

COPD: The Not So Good, the Bad, and the Ugly!

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In the United States, it is estimated that 12.7 million adults, aged 18 and above, have chronic obstructive pulmonary disease (COPD).^{1,2} Moreover, another 24 million US adults are reported to have evidence of impaired lung function,^{1,3} perhaps representing undiagnosed COPD. COPD claimed the lives of almost 135,000 Americans in 2010, and is one of the top 5 leading causes of death in the United States.^{1,4} In the last decade, more females have consistently died from COPD than males in the United States.^{1,4} An estimated 715,000 hospital discharges were reported in 2010 for COPD.^{1,5} In that same year, the cost to the nation for COPD was projected to be approximately \$50 billion.¹ These statistics are staggering. Anyone seeing adult patients with lower respiratory complaints will be faced with how to diagnose and manage COPD as it should always be in the differential diagnosis. This issue provides valuable information on the appropriate use of spirometry, complete lung function tests, genetic testing, and chest CT scans for diagnosing and evaluating COPD. In addition, therapeutic interventions are reviewed including the role of pulmonary rehabilitation and smoking cessation strategies, including the potential utility of e-cigarettes.

Soler and Ramsdell discuss the key clinical, genetic, and mechanistic features that distinguish between asthma and COPD.⁶ Asthma is predominately an airway disease without lung parenchyma involvement. Patients with asthma have airway hyperreactivity and reversibility, and the inflammation often involves eosinophils and TH2 cells. These patients usually respond to inhaled corticosteroids and biologics targeting TH2 inflammation and eosinophilia. A neutrophil predominant picture is seen in some asthmatics, and this group of patients are less or nonresponsive to corticosteroid treatment. These characteristics have been noted in certain asthma phenotypes such as >20% of asthmatics who smoke combustible cigarettes and the majority of patients with COPD. These patients might be best treated with antineutrophil strategies, and have not shown good responses to the 3 anti-IL-5 monoclonal antibody strategies in development (mepolizumab, reslizumab, and benralizumab).⁷⁻⁹

COPD includes chronic bronchitis and emphysema. The former typically has excess mucus accumulation and relatively limited parenchymal destruction, whereas the latter has significant parenchymal damage that leads to air trapping and airway

obstruction. Although seemingly straightforward to distinguish from asthma, COPD and asthma often have overlapping symptoms. Indeed, the asthma COPD overlap syndrome (ACOS) is defined as airflow limitation with features typical of both disorders.¹⁰ Soler and Ramsdell point out that patients with ACOS tend to experience frequent exacerbations, poor quality of life, increased use of health care resources, a more rapid decline in lung function, and high mortality. These patients tend to have eosinophilic inflammation and increased responsiveness to inhaled corticosteroids. Because of the heterogeneity of each of these 3 subgroups of airway diseases, COPD, asthma, and ACOS, Soler and Ramsdell discuss the importance of defining disease-specific endotypes to provide a more rational therapeutic approach. As specialists treating lower airway diseases, it behooves us to be able to distinguish and manage all 3 of these conditions appropriately.

Bellinger and Peters¹¹ discuss the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for managing COPD.¹² Their review discusses the categories of pharmacologic therapy used including anticholinergics, methylxanthines, β -agonists, corticosteroids, phosphodiesterase inhibitors, and combination therapy. As with asthma guidelines, GOLD guidelines categorize patients based on severity and treatment is recommended accordingly. In contrast to asthma, bronchodilator therapies alone or in combination often represent the best therapeutic option for many patients with COPD, with the role of inhaled corticosteroids often reserved for patients with frequent exacerbations. Bellinger and Peters also review nonpharmacologic therapies including lung volume reduction and lung transplant. They stress the need for managing comorbidities including heart disease, diabetes, osteoporosis, and depression, frequently found in patients with COPD.

Sze et al provide excellent examples of the utility of CT scans to differentiate between asthma and COPD.¹³ They provide images of patients with emphysema (hypodensities and bullae) and chronic bronchitis (thickened airway walls and mucus) to help distinguish between these disorders and asthma. Bronchiectasis is often in the differential diagnosis of this group of disorders, and the CT features are reviewed as well.

Craig reviews when to suspect and test for alpha-1 antitrypsin deficiency (AATD), a disorder characterized by decreased levels or function of the proteinase inhibitor alpha-1 antitrypsin.¹⁴ Unfortunately, of more than 100,000 Americans likely to have this disorder, <10% are diagnosed. He points out that the respiratory symptoms in AATD overlap with those of asthma and COPD probably accounting for the lack of appropriate diagnosis. Unlike COPD, these patients often present earlier with nonreversible airway obstruction and panlobular emphysema. Individuals who should be tested for AATD include patients with COPD, asthmatics with incomplete reversible airway obstruction, asymptomatic adults with evidence of lung disease and smoking or occupational exposure, adults with necrotizing panniculitis, and newborns, children, or adults with unexplained

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liver disease. Craig urges us to have a high index of suspicion, test appropriately, and when diagnosed, manage patients with replacement therapy and genetic counseling.

One of the most important contributors to the pathogenesis of COPD is the use of combustible tobacco products. Smokers are approximately 12 times more likely to die from COPD than nonsmokers, regardless of gender.^{1,15} Almost 18% of US adults aged 18 years or older were reported to be current cigarette smokers in 2013.¹⁶ According to the US Department of Health and Human Services, each day more than 3200 people younger than 18 years of age smoke their first cigarette.¹² Surprisingly, the percentage of people with asthma who smoke is higher, 21%, than in the general population,¹⁷ which makes the distinction between asthma and COPD more relevant to best guide therapy. The most recent information on smoking cessation strategies is reviewed in this issue by Baldassarri et al.¹⁸ They provide a comprehensive review on tobacco dependence interventions and the benefits of tobacco cessation including a decreased rate of normal age-related decline in FEV1, lower risk of hospital admission, and improved survival. The utility of both long-acting and short-acting drugs, including appropriate dosing, treatment duration, side effects, and contraindications, are reviewed. Clinicians should be aware of the need to counsel patients about smoking cessation that starts with an accurate assessment of nicotine dependence and tobacco withdrawal symptoms from previous cessation attempts so as to best use available pharmacologic therapy.

