    • Mediation by G protein (guanine nucleotide)-linked receptors (e.g., β-adrenergic agonists, anti-muscarinic agents)
    • Attachment to intracellular receptors by lipid-soluble drugs (e.g., corticosteroids)
Airway receptors & neural control of lung

- Sympathetic (adrenergic) & parasympathetic (cholinergic) receptors are in lung
- Neurotransmitter in sympathetic system is norepinephrine (epinephrine)
- Neurotransmitter in parasympathetic system is acetylcholine
Airway receptors & neural control of lung (cont.)

- Agonists (stimulating agents) & antagonists (blocking agents) that act on receptors are given to following classification:
  - Adrenergic: drug that stimulates receptor responding to norepinephrine or epinephrine
  - Antiadrenergic: drug that blocks receptor for norepinephrine or epinephrine
  - Cholinergic: drug that stimulates receptor for acetylcholine
  - Anticholinergic: drug that blocks receptor for acetylcholine
A medication that blocks a receptor for norepinephrine or epinephrine is classified as:

A. andrenergic  
B. antiadrenergic  
C. cholinergic  
D. anticholinergic
3 Ways to Express Drug Strength

- X mg/ml
- % solution
- Dilution ratio
“X” mg/ml

- Tells how many milligrams of drug (solute) are in each ml of solution (solvent)

- 10 mg/ml = 10 milligrams of drug in each ml of solution

- Best form to use for most calculations!
% Solution

- “X” grams of solute (drug) in each 100 ml of solvent (solution)

- 1% solution = 1 gram of solute (drug) in each 100 ml of solvent (solution)
  - Is also the same strength as 10 mg/ml since 1% = 1gm/100ml = 1000mg/100 ml = 10 mg/ml
Dilution Ratio

- 1 gram solute (drug) per “X” grams (or ml) of solvent (solution)
  - 1:100 = 1 grams of drug (solute) per 100 grams of solvent (or ml of solution)
    - $1:100 = 1000\text{mg}/100\text{ml} = 10\text{mg/ml}$
10 mg/ml, 1% and 1:100 are all the same strength just expressed 3 different ways
Conversions: mg/ml to % solution

- Move decimal point 1 place to the left! (divide by 10)

- 10 mg/ml = 1%

- 75 mg/ml = 7.5%
Conversions: % solution to mg/ml

- **Move decimal point 1 place to the right!** (multiply by 10)

- 2% =
  - 20 mg/ml

- .5% =
  - 5 mg/ml

- 7.5% =
  - 75 mg/ml
Conversions: Dilution Ratio to % Solution

- *Convert to mg/ml and then move decimal point 1 place to the left!*
- 1:1000 = 1 gram per 1000 ml = 1000mg/1000 ml (why?) = 1 mg/ml = .1 %
Calculations

- To determine how many mg of drug are in “X” ml of solution, or to determine how many ml of solution contain “X”mg of drug, use:
  \[ \text{mg/ml (available)} = \text{mg/ml (desired)} \]
- where mg/ml (available) is the strength of the drug. Solve for the desired variable on the right side (“desired”) side of the equation.
Calculation Example:
How many ml of 1% Isoetharine (Bronkosol) are needed to give the patient 2.5 mg of drug?

- Convert 1% to mg/ml and use the equation
  \[ \text{mg/ml (available)} = \text{mg/ml (desired)} \]
- 1% = 10 mg/ml, so
- 10 mg/ml = 2.5 mg/”X” ml
  - Using algebra, solve for “X”
- \[ X = .25 \text{ ml} \]
Thus, to give a patient 2.5 mg of 1% Isoetharine (Bronkosol), you would need to administer .25 ml of 1% Isoetharine (Bronkosol)
Calculation Example: How much drug does a patient get if you administer .5 ml of 0.5% Albuterol (Proventil)?

