Learning Objectives

- Review normal lung function and COPD pathophysiology
- Discuss pharmacological management of COPD in hospice patients
- Identify effective inhaler techniques for aerosol and dry powder inhalers
- Describe dyspnea management for hospice patients with COPD
Prevalence

- 4th leading cause of death in United States
  - Expected to be 3rd by 2020
- 6% of the population have been diagnosed
  - Estimated that 25% actually have air flow limitation without diagnosis

Healthcare Utilization

- Overall patients in 2000
  - 8 million physician and hospital visits
  - 1.5 million emergency department visits
  - 673,000 hospitalizations
- Hospice patients 2010
  - 1,029,000 patients total all diagnoses
  - 85,407 (8.3%) patients with lung disease

COPD Definition

- COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.
  - Global Initiative for Chronic Obstructive Lung Disease, 2010
Other Names for COPD

- Emphysema
  - Destruction of alveoli
  - Pathological term
- Chronic bronchitis
  - Presence of cough and sputum production for at least 3 months in each of 2 consecutive years

Lung Anatomy

- Lungs
  - Located on each side of the chest
  - Encased in the pleura
- Bronchi
- Bronchioles
- Alveoli
- Conducting airways
  - Conduct air from the trachea to the alveoli

Lung Functions

- Gas exchange
  - Blood – Air interface
  - Two cell layers thick
  - 300 million alveoli
  - 450-1000 square feet of surface area
- Filtering and detoxification
- Metabolic/Synthetic functions
  - Surfactant
  - Mucopolysaccharides
  - Angiotensin conversion
  - Endocrine functions
Normal Lung Function and Elasticity
- Lungs tend to collapse to a smaller size
- Chest wall tends to expand outward
- Lung expansion is maintained by a negative pressure in the pleural space
- Lungs distend easily with little pressure

Air Movement During Inspiration
- The diaphragm contracts
  - Pushes down on abdominal contents
  - Lengthens the thoracic cavity
- Intercostal muscles contract
  - Raise and lift ribs outward
  - Expand the chest laterally
- Result is negative pressure in the chest
  - Air flows in easily to fill the "empty space"

Air Movement during Expiration
- Respiratory muscles relax
- Chest wall moves inward
- Elastic recoil pulls the lung inward
- Pressure within the chest increases
- Air flows outward passively
Air Movement in COPD

- Lungs are chronically overinflated
  - Chest wall and diaphragm move less
  - Less negative pressure is generated in inspiration
  - Patients use accessory muscles or arms to lift and lengthen thoracic cavity
- Elastic recoil is reduced
  - Positive pressure in expiration is reduced
  - Expiration no longer passive, requires effort
- Airways are narrowed by inflammation
- Airways may collapse
  - Expiration is slower
  - Expiration takes more effort
- Elastic recoil is reduced
  - Positive pressure in expiration is reduced
  - Expiration no longer passive, requires effort

Normal Lungs vs. COPD Lungs


Stages of COPD

<table>
<thead>
<tr>
<th>Stage</th>
<th>FEV1/FVC</th>
<th>FEV1 (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Mild</td>
<td>FEV1/FVC &gt; 75%</td>
<td>FEV1 &gt; 80%</td>
<td>Mild airflow limitation. Symptoms of cough and sputum production may be present, but not always. The individual is usually unaware that his/her lung function is abnormal.</td>
</tr>
<tr>
<td>II: Moderate</td>
<td>FEV1/FVC &gt; 75%, 50% ≤ FEV1 &lt; 80%</td>
<td>bronchodilators often help if symptoms are not severe.</td>
<td></td>
</tr>
<tr>
<td>III: Severe</td>
<td>FEV1/FVC &gt; 75%, 30% ≤ FEV1 &lt; 50%</td>
<td>Slow walking, dyspnea on exertion, fatigue, and repeated exacerbations affect QOL.</td>
<td></td>
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<tr>
<td>IV: Very Severe</td>
<td>FEV1/FVC &lt; 75%, FEV1 &lt; 30% or FEV1 &lt; 50% predicted plus chronic respiratory failure</td>
<td>Respiratory failure may lead to effects on the heart.</td>
<td></td>
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</tbody>
</table>
End-Stage COPD: Hospice Eligibility

