



## Editorial

Chronic Obstructive Pulmonary Disease in Non-Smokers<sup>☆</sup>

## Enfermedad pulmonar obstructiva crónica de origen no tabáquico

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Multiple epidemiological studies have been published in the last 10 years highlighting the significant prevalence of chronic obstructive pulmonary disease (COPD) among never smokers. Figures tend to be higher in developing countries (35%–40%) than in developed countries (25%).<sup>1</sup> Some of the possible etiological factors include: biomass inhalation, asthma and small airways disease, tuberculosis (TB) sequelae, and occupational diseases.<sup>2</sup> Great importance has recently been attributed to the effects of changes in pulmonary development in the early years of life on the natural history of COPD.<sup>3</sup> These factors can produce a spirometric pattern of chronic airflow obstruction; however, if we agree that a diagnosis of COPD is dependent on a history of inhalation of toxic gases, only COPD caused by biomass inhalation should be included in this definition. Nevertheless, this notion is still poorly defined, and these factors may interact with tobacco smoke or the inhalation of biomass smoke.

**Inhalation of Biomass Smoke**

Exposure to biomass smoke from the combustion of animal waste or biological materials affects a large proportion of the world's population (more than tobacco smoke), even in developed countries such as Australia, the USA or Spain,<sup>1,4,5</sup> and is associated with a greater risk (2.3-fold) of COPD.<sup>1</sup> It occurs more frequently in women cooking over wood fires, and is generally characterized by more bronchial involvement and less emphysema.<sup>6</sup> It manifests in the form of COPD with mild obstruction and less decline in lung function (FEV1) over time compared to COPD caused by smoking.<sup>5</sup> Although COPD caused by smoking is associated with higher mortality due to cancer, no differences are observed after mortality figures are adjusted for airway obstruction. These survival data have been described in developing countries and recently corroborated in Spain.<sup>6</sup>

**Changes in Lung Development**

In the last 10 years, data from the Tucson cohort have shown that diminished lung function in the first 6 years of life may possibly affect airway obstruction in adolescence and young adulthood.<sup>7</sup> Factors that have been involved in early airway development changes include: a history of asthma and atopy, respiratory infection in infancy (syncytial respiratory virus or rhinovirus in the first 2–3 years of life), bronchial hyperreactivity, symptoms and wheezing, low birth weight, smoking in the mother, prematurity, and low CC16 concentrations in blood.<sup>8</sup>

**Other Factors**

Other factors that could come under the heading of COPD may contribute to chronic airflow obstruction, provided there has been exposure to tobacco smoke or other toxic gases:

- *Bronchial asthma.* Bronchial asthma, and, to a greater extent, severe asthma in infancy, and bronchial asthma in both parents have been identified as risk factors for chronic airflow obstruction.<sup>1</sup> In a cohort of 3099 adults in Tucson who were followed up for 20 years, it was observed that patients with symptomatic asthma were 10 times more likely to develop symptoms of chronic bronchitis and 17 times more likely to be diagnosed with emphysema than patients without asthma, even after adjusting for confounding factors, such as smoking. Asthma was the most important risk factor in the diagnosis of COPD, even more so than tobacco consumption (odds ratio: 12.5 vs 2.9).

The co-existence of asthma, smoking and chronic airway obstruction may lead to what we now know as the asthma-COPD overlap syndrome (ACOS); the pathophysiology of this syndrome may differ from COPD, and its clinical identification is complex, but some proposals have been made, based on clinical and laboratory criteria.<sup>9</sup>

- *Pulmonary tuberculosis.* Recent epidemiological studies suggest that one of the risk factors for COPD in non-smokers is a history of pulmonary TB,<sup>10</sup> which increases the probability of COPD by between 4.5-fold and 23.4-fold, depending on the population under study. Moreover, the risk of developing COPD is more

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closely related with a previous history of pulmonary TB than to exposure to biomass smoke or age.<sup>10</sup>

Growing evidence appears to point to a bidirectional association between these two lung diseases, in which each can act as a stand-alone risk factor. Thus, a better understanding of the interactions between these two diseases is essential if a possibly new COPD phenotype needs to be characterized and new preventive strategies designed.

## Conclusions

COPD must not be confused with chronic airway obstruction. COPD appears alongside chronic airway obstruction, but requires exposure to tobacco or biomass smoke, while chronic airway obstruction can develop in other ways. Defining a disease according to only one spirometric criterion can generate this type of confusion, when it is clear that other diseases can overlap with the effects of smoking. In the future, this type of terminology may have to be abandoned, and all airway obstructive diseases will come under the same umbrella, permitting treatment to be tailored according to inflammatory substrate, irrespective of its origin. Until then, at least in Spain, COPD must be associated with smoking (or biomass in Lugo), and other diseases characterized by chronic airway obstruction must never be classified as COPD.

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