- Convert 0.5% to mg/ml and use the equation mg/ml (available) = mg/ml (desired)
- 0.5% = 5 mg/ml, so
- 5 mg/ml = “X” mg/0.5 ml
  - Use algebra and solve for X
- X = 2.5 mg
Thus, if a patient receives .5 ml of .5% Albuterol (Proventil), he receives 2.5 mg of Albuterol (Proventil)!
Classes of Respiratory Drugs

- Bronchodilators
  - Adrenergic
  - Anticholinergic
- Antiinflammatory medications
  - Steroidal
  - Non-steroidal
- Mucus controlling agents (Mucolytics)
- Aerosolized antiinfective agents
- Inhaled pulmonary vasodilators
Adrenergic Bronchodilators

Indications for use

- **Short-acting agents (SABA) (rescuer or reliever agents)**
  - For relief of *acute reversible* airflow obstruction
  - E.g. albuterol, levalbuterol.

- **Long-acting agents (LABA) (controller agents)**
  - For *maintenance* bronchodilation in patients with obstructive lung disease
  - E.g. salmeterol, formoterol

- **Racemic epinephrine**
  - It has α-adrenergic vasoconstricting effect.
  - To reduce airway swelling after extubation or with acute upper airway inflammation from croup, epiglottitis, or broncholitis
  - To control airway bleeding during endoscopy
  - It is often used either as inhaled aerosol or by direct instillation
## KEY POINT

The adrenergic bronchodilator group is used for treatment of **reversible airway obstruction** in diseases such as asthma and COPD.

These agents produce bronchodilation by stimulating β2 receptors on airway.
Adrenergic Bronchodilators (cont.)

- Mode of action & effects
  - $\alpha$-Receptor stimulation: causes vasoconstriction & vasopressor effect
  - $\beta_1$-Receptor stimulation: causes increased heart rate & heart contractility
  - $\beta_2$-Receptor stimulation: relaxes bronchial smooth muscle, stimulates mucociliary activity, & has some inhibitory action on inflammatory mediator release
Adrenergic Bronchodilators (cont.)

Diagram showing the action of adrenergic bronchodilators on smooth muscle relaxation.
Adrenergic Bronchodilators (cont.)

Three subgroups:

1. Ultra-short acting catecholamine agents
   • Duration of action is less than 3 hours
   • racemic epinephrine
   • Metabolized rapidly by enzyme catechol o-methyltransferase (COMT)

2. Short-acting non-catecholamine agents
   • Albuterol, & levalbuterol, Metaproterenol
   • Duration of action is about 4-6 hours

3. Long-acting adrenergic bronchodilators
   • Salmeterol, formoterol, arformoterol
   • Duration of action is about 12 to 24 hours
Figure 6-3 Chemical structures of inhaled adrenergic bronchodilators currently available in the United States. With the exception of natural epinephrine and levalbuterol, all formulations are racemic mixtures and are shown in the same orientation for clarity. The isomers of racemic albuterol and levalbuterol are labeled to indicate the difference between these two drugs. Formoterol and arformoterol, not shown, are illustrated in Figure 6-8. (From Rau JL: Inhaled adrenergic bronchodilators: historical development and clinical application, Respir Care 45:854, 2000.)
Adrenergic Bronchodilators (cont.)

- Adverse effects
  - Older adrenergic agents such as isoproterenol commonly caused tachycardia, palpitations, & nervousness
  - Newer $\beta_2$-selective agents are safe, with tremor as primary side effect
  - Dizziness, hypokalemia, loss of bronchoprotection, nausea, & tolerance to drug may occur
Adrenergic Bronchodilators (cont.)