- Patient has ALL of the following:
  - Disabling dyspnea at rest or with minimal exertion
  - Little or no response to bronchodilators
  - Decreased functional capacity
- AND
  - Progression of disease (physician visits, ER visits, hospitalizations)
  - Documentation of one of the following in the past 3 months
    - Hypoxemia (pO2 < 55mmHg or O2 sat. <88%)
    - Hypercapnia (pCO2 > 50mmHg)

Causes of Death in COPD

- Infection
- Ventilatory failure
- Heart failure

Treatments for COPD

- Bronchodilators
  - Beta 2 agonists
  - Anticholinergics
  - Methylxanthines (theophylline)
- Corticosteroids
- Phosphodiesterase-4 Enzyme Inhibitor
Bronchodilators
- Less benefit in end-stage disease
- Nebulizers vs. multi-dose inhalers +/− spacer
- Beta 2 agonists
- Anticholinergics
- Theophylline
- Patient may become psychologically dependent

Beta 2 Agonists: Short-acting
- Albuterol (Proventil, Ventolin, ProAir HFA)
  - ProAir HFA inhaler: 90mcg/act
    - 2 puffs every 4-6 hours ($88/30 DS)
  - Nebs: 0.63mg, 2.5mg/3ml
    - 1 vial every 4-6 hours ($316, $140/30 DS)
- Levalbuterol (Xopenex)
  - Inhaler: 45mcg/act
    - 2 puffs every 4-6 hours ($120/30 DS)
  - Nebs: 0.31mg, 0.62mg, 1.25mg/3ml
    - 1 vial every 6-8 hours ($605 - $675/30 DS)

Beta 2 Agonists: Long-acting
- Salmeterol (Serevent)
  - Inhaled powder: 50mcg/act
    - Every 12 hours ($181/30 DS)
- Formoterol (Foradil Aerolizer)
  - Inhaled powder: 12mcg/capsule
    - Every 12 hours ($176/30 DS)
- Arformoterol (Brovana)
  - Nebs: 15mcg/2ml
    - Every 12 hours ($280/30 DS)
- Indacaterol (Arcapta Neohaler)
  - Inhaled powder: 75mcg/capsule
    - Every 24 hours ($195/30 DS)
### Anticholinergics

- **Ipratropium (Atrovent, Atrovent HFA)**
  - Inhaler: 17mcg/act
    - 2 puffs every 6 hours ($172/30 DS)
  - Neb: 0.02%
    - 1 vial every 6-8 hours ($70/30 DS)

- **Tiotropium (Spiriva)**
  - Inhaled powder: 18mcg/capsule
    - Every 24 hours ($246/30 DS)

### Theophylline

- Bronchodilator
  - Exact mechanism unknown
  - Thought to non-specifically inhibit all phosphodiesterase enzymes
- Inexpensive
  - 200mg CR tablets ($25/30 DS)
- Narrow therapeutic index
  - Consider 3rd line therapy due to side-effects and potential toxicity
- Side-effects include: tachycardia, headache, restlessness, seizures, nausea/vomiting, reflux, tremor

### Inhaled Corticosteroids

- Fluticasone (Flovent)
  - HFA inhaler: 44mcg, 110mcg, 220mcg/act ($120, $154, $247/30 DS)
  - Aerosol discs: 50mcg, 100mcg, 250mcg ($115, $116, $155/30 DS)
    - Every 12 hours
- Budesonide (Pulmicort, Pulmicort Flexhaler)
  - Aerosol inhaler: 90mcg, 180mcg/act ($122, $160/30 DS)
  - Neb: 0.25mg, 0.5mg/2ml
    - Every 12 hours
- Beclomethasone (QVAR)
  - Inhaler: 40mcg, 80mcg/act
    - Every 12 hours
- Mometasone (Asmanex Twisthaler)
  - Aerosol powder: 110mcg, 220mcg/act
    - Every 12 to 24 hours

Oral corticosteroids are more cost-effective than inhaled corticosteroids in end-stage disease.
Oral Corticosteroids
- Prednisone
  - 10-20mg daily ($12/30 DS)
- Dexamethasone
  - 2-4mg daily ($22/30 DS)
- Multiple palliative benefits
  - Improvement of shortness of breath due to inflammation
  - Improvement of inflammatory pain
  - Appetite stimulation
- Use caution with brittle diabetics or recent GI bleed

