Key Inforbits

- Introduction to COPD
- Diagnosis of COPD
- Management of Stable COPD
- Smoking Cessation: The 5 A’s
- Recent Developments
- Management of Stable COPD

November is…

COPD AWARENESS
Month

INTRODUCTION TO COPD

More than 12 million Americans 18 years or older report having chronic obstructive pulmonary disease (COPD). However, prevalence of the disease is expected to be higher due to the lack of symptoms in the earlier stages of COPD.¹ It is the fourth leading cause of death only surpassed by cancer, heart disease, and cerebrovascular accidents. This accounted for 126,005 deaths in the U.S. in 2005. By 2020, it is expected to be the third leading cause of death across the globe.¹

Cigarette smoking is the most common risk factor and leading cause of COPD. This accounts for 85-90% cases of COPD.² Approximately 25% of Americans smoke currently. The prevalence of smoking has decreased since 1965; however the increasing rise in mortality is likely due to the long latency period between smoking exposure and the problems associated with COPD.² Other factors such as environmental and occupational exposures can lead to COPD; and genetics can additionally play a part. The most documented genetic link is a hereditary deficiency of α₁-antitrypsin (ATT).¹ A severe deficiency in this enzyme can lead to an early onset of emphysema.

COPD is characterized by chronic airflow limitation that is not fully reversible and chronic inflammation that leads to pathological changes in the lungs.³ This chronic limitation of airflow is caused by obstructive bronchitis (small airway disease) and emphysema (parenchymal destruction). Chronic inflammation in the lungs due to repeated exposure of noxious gases, such as cigarette smoke or other chemicals, is responsible for the changes found in the central and peripheral airways, lung parenchyma, and pulmonary vasculature.¹ These noxious irritants impair the lungs’ normal protective and repairing processes.

Additional changes in the lungs seen in COPD include hypersecretion, ciliary dysfunction, airflow limitation, pulmonary hyperinflation, alveolar gas exchange abnormalities, and pulmonary vascular disease.⁴ Recurrent exacerbations associated with increased symptoms and a decline in overall health status is a common problem in patients with COPD. Exacerbations are
defined changes in the baseline symptoms (dyspnea, cough, or sputum production) sufficient to warrant a change in disease management. Exacerbations may progress to acute respiratory failure requiring mechanical ventilatory support. Infections, mostly viral and some bacterial, are the leading cause of COPD exacerbations.


**DIAGNOSIS OF COPD**

When diagnosing COPD, a patient’s symptoms and history of exposure to risk factors should be obtained. For a confirmed diagnosis of COPD, the gold standard is spirometry (refer to Table 1).

An FEV₁/FVC of <70% confirms an airflow limitation that is not completely reversible. The FEV₁ indicates which stage of COPD into which the patient is categorized.

**MANAGEMENT OF STABLE COPD**

### Table 1

**SPIROMETRIC CLASSIFICATION OF COPD SEVERITY BASED ON POST-BRONCHODILATOR FEV₁**

<table>
<thead>
<tr>
<th>Stage</th>
<th>FEV₁/FVC &lt; 70%</th>
<th>FEV₁ ≥ 80% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I: Mild</td>
<td></td>
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<tr>
<td>Stage II: Moderate</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>50% ≤ FEV₁ &lt; 80% predicted</td>
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<tr>
<td>Stage III: Severe</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>30% ≤ FEV₁ &lt; 50% predicted</td>
</tr>
<tr>
<td>Stage IV: Very Severe</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>FEV₁ &lt; 30% predicted or FEV₁ &lt; 50% predicted plus chronic respiratory failure</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduction of active risk factors*</td>
<td>• Reduction of active risk factors*</td>
<td>• Reduction of active risk factors*</td>
<td>• Reduction of active risk factors*</td>
<td></td>
</tr>
<tr>
<td>• Influenza vaccine yearly</td>
<td>• Influenza vaccine yearly</td>
<td>• Influenza vaccine yearly</td>
<td>• Influenza vaccine yearly</td>
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<tr>
<td>• Short acting bronchodilators</td>
<td>• Short acting bronchodilators</td>
<td>• Short acting bronchodilators</td>
<td>• Short acting bronchodilators</td>
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<tr>
<td>• 1 or more long acting bronchodilators (when needed)</td>
<td>• 1 or more long acting bronchodilators</td>
<td>• 1 or more long acting bronchodilators</td>
<td>• 1 or more long acting bronchodilators</td>
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</tr>
<tr>
<td>• Rehabilitation</td>
<td>• Rehabilitation</td>
<td>• Rehabilitation</td>
<td>• Rehabilitation</td>
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<tr>
<td></td>
<td></td>
<td>• Glucocorticoids for repeated exacerbations</td>
<td>• Glucocorticoids for repeated exacerbations</td>
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<td></td>
<td></td>
<td></td>
<td>• Long term O₂ for chronic respiratory fail.</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Consider surgery</td>
<td></td>
</tr>
</tbody>
</table>