- Assessment of bronchodilator therapy
  - Based on indication(s) for aerosol agent
  - Vital signs, breath sounds, & breathing pattern should be evaluated before & after treatment
  - Patient’s subjective response is important to evaluate
<table>
<thead>
<tr>
<th>DRUG</th>
<th>BRAND NAME</th>
<th>RECEPTOR PREFERENCE</th>
<th>ADULT DOSAGE</th>
<th>TIME COURSE (ONSET, PEAK, DURATION)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultra-Short-Acting Adrenergic Bronchodilator Agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Adrenalin Chloride, Primatene Mist</td>
<td>α, β</td>
<td>SVN: 1% solution (1:100), 0.25-0.5 mL (2.5-5.0 mg) qid</td>
<td>Onset: 3-5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MDI: 0.22 mg/puff, puffs as ordered or needed</td>
<td>Peak: 5-20 min</td>
</tr>
<tr>
<td><strong>Raceemic epinephrine</strong></td>
<td>microNefrin, Nephron, 5-2</td>
<td>α, β</td>
<td>SVN: 2.25% solution, 0.25-0.5 mL (5.63-11.25 mg) qid</td>
<td>Onset: 3-5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peak: 5-20 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 0.5-2 hr</td>
</tr>
<tr>
<td><strong>Short-Acting Adrenergic Bronchodilator Agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metaproterenol</td>
<td>Alupent</td>
<td>β2</td>
<td>SVN: 0.4%, 0.6% solution, tid, qid</td>
<td>Onset: 1-5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tab: 10 mg and 20 mg, tid, qid</td>
<td>Peak: 60 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Syrup: 10 mg per 5 mL</td>
<td>Duration: 2-6 hr</td>
</tr>
<tr>
<td>Albuterol</td>
<td>Proventil HFA, Ventolin HFA, ProAir HFA, AccuNeb, VoSpire ER</td>
<td>β2</td>
<td>SVN: 0.5% solution, 0.5 mL (2.5 mg), 0.63 mg, 1.25 mg and 2.5 mg unit dose, tid, qid</td>
<td>Onset: 15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MDI: 90 μg/puff, 2 puffs tid, qid</td>
<td>Peak: 30-60 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tab: 2 mg, 4 mg, and 8 mg, bid, tid, qid</td>
<td>Duration: 5-8 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Syrup: 2 mg/5 mL, 1-2 tsp tid, qid</td>
<td></td>
</tr>
<tr>
<td>Pirbuterol</td>
<td>Maxair Autohaler</td>
<td>β2</td>
<td>MDI: 200 μg/puff, 2 puffs q4-6h</td>
<td>Onset: 5 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peak: 30 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 5 hr</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex, Xopenex HFA</td>
<td>β2</td>
<td>SVN: 0.31 mg/3 mL tid, 0.63 mg/3 mL tid, or 1.25 mg/3 mL tid; Concentrate</td>
<td>Onset: 15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.25 mg/0.5 mL tid</td>
<td>Peak: 30-60 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 5-8 hr</td>
</tr>
<tr>
<td><strong>Long-Acting Adrenergic Bronchodilator Agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent Diskus</td>
<td>β2</td>
<td>DPI: 50 μg/blister bid</td>
<td>Onset: 20 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peak: 3-5 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 12 hr</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Perforomist, Foradil</td>
<td>β2</td>
<td>SVN: 20 μg/2 mL unit dose, bid</td>
<td>Onset: 15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPI: 12 μg/inhalation, bid</td>
<td>Peak: 30-60 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 12 hr</td>
</tr>
<tr>
<td></td>
<td>Foradil Certihaler</td>
<td>β2</td>
<td>DPI: 8.5 μg/inhalation, bid</td>
<td>Onset: 15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peak: 30-60 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 12 hr</td>
</tr>
<tr>
<td>Arformoterol</td>
<td>Brovana</td>
<td>β2</td>
<td>SVN: 15 μg/2 mL unit dose, bid</td>
<td>Onset: 15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Peak: 30-60 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 12 hr</td>
</tr>
</tbody>
</table>

*DPI, dry powder inhaler; MDI, metered dose inhaler; SVN, small volume nebulizer.*
Anticholinergic Bronchodilators

- Indications for use
  - anticholinergic bronchodilator
    - Ipratropium & tiotropium are indicated as maintenance bronchodilator therapy for COPD patients
  - combined anticholinergic & β-agonist
    - Ipratropium bromide & albuterol (Combivent, Duoneb) is indicated for patients with COPD or asthma
Anticholinergic Bronchodilators (cont.)

- **Mode of action**
  - Agents act as competitive antagonists for acetylcholine on airway smooth muscle

- **Adverse effects**
  - Atropine produces many side effects when inhaled since it is easily absorbed into bloodstream
    - Side effects include dry mouth, pupillary dilation, lens paralysis, increased intraocular pressure, increased heart rate, urinary retention, & altered mental state
  - Protect eye from drug exposure with aerosol use due to accidental spraying from MDI or with nebulizer-mask delivery.
Anticholinergic Bronchodilators (cont.)

