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Guest Editors: Margaret Williamson, Shaun Osborn, and Pratyusha Patel, Pharm.D. Candidates, 2012; Wesley Lindsey, Pharm.D.

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 α_1-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.[2] Exacerbations may progress to acute respiratory failure requiring mechanical ventilatory support.[4] Infections, mostly viral and some bacterial, are the leading cause of COPD exacerbations.

1. Whetsel TR, Verkleeren ND. Chronic Obstructive Pulmonary Disease. In: Chisholm-Burns MA, Schwinghammer TL, Wells BG, Malone PM, Kolesar JM, Dipiro JT, eds. Pharmacotherapy. 2nd ed. New York: McGraw-Hill Medical; c2010. Pg. 443-484
2. Williams DM, Bourdet SV. In: Chronic Obstructive Pulmonary Disease. In: Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A Pathophysiologic Approach. 7th ed. New York: McGraw-Hill Medical; c2008. Pg. 495-517
3. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2010 update. (http://www.goldcopd.com.)
4. Yusen RD, Mayse ML, Chakinala M, Russell T, Rosenbluth DB. Pulmonary Disease. In: Cooper DH, Krainik AJ, Lubner SJ, Reno HE. Washington Manual of Medical Therapeutics. 32nd ed. Lippincott Williams & Wilkins; c2007. Pg. 265-275

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 FEV_1/FVC of <70% confirms an airflow limitation that is not completely reversible. The FEV_1 indicates which stage of COPD into which the patient is categorized.

Table 1

SPIROMETRIC CLASSIFICATION OF COPD SEVERITY BASED ON POST-BRONCHODILATOR FEV_1[1]	
Stage I: Mild	FEV1/FVC < 70% FEV1 ≥ 80% predicted
Stage II: Moderate	FEV1/FVC < 70% 50% ≤ FEV1 < 80% predicted
Stage III: Severe	FEV1/FVC < 70% 30% ≤ FEV1 < 50% predicted
Stage IV: Very Severe	FEV1/FVC < 70% FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure

MANAGEMENT OF STABLE COPD[1]

Table 2

DISEASE SEVERITY			
Mild	**Moderate**	**Severe**	**Very Severe**
• Reduction of active risk factors* • Influenza vaccine yearly • Short acting bronchodilators	• Reduction of active risk factors* • Influenza vaccine yearly • Short acting bronchodilators Plus • 1 or more long acting bronchodilators (when needed) • Rehabilitation	• Reduction of active risk factors* • Influenza vaccine yearly • Short acting bronchodilators Plus • 1 or more long acting bronchodilators • Rehabilitation Plus • Glucocorticoids for repeated exacerbations	• Reduction of active risk factors* • Influenza vaccine yearly • Short acting bronchodilators Plus • 1 or more long acting bronchodilators • Rehabilitation Plus Glucocorticoids for repeated exacerbations Plus • Long term O_2 for chronic respiratory fail. • Consider surgery

*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

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2010 update. (http://www.goldcopd.com.)

SMOKING CESSATION: The 5 A's

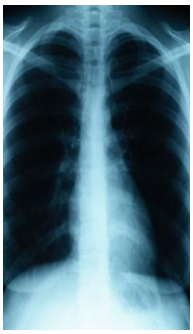
Cigarette smoking is the most common risk factor for COPD worldwide.[1] The most effective treatment for COPD is to quit smoking. Quitting can prevent or delay the development of airway limitation or reduce the progression of COPD. Even brief (3 minute) encounters in which counseling is provided have resulted in smoking cessation rates of 5-10%.[1] 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]

1. **A**sk: Identify patients at each encounter that are tobacco users.
2. **A**dvise: Urge patients in a clear, strong, and personalized manner that they should quit and the importance of quitting for their health.
3. **A**ssess: Evaluate the patient's willingness to quit.
4. **A**ssist: 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. **A**rrange: Schedule a follow-up with the patient either in person or on the telephone.

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2010 update. (http://www.goldcopd.com.)

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.[1] 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.

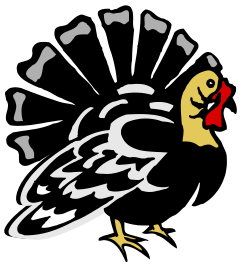
1. Albert R, Connett J, Bailey W, Casaburi R, Cooper A et al. Azithromycin for prevention of exacerbations of COPD. N Engl J Med, 2011;365(8):689-698

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 chlorofluorcarbons (CFCs).[1] 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.[2] 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, FEV_1 at hours 0-6 post dose.[3] 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%).[3] Combivent Respimat® will be available beginning in mid-2012, allowing for Combivent® MDI to be phased out by December 31, 2013.[2]

1. FDA Approves Combivent Respimat. In: Drug Facts and Comparisons (Facts and Comparisons eAnswers) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health [updated 2011, cited 2011 Oct 18]. [about 1 p.]. Available from http://online.factsandcomparisons.com/News/NewsArticle.aspx?id=1009362
2. Zuwallack R, De Salvo MC, Kaelin T, Bateman ED, Park CS, Abrahams R, Fakih F, Sachs P, Pudi K, Zhao Y, Wood CC; Combivent Respimat Inhaler Study Group. Efficacy and safety of ipratropium bromide/albuterol delivered via Respimat inhaler versus MDI. Respir Med. 2010 Aug;104(8):1179-88.
3. Boehringer Ingelheim's Combivent Respimat Inhalation Spray OKed in USA to replace aerosol. The Pharma Letter 2011 Oct 9 [cited 2011 Oct 17]; [about 1 screens]. Available from: http://www.thepharmaletter.com/file/107902/boehringer-ingelheims-combivent-respimat-inhalation-spray-oked-in-usa-to-replace-aerosol.html .

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)]

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