*Tobacco smoke, occupational dust and chemicals, indoor air pollutants (coal, animal dander, etc), outdoor pollutants
Other Therapies:
- **Alpha-1 antitrypsin augmentation therapy (Prolastin®, Aralast®, Zemaira®):** Very expensive; not recommended for COPD not associated with alpha-1 antitrypsin deficiency
- **Antibiotics (tetracyclines, macrolides, trimethoprim-sulfamethoxazole):** No effect has been seen in preventing exacerbations when used prophylactically.
- **Mucolytic agents (ambroxol, erdosteine, carbostein, iodinated glycerol):** Very small benefit, regular use not recommended
- **Antioxidants (N-acetylcysteine):** Limited evidence supporting use, not recommended
- **Immunoregulators:** Have been shown to decrease severity and frequency of exacerbations. More evidence needed before regular use can be recommended
- **Antitussives (dextromethorphan, hydrocodone, codeine, ephedrine):** Cough may play a protective role; regular use of antitussives is not recommended
- **Vasodilators (Nitric oxide):** can worsen COPD and is contraindicated
- **Morphine:** May be useful for dyspnea in severe disease
- **Nedocromil/Infliximab/herbal remedies:** Limited evidence, therefore not recommended


**SMOKING CESSATION: The 5 A’s**

Cigarette smoking is the most common risk factor for COPD worldwide. The most effective treatment for COPD is to quit smoking. Quitting can prevent or delay the development of airway limitation or reduce the progression of COPD. Even brief (3 minute) encounters in which counseling is provided have resulted in smoking cessation rates of 5-10%. One strategy recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines is to use the 5 A’s at each encounter with a COPD current smoker:

1. **Ask:** Identify patients at each encounter that are tobacco users.
2. **Advise:** Urge patients in a clear, strong, and personalized manner that they should quit and the importance of quitting for their health.
3. **Assess:** Evaluate the patient’s willingness to quit.
4. **Assist:** Help the patient formulate a plan to quit. Provide practical counseling and suggestions for group and/or psychosocial support. Recommend use of pharmacotherapy when appropriate. Provide supplementary materials.
5. **Arrange:** Schedule a follow-up with the patient either in person or on the telephone.


**RECENT DEVELOPMENTS**

**Azithromycin for acute COPD exacerbations** .... Acute COPD exacerbations result in frequent E.R. visits, hospitalizations and days lost from work thus taking a toll on a patient’s quality of life as well as affecting healthcare costs. Patients who have frequent COPD exacerbations have increased airway inflammation in the stable state and have a faster decline in lung function. Macrolides are thought to be helpful in reducing acute COPD exacerbations due to their anti-inflammatory activity. The anti-inflammatory activity of macrolides is not related to their antimicrobial effect and so macrolides can be used at low concentrations (below MIC) and still produce anti-inflammatory effects. The advantage of using macrolides in low doses is fewer ADRs, but the disadvantage is that we would be
encouraging the development of resistance. A recent trial involving 1142 COPD patients showed that the addition of azithromycin 250 mg daily for 1 year to COPD treatment led to decreased exacerbations (median time to first exacerbation was 266 days in the macrolide arm vs. 174 days in the placebo arm) and an improvement in quality of life of patients with COPD. However, there was an increase in the incidence of colonization with macrolide resistant organisms as well as a slight increase in hearing loss in the azithromycin group. The findings of this study show that azithromycin can be used to decrease exacerbations and possibly help to slow down the progression of COPD. Practitioners should weigh the benefits vs. the risks when initiating this drug in their patients as there has been hearing loss and macrolide resistance associated with chronic use of azithromycin.


**Combivent® Respimat® (ipratropium bromide and albuterol)...** approved by the FDA as a propellant-free inhaler with the same components of the previously approved Combivent® metered dose inhaler (MDI) that contained chlorofluorocarbons (CFCs). Ipratropium/albuterol delivered through a Respimat® inhaler meets the requirements of the Montreal Protocol, an international treaty that requires discontinued use of CFCs as propellants. In a 12-week, randomized, double-blinded, placebo and active control trial involving 1209 COPD patients, ipratropium/albuterol Respimat® inhaler was non-inferior to ipratropium/albuterol MDI inhaler in regards to the studies primary efficacy endpoint, FEV1 at hours 0-6 post dose. The study also showed that Ipratropium/albuterol Respimat® inhaler had the slightly lower rates of all adverse events versus ipratropium/albuterol MDI (45.7% versus 51.7%). Combivent Respimat® will be available beginning in mid-2012, allowing for Combivent® MDI to be phased out by December 31, 2013.


**OTHER IMPORTANT DATES IN NOVEMBER**
- Lung Cancer Awareness Month
- World COPD Day: November 16th
- Great American Smoke Out: November 17th
- Thanksgiving: November 24th

The last “dose” …

“To cease smoking is the easiest thing I ever did. I ought to know because I've done it a thousand times.”

~Mark Twain, attributed [Samuel Langhorne Clemens (1835-1910)]