**Box 32-2** Side Effects Seen with Anticholinergic Aerosol Agents*

SVN, MDI, and DPI (common)
- Cough, dry mouth
MDI (occasional)
- Nervousness, irritation, dizziness, headache, palpitation, rash
SVN and DPI
- Pharyngitis, dyspnea, flu-like symptoms, bronchitis, upper respiratory infections, nausea, occasional bronchoconstriction, eye pain, urinary retention

*Side effects were reported in a small percentage (1% to 5%) of patients. Precautions: Use with caution in patients with narrow-angle glaucoma, prostatic hypertrophy, bladder neck obstruction, constipation, bowel obstruction, or tachycardia.
Inhaled Corticosteroids

- Indications & purposes
  - Inhaled preparations used for antiinflammatory maintenance therapy of persistent asthma & severe COPD
  - Use of intranasal steroids is for control of allergic & non-allergic rhinitis.

- Mode of action
  - Lipid-soluble drugs that act on intracellular receptors
  - Full antiinflammatory effects require hours to days
    - Will not provide immediate relief of dyspnea from airways obstruction
Inhaled Corticosteroids (cont.)

[Diagram showing the mechanism of action of inhaled corticosteroids, including the interaction of hsp90 and GR, the role of inflammatory factors like AP-1 and NF-kB, and the resulting inhibition of pro-inflammatory proteins and increased anti-inflammatory proteins, leading to decreased airway responsiveness.]
Inhaled Corticosteroids (cont.)

- Special consideration
  - Modes of action of all inhaled glucocorticoids are same with exception of ciclesonide
  - Ciclesonide is *prodrug* given as inactive compound & is converted to active metabolite by intracellular enzyme
    - Available as intranasal formulation name Omnaris & pressurized metered dose inhaler named Alvesco
## Inhaled Corticosteroids (cont.)

Adverse effects

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### Box 32-3

**Potential Hazards and Side Effects of Aerosolized Corticosteroids**

**SYSTEMIC**
- Adrenal insufficiency*
- Extrapulmonary allergy*
- Acute asthma*
- HPA suppression (minimal, dose dependent)
- Growth retardation†
- Osteoporosis†

**LOCAL (TOPICAL)**
- Oropharyngeal fungal infections
- Dysphonia
- Cough, bronchoconstriction
- Incorrect use of MDI

*HPA, Hypothalamic, pituitary, adrenal.
*Following substitution for systemic corticosteroid therapy.
†Effect with inhaled corticosteroids alone is unclear.
Inhaled Corticosteroids (cont.)

- Assessment of drug therapy
  - Use strategies for assessment similar to those used for evaluation of bronchodilators
  - In addition
    - Make sure patient understands importance of consistent use & not to use it as rescue drug
    - Instruct patient in use of peak flowmeter
    - Assess patient for side effects
Nonsteroidal Antiasthma Drugs

- Growing class of drugs for treatment of asthma
- Three types exist:
  1. Mast cell stabilizers (Cromolyn sodium)
  2. Antileukotrienes (zafirlukast, monteleukast, zileuton)
  3. Monoclonal antibodies or anti-IgE agents (omalizumab)
Nonsteroidal Antiasthma Drugs (cont.)

- Indications for use
  - prophylactic management (control) of persistent asthma
  - Offer no benefit for acute airways obstruction in asthma
  - Cromolyn sodium & antileukotrienes may be used as alternative to steroids in patients with persistent asthma symptoms
  - Monoclonal antibody omalizumab is available for consideration in correct population
Nonsteroidal Antiasthma Drugs (cont.)