Combination Products
- Albuterol & Ipratropium
  - Combivent inhaler: 90-18mcg/act ($280/30 DS)
  - Duoneb nebs: 2.5-0.5mg/3ml ($160/30 DS)
  - Every 6 hours
- Fluticasone & Salmeterol (Advair Diskus, Advair HFA)
  - Inhaler: 45-21mcg, 115-21mcg/act, 230-21mcg/act ($209-$304/30 DS)
  - Aerosol powder: 190-50mcg/dose ($186/30 DS)
  - Aerosol powder: 250-50mcg/dose ($216/30 DS)
  - Aerosol powder: 500-50mcg/dose ($317/30 DS)
  - Every 12 hours
- Budesonide & Formoterol (Symbicort)
  - Inhaler: 80-4.5mcg, 160-4.5mcg/act ($197, $230/30 DS)
  - Every 12 hours
- Mometasone & Formoterol (Dulera)
  - Inhaler: 100-5mcg, 200-5mcg/act ($188/30 DS)
  - Every 12 hours

Phosphodiesterase-4 Enzyme Inhibitor
- Daliresp (Roflumilast)
  - FDA approved in 2011 for severe COPD
  - First and only selective PDE-4 inhibitor
  - Anti-inflammatory activity
- Oral tablet
  - 500mcg once daily
  - $250/30 DS

Oral corticosteroids are still the preferred anti-inflammatory therapy for hospice patients with COPD
Inhaled vs. Nebulized Treatments

- **Inhalers**
  - Available as aerosol or dry powder inhalers
  - Requires coordination
  - Requires variable inhalation effort
  - Rescue inhalers may still be appropriate for ambulatory patients

- **Nebulizers**
  - Solution is placed in the nebulizer machine
  - Patient breathes normally through the mouth for the duration of the treatment
  - Mouthpiece or mask used for inhalation

Nebulizer treatments are preferred in hospice patients to successfully deliver medications to the lungs.

Factors for Device Selection

- Ability to use device
  - Cognitive function
  - Dexterity and strength
- Medication availability in desired device
- Cost and reimbursement
- Patient preferences and device considerations
- Educational challenges

Importance of Inhaler Technique

- 2008 observational study of dry powder inhaler use in 224 patients
  - Diskus, Handihaler, Turbohaler, Aerolizer
  - Observed for ineffective inhaler use
    - Technical errors
    - Inadequate respiratory flow
  - 67 patients with COPD
    - 33 patients GOLD I or II
    - 34 patients GOLD III or IV
Results: Influence of Age

- Error rate increased with age ($p<0.01$)
- Significance remained even after adjustment for severity of obstruction and type of training ($p<0.05$)

Results: Influence of Severity

- Error rate increased with severity of obstruction for the whole group ($p<0.01$)
- Error rate also increased within COPD group alone ($p<0.05$)

Inhaler Technique

- **Aerosol Inhalers**
  - Require priming before first use
  - Exhale as much air as possible
  - Inhale slowly and deeply while depressing canister
  - Hold breath for 10 seconds
  - Breathe normally

- **Dry Powder Inhalers**
  - Require various methods of readying the dose
  - Breath out fully
  - Inhale quickly and deeply
  - Hold breath for 10 seconds
  - Breathe out slowly
Inhaler Technique Demonstration

Volunteers Please!

- Aerosol inhaler
- Advair Diskus
- Spiriva Handihaler

Aerosol Inhalers

- Priming the inhaler
  - Before first use, if not used in 14 days, or if dropped
- Shake well before each puff
- Wait at least 1 minute between puffs
- Cleaning the inhaler
  - Running actuator under warm water for 30 seconds
  - Must be done at least weekly

Advair Diskus

- Open, Click, Inhale
  - Open by sliding thumb grip
  - Click lever away from you
  - Inhale
- Tips
  - Always keep inhaler level
  - Never breath out into the inhaler
Spiriva Handihaler
- Open
  - Release cap and lift mouthpiece
- Insert capsule
  - Open immediately before use
- Pierce the capsule
  - Hold inhaler upright
  - Do not pierce more than once
  - Do not shake
- Inhale dose
  - Must inhale twice
  - Capsule should rattle inside of inhaler