Unfortunately, more adults and children are aware of and beginning to use e-cigarettes. In this issue, Cooke et al¹⁹ review the potential downsides of using e-cigarettes and discuss their putative role in smoking cessation. They review the possible “good” features of e-cigarettes versus combustible cigarettes including fewer toxins in the vapors and fewer effects on airway functions. Their utility in smoking cessation remains to be definitively determined. There is, however, a lack of regulation of e-cigarettes and -liquids so that individuals might not get what they thought they purchased. For example, analysis of some e-cigarette liquids labeled as having zero nicotine had nicotine. Furthermore, although present in lower concentrations, the vapors do contain carcinogens and appear to have secondhand effects. The uptake and use of e-cigarettes have been increasing dramatically, we do not know their true health effects, and there is a need for research and regulation.

Finally, for those patients with severe asthma or COPD, Nici and ZuWallack discuss the benefits of pulmonary rehabilitation.²⁰ They review the patient-centered approach for those individuals who remain symptomatic or have decreased exercise tolerance, functional status, or health status despite standard medical therapy. Although pulmonary rehabilitation has not been shown to increase or improve lung functions in patients with COPD, there are significant improvements in dyspnea, exercise tolerance, and health status. These same benefits are often achieved in patients with severe asthma. Clinicians need to recognize the value of pulmonary rehabilitation in helping their patients achieve physical and social goals.

In summary, this issue provides an opportunity for clinicians managing lower airway diseases to have a better understanding of the important distinguishing features between asthma, COPD, and the overlap syndrome. The excellent reviews in this issue give

guidance on the diagnosis and management of patients with COPD including pharmacologic, interventional, smoking cessation, and pulmonary rehabilitation strategies. Based on the number of patients with COPD in the United States, all of us should be aware of the latest information on how best to provide optimal care for our patients with COPD.

REFERENCES

1. Chronic Obstructive Pulmonary Disease (COPD) Fact Sheet. <http://www.lung.org/lung-disease/copd/resources/facts-figures/COPD-Fact-Sheet>. Accessed May 21, 2015.
2. Centers for Disease Control and Prevention. National Center for Health Statistics. National Health Interview Survey Raw Data, 2011. Analysis performed by the American Lung Association Research and Health Education Division using SPSS and SUDAAN software.
3. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971–2000. *MMWR Surveill Summ* 2002;51:1–16.
4. Centers for Disease Control and Prevention; National Center for Health Statistics. Deaths: Final Data for 2010. *National Vital Statistics Report* 2013; 61(4):1–117.
5. Centers for Disease Control and Prevention. National Center for Health Statistics. National Hospital Discharge Survey Raw Data, 2010. Analysis performed by the American Lung Association Research and Health Education Division using SPSS software.
6. Soler X, Ramsdell JW. Are asthma and COPD a continuum of the same disease? *J Allergy Clin Immunol Pract* 2015;3:489–95.
7. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, et al, MENSA Investigators. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014;371:1198–207.
8. Castro M, Wenzel SE, Bleecker ER, Pizzichini E, Kuna P, Busse WW, et al. Benralizumab, an anti-interleukin 5 receptor α monoclonal antibody, versus placebo for uncontrolled eosinophilic asthma: a phase 2b randomised dose-ranging study. *Lancet Respir Med* 2014;2:879–90.
9. Castro M, Zangrilli J, Wechsler ME, Bateman ED, Brusselle GG, Bardin P, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med* 2015;3(5):355–66.
10. Global Initiative for Asthma. Diagnosis of asthma, COPD, and asthma-COPD overlap syndrome (ACOS); 2015. Available from: <http://www.ginasthma.org>. Accessed April 21, 2015.
11. Bellinger CR, Peters SP. Outpatient COPD management: going for the GOLD. *J Allergy Clin Immunol Pract* 2015;3:471–8.
12. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease—Updated 2015. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2015.pdf. Accessed April 15, 2015.
13. Sze TFC, Ditzler MG, Walser EM, Calhoun WJ. The role of computed tomography in chronic obstructive pulmonary diseases. *J Allergy Clin Immunol Pract* 2015;594–6.
14. Craig T. Suspecting and testing for alpha-1 antitrypsin deficiency—an allergist's perspective. *J Allergy Clin Immunol Pract* 2015;3:506–11.
15. US Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. US Department of Health and Human Services. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014. <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>. Accessed April 19, 2015.
16. Centers for Disease Control and Prevention. Current cigarette smoking among adults—United States, 2005–2013. *MMWR Morb Mortal Wkly Rep* 2014;63:1108–12.
17. Asthma Stats: Percentage of people with asthma who smoke. http://www.cdc.gov/asthma/asthma_stats/asthma_stats_factsheet.pdf. Accessed April 19, 2015.
18. Baldassarri SR, Toll BA, Leone FT. A comprehensive approach to tobacco dependence interventions. *J Allergy Clin Immunol Pract* 2015;481–8.
19. Cooke A, Ferguson J, Bulkhi A, Casale TB. The electronic cigarette: the good, the bad, and the ugly. *J Allergy Clin Immunol Pract* 2015;3:498–505.
20. Nici L, ZuWallack R. Pulmonary rehabilitation for COPD and severe asthma. *J Allergy Clin Immunol Pract* 2015;3:512–8.

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