Mode of action

- Mast Cell stabilizers:
  - Cromolyn sodium inhibits degranulation of mast cells in response to allergic & nonallergic stimuli
  - Prevents release of histamine & other mediators of antihistamine

- Antileukotrienes:
  - Zafirlukast & montelukast act as leukotriene receptor antagonists & are selective competitive antagonists of leukotriene receptors
  - Leukotrienes Cause bronchoconstriction, mucus secretion, vascular permeability, & plasma exudation into airway
  - Drug inhibits reactions induced by exercise, cold air, allergens, & aspirin
Nonsteroidal Antiasthma Drugs (cont.)

Mode of action (cont.)

- **Antileukotrienes:**
  - Zileuton inhibits 5-lipoxygenase enzyme that catalyzes formation of leukotriene from arachidonic acid

- **Monoclonal antibodies or anti-IgE agents:**
  - Omalizumab inhibits attachment of IgE to mast cells & basophils, reducing release of chemical mediators of allergic response
Nonsteroidal Antiasthma Drugs (cont.)
Nonsteroidal Antiasthma Drugs (cont.)

- Adverse effects
  - Antileukotriene agents
    - Headache
    - Dyspepsia (indigestion)
    - Liver enzyme elevation
  - Omalizumab
    - Injection site reaction
    - Viral infections
    - Headache
    - Sinusitis
    - Pharyngitis
Assessment of drug therapy

- Strategies similar to those used to assess initial bronchodilator therapy
- Clinician should verify that patient understands that medications are controller drugs & not rescue agents
Mucus-Controlling Agents

- **N-Acetyl-cysteine (NAC)**
  - Given by aerosol or direct tracheal instillation
  - Given to reduce accumulation of airway mucus
  - May cause bronchospasm due to irritating side effects
  - Used as antidote for acetaminophen overdose (oral)
  - Mode of action
    - NAC substitutes its own sulfhydryl group for disulfide group in mucus, breaking portion of bond forming gel structure
Figure 9-9  Mechanisms of action by which acetylcysteine reduces the viscosity of mucus. Acetylcysteine substitutes the sulfhydryl for the disulfide bonds.
Mucus-Controlling Agents (cont.)

- N-Acetyl-cysteine (NAC) (cont.)
  - Side effects
    - Airway obstruction due to rapid liquefaction of secretions
    - Disagreeable odor due to hydrogen sulfide
    - Increased concentration & toxicity of nebulizer solution toward end of treatment
    - Nausea & rhinorrhea
    - Stomatitis
    - Reactivity of acetylcysteine with rubber, copper, iron, & cork
Mucus-Controlling Agents (cont.)

- Dornase alfa
  - Indicated for management of cystic fibrosis
  - Mode of action
    - Solution of (rhDnase) cleaving DNA in mucus
  - Side effects
    - Voice alteration
    - Pharyngitis
    - Rash
    - Chest pain
Mucus-Controlling Agents (cont.)

<table>
<thead>
<tr>
<th>Reduction in Viscosity: (Pourability)</th>
<th>0 min</th>
<th>15 min</th>
<th>30 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>0</td>
<td>+1</td>
<td>+1</td>
</tr>
<tr>
<td>rhDNase, 50 µg/ml</td>
<td>0</td>
<td>+3</td>
<td>+4</td>
</tr>
<tr>
<td>Bovine DNase, 50 µg/ml</td>
<td>0</td>
<td>+2</td>
<td>+4</td>
</tr>
</tbody>
</table>

Thick purulent mucus

DNA strands

Mucus

Neutrophil

rhDNase

Lower viscosity mucus

Bronchial epithelium
Dornase alfa has which of the following common side effect(s)?

A. voice alteration
B. rash
C. chest pain
D. all of the above
Mucus-Controlling Agents (cont.)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Adult Dosage</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-Acetylcysteine 10%</td>
<td>Mucomyst</td>
<td>SVN: 3-5 ml</td>
<td>Bronchitis, efficacy not proven</td>
</tr>
<tr>
<td>N-Acetylcysteine 20%</td>
<td>Mucomyst</td>
<td>SVN: 3-5 ml</td>
<td>Bronchitis, efficacy not proven</td>
</tr>
<tr>
<td>Dornase alfa</td>
<td>Pulmozyme</td>
<td>SVN: 2.5 mg/ampule, 1 ampule daily*</td>
<td>CF</td>
</tr>
<tr>
<td>Aqueous aerosols: water, saline (0.45%, 0.9%, 5%-10%)</td>
<td>NA</td>
<td>SVN: 3-5 ml, as ordered</td>
<td>Sputum induction, secretion mobilization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>USN: 3-5 ml, as ordered</td>
<td></td>
</tr>
</tbody>
</table>

NA, Not applicable.

