Of Dung and Dynein Arms: Understanding COPD in Nonsmokers

A frequent conundrum to a pulmonologist is understanding and therefore properly diagnosing COPD in a nonsmoker or minimal smoker (after confirming that this is indeed the case). The questions then become:

- What exposures other than cigarette smoking may cause COPD?
- What other pathologic processes may result in COPD, in the absence of inhaled noxious agents?

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The article by Köksal et al in this issue of RESPIRATORY CARE provides useful information on the first question.[1] The authors, from Turkish federal referral hospitals for respiratory disorders, report on 55 female patients selected for respiratory symptoms and biomass exposure. All were nonsmokers, although 24 (44%) were passively exposed. Cough was noted by 80%, dyspnea by 75%, sputum by 55% and wheezing by 35%. The authors reported that FEV_1, FVC, and FEV_1/FVC varied inversely with biomass exposure: FEV_1 was 70% of predicted in the least exposed, 55% in the intermediate, and 46% in the most exposed. Dung exposure was associated with a lower FEV_1/FVC than other forms of biomass (odds ratio 3.5). Their findings confirm that use of biomass fuels for cooking and heating leads to symptoms and pulmonary function impairments typical of COPD. Many of these women had emigrated from their rural villages to cities but continued their use of biomass fuel. The authors cite references for the great import of biomass fuel in causing COPD around the world. It is estimated to contribute to the annual deaths of 2 million women and children, and to account for nearly 35% of COPD in less developed countries.[2–4]

Certain questions need be raised about this paper. The absence of a control group unexposed to biomass fuel is difficult to understand at referral centers for respiratory disorders. The predicted norm set is inapplicable to these ethnically distinct women. This does not vitiate the significant differences between exposure groups, but is critical for understanding the reported seemingly low absolute values of lung function: FEV_1 1.26 L and FVC 1.52 L in the least exposed group.

This editorial will now address issues beyond the report of Köksal and co-workers. They have contributed to answering the first question: what exposures other than cigarette smoking may cause COPD? In addition to COPD, there is a spectrum of smoking-related interstitial lung diseases that originate in the small airways. These range in severity from respiratory bronchiolitis interstitial lung disease to desquamative interstitial pneumonia to pulmonary Langerhans cell histiocytosis (previously named histiocytosis-X or eosinophilic granuloma).[5] The cystic cavities in PLHC result from the destruction of bronchiolar walls by the Langerhans cell granuloma. Smoking predominates in patients with the newly described syndrome of combined pulmonary fibrosis and emphysema,[6,7] which is characterized by near normal or normal spirometry and lung volumes but severely decreased diffusing capacity. In this syndrome, airway obstruction is evident on CT imaging but not on pulmonary function testing.

Those concerned with obstructive airways disorders may consider other exposures to tobacco smoke (from secondhand smoke and from pipes or cigars, especially if inhaled), to tobacco that is not smoked but inhaled into the upper respiratory tract (snuff), and to other plant products that are not only inhaled but retained at full inspiration (marijuana). The role of a wide variety of inhaled sensitizing and irritating agents in causing occupational asthma, reactive airways syndrome, bronchitis, and bronchiolitis should be included here as well. These overlapping disorders may become persistent or permanent and indistinguishable from COPD of typical origin. Bronchiolitis (constrictive and obliterative) following massive fires in a military setting[8,9] and the World Trade Center plume are timely examples. The likely role of bronchiolitis in causing World Trade Center obstructive lung disease, with its characteristic low FVC, has been reviewed.[10]

It has been recognized for many years that certain interstitial lung diseases caused by inhalation of particles (eg, asbestosis) begin in the small airways and show characteristic changes on histologic examination and pulmonary function testing.[11,12] The latter disappears with progressive interstitial fibrosis, resulting in a typical restrictive impairment.[13]

The second question, what other pathologic processes may result in COPD in the absence of inhaled toxins, is

one of great interest to those who practice and teach pulmonary medicine. How do we explain and then diagnose these familiar symptoms, physical signs, and spirometric abnormalities in a 50-year-old nonsmoking man or 70-year-old nonsmoking woman? Unrecognized asthma is certainly a contending diagnosis. Asthma transiting or "remodeling" into COPD has a vast literature, of which only a few references are cited.[14,15] This phenotype is often neutrophilic rather than eosinophilic, and poorly responsive to corticosteroids. Many findings that we employ to confirm the diagnosis of asthma are likely to be negative (eg, immunoglobulin E level, radioallergosorbent test, exhaled nitric oxide, acute bronchodilator response).

Other pathologic processes that result in chronic airways obstruction include primary ciliary dyskinesia (in which the dynein arms are dysfunctional) and certain parenchymal lung diseases, including late stage sarcoidosis,[16] diffuse bronchiectasis/cystic fibrosis, and complicated pneumoconiosis (progressive massive fibrosis due to silica or coal dust). A diverse consideration is bronchiolitis not caused by inhalational toxins (panbronchiolitis in Japanese and Koreans),[17,18] bronchiolitis following lung and bone marrow transplantation,[19] medication, and hepatitis C,[20] and associated with human T-lymphotrophic virus-1 (HTLV-1) infection,[21,22] Sjögren syndrome and connective tissue disease,[23,24] adult T cell leukemia/lymphoma,[25,26] and inflammatory bowel disease.[27] Additionally, I have been impressed in my many years of experience by severe obstructive impairment in nonsmoking patients with healed tuberculosis and architecturally distorted lungs. Like stage IV sarcoidosis, this is another example of obstructive impairment due to longstanding granulomatous inflammation.

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