Benefits of a Spacer
- Helps to overcome common technique problems in the elderly
- Slows aerosol spray
- Allows propellant to evaporate, reducing particle size
  - Reduces oropharyngeal deposition
- Holds dose until inhaled
  - Reduces need for hand-breath coordination
  - Some signal when inhalation is occurring to quickly

Downside of a Spacer
- Bulky
- Require assembly
  - Increased dexterity may be needed
- Walls of spacer may have electrostatic charges attracting drug particles
  - Reduces size of available dose
  - Minimized by weekly washing and air drying
spacer use

http://www.asthma.ca/adults/treatment/spacers.php

Discontinuing Inhalers

- Video

Dyspnea

- Dyspnea is the sensation of difficulty breathing
  - Mechanism is not entirely clear

- Occurs in 70-80% of hospice patients
  - Often not successfully treated
Dyspnea
- May represent abnormal relationships between neuromuscular effort and air movement in the lung
  - Respiratory muscle fatigue may contribute
- Patient perception of the underlying cause may increase distress
- May occur with or without cardiac or lung disease

Palliative Care of Dyspnea
- Identify potentially reversible causes
  - Bronchospasm, congestive heart disease (CHF), infection, pulmonary embolism, effusion, anemia
- Treat reversible causes, if appropriate
- Evaluate for use of oxygen or a fan
- Consider bronchodilators
  - Especially if bilateral wheezing
- Consider corticosteroids
  - COPD, pulmonary fibrosis, asthma or tumor are present

Benzodiazepines for Dyspnea
- Schedule ATC with higher dose at bedtime
- Anxiety is always a component of feeling short of breath
- Start low and titrate up
  - Lorazepam (Ativan) 0.25-0.5mg every 6-8 hours
  - Alprazolam (Xanax) 0.125-0.25mg every 6-8 hours
  - Diazepam (Valium) 1-2.5mg every 8-12 hours
- Goal is to relieve anxiety and calm patient
  - Appropriate doses should not sedate
Opioids for Dyspnea

- Use morphine unless contraindicated
  - Oxycodone is preferred in renal failure
- Start with morphine 2.5-5mg every 1-2 hours prn
  - For opioid naïve patients
  - Higher starting dose may be needed for opioid tolerant patients
- Schedule every 4 hours if needed frequently
  - Continue to have prn doses available
- Seldom need more than 5-10mg every 4 hours in an opioid naïve patient
- Increase benzodiazepine before going above 10-20mg every 4 hours

Risk of Treating Dyspnea

- Easy to overdose if treating physical signs rather than symptoms
- Treat patient reports of discomfort
  - Not respiratory rate or effort
- Goal is to relieve subjective symptoms of distress
  - Not necessary to decrease respiratory rate for comfort

Role of Oxygen in Dyspnea

- Duke University Medical Center
  - For those who do benefit from oxygen therapy, researchers discovered that regular room air was just as effective as pure oxygen. The results of the study suggest that any air streams directed toward the nose offer relief from shortness of breath, and that in some cases, a room fan might even be as effective as an oxygen mask.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)61115-4/abstract
Patient Case

- 72 yo male with end stage COPD, CHF, osteoarthritis, glaucoma, and gout
- PPS 30%
  - Bedbound, normal swallowing, requires total care
- NKDA
- Medications:
  - Advair 250/50: Inhale 1 puff BID
  - Spiriva 18mcg: Inhaler content of 1 cap daily
  - Metoprolol tartrate 25mg: take 1 tab PO BID
  - Lisinopril 20mg: take 1 tab PO daily
  - Allopurinol 100mg: take 1 tab PO daily
  - Ibuprofen 200mg: take 2 tablets PO q8h
  - Tylenol 500mg: Take 1 tab PO q4h pm pain or fever
  - Xalatan 0.005% soln: Instill 1 drop in each eye at bedtime

Patient Case

- SOB symptoms have worsened over the last few weeks.
  - Upon observation of this patient’s inhaler technique, you notice patient is having difficulty inhaling quickly and forcefully when using Advair and Spiriva inhalers.
  - Patient is also not able to consistently rinse mouth after use of Advair.
- What recommendations would you make for this patient?

Questions??
References

- LexiComp Online. Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc; April 24, 2012.
- Spiriva HandiHaler (tiotropium bromide) package insert. Ridgefield, CT: Boehringer Ingelheim; 2012.