*Use recommended nebulizer system (see package insert). Approved nebulizers include Hudson T Updraft II, Marquest II with Pulmo-Aide compressor, or PARI LC Jet Plus with PARI Inhaler Boy compressor.
Pentamindine isethionate (NebuPent)

- Has been used in past for treatment of opportunistic pneumonia caused by Pneumocystis jiroveci which is causative agent of *Pneumocystis* pneumonia (PCP)
- Due to limited efficacy, pentamindine is no longer recommended for PCP treatment
- Common side effects include cough, bronchospasm & wheezing, dyspnea.
Aerosolized Antiinfective Agents (cont.)

- Ribavirin
  - Antiviral agent used in treatment of severe lower respiratory tract infections caused by respiratory syncytial virus (RSV)
  - Administration of aerosol requires use of small particle aerosol generator (SPAG).
  - Cost-effectiveness continues to be debated
  - Adverse effects
    - Skin rash
    - Eyelid erythema
    - Conjunctivitis
  - Pregnant patients & practitioners should not be exposed
Inhaled tobramycin

- Intended to manage chronic infection with *P. aeruginosa* in patients with cystic fibrosis
- Side effects with inhaled route are usually minimal & include voice alteration & tinnitus
Aerosolized Antiinfective Agents (cont.)

- Inhaled aztreonam (Cayston)
  - Monobactam- synthetic bactericidal antibiotic given as intravenous (IV) solution
  - Improves pulmonary symptom in CF patients colonized with *P. aeruginosa*
  - Not indicated for patients younger than 7-years old, or those with *Burkholderia cepacia*
  - Possible side effects include bronchospasm, decrease in FEV1, & allergic reactions
Aerosolized Antiinfective Agents (cont.)

- Colistimethate sodium
  - Antibiotic used to treat sensitive strains of gram-negative bacilli, particularly *P. aeruginosa*
  - Parenteral side effects include nephrotoxicity & neurotoxic events (dizziness, confusion, & muscle weakness)
  - Bronchospasm is most common side effect seen with aerosol route
    - Pretreatment with a β-agonist can decrease potential for this complication
Inhaled zanamivir

- Inhaled powder aerosol (DPI)
- Indicated for treatment of uncomplicated acute illness due to influenza virus in adults & children at least 5 years of age
  - Has off-label use for treatment & prophylaxis of H1N1 influenza A
- Can cause bronchospasm & allergic reactions
Which of the following is NOT an aerosolized antiinfective agent?

A. ribavirin
B. tobramycin
C. aztreonam
D. treprostinil
Inhaled Pulmonary Vasodilators

- Medications being tested for pulmonary hypertension
  - Epoprostenol (Flolan)
  - Alprostadil (Prostin VR Pediatrics)
  - Only Iloprost & Treprostenil are FDA approved
Inhaled Pulmonary Vasodilators (cont.)

- Nitric oxide (INOmax)
  - Indicated for treatment of neonates with persistent pulmonary hypertension (PPH)
  - Relaxes vascular smooth muscle in pulmonary vasculature
  - When inhaled, produces pulmonary vasodilation, reducing pulmonary artery pressure & improving V/Q mismatching
  - Hypotension is most common side effect
Inhaled Pulmonary Vasodilators (cont.)

- Iloprost (Ventavis)
  - Used in treatment of pulmonary hypertension
  - Administered with I-neb nebulizer
  - Acts by dilating pulmonary vasculature & affecting platelet aggregation
  - Side effects include headache & increased cough
Role of the Respiratory Therapist in Airway Pharmacology

- Recommend for given clinical situation:
  - Appropriate drug class
  - Most suitable mode of administration

- Assess Outcomes
  - Effectiveness of therapy
  - Adverse effects