

# Chronic Obstructive Pulmonary Disease (COPD): Not Always Related to Smoking

*Enfermedad pulmonar obstructiva crónica (EPOC): no siempre relacionada con tabaquismo*

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## ABSTRACT

There are a lot of risks unrelated to tobacco that can cause COPD, so the burden of non-smoking COPD is much greater than previously thought. In the Third World countries, there is a significant number of non-tobacco-related risk agents capable of causing COPD.

The pathogenesis of COPD and its relationship with occupational exposure to dust, gases, and fumes is not fully understood. Further experimental and epidemiological research on a larger scale is needed to confirm the relationship between these two variables.

Approximately 15 % of COPD is related to work, and aggravated by smoking. New agents causing COPD continue to be reported and published.

Women exhibit a different clinical manifestation of COPD and, under similar exposures, are more prone to developing the disease compared to men.

Personal protection for workers is of particular importance since it is challenging to assess the nature of dust, smoke, or gases, their ambient concentration, and the duration of the exposure.

**Key words:** COPD; Biomass; Tasks

## RESUMEN

Existen un número importante de riesgos no relacionados al tabaco pasible de provocar la EPOC por lo que la carga de la EPOC no tabáquica es mucho mayor de lo pensado. En los países del 3er. Mundo, hay importantes agentes de peligro no relacionados al tabaco pasibles de provocar la EPOC.

No está aclarada la patogenia de la EPOC y su relación con la exposición laboral a polvos, gases y humos. Son necesarias más investigaciones experimentales y epidemiológicas de mayor magnitud, para confirmar la relación entre estas 2 variables.

Aproximadamente el 15 % de la EPOC relacionada con el trabajo, está agravada por el tabaquismo y continúan publicándose nuevos agentes que causan EPOC.

Las mujeres presentan una manifestación clínica diferente de la EPOC siendo, –ante exposiciones semejantes–, más propensas a desarrollar la enfermedad que los hombres.

La protección personal de los trabajadores es de importancia, ya que es dificultoso valorar la naturaleza del polvo, humo o gases, su concentración ambiente y el tiempo de exposición.

**Palabras clave:** EPOC; Biomasa; Tareas

Chronic Obstructive Pulmonary Disease (COPD) is a condition resulting from a constant limitation of the airflow and gradually progressive respiratory symptoms culminating in the destruction of the lung parenchyma. It is a complex condition with different mechanisms and components that contribute to its physiopathology and clinical presentation. After cerebrovascular and cardiovascular diseases, it constitutes the third leading cause of mortality. In Argentina, the EPOC.AR study conducted by Chazarreta et al between May 2014 and May 2016 estimated that there were approximately 2,300,000 cases of COPD, among which 309 were related to occupational exposure, without specifying the occupation. The study also highlighted a high number of both misdiagnoses and underestimated cases.<sup>1-4</sup> Frequently, in highly industrialized countries, statistics are challenging to compile. In the developing world, which includes Argentina, the task is even more difficult.

## ASSOCIATION BETWEEN COPD AND COVID 19

Most COPD patients are of advanced age and often have frequent comorbidities. So, at present and also during the pandemic, patients diagnosed with COVID 19 experience a worse outcome, including higher mortality rates, elevated hospitalization rates, and consequently, a possible admission to the Intensive Care Unit (ICU).<sup>5,6</sup>

## COPD – PREVALENCE

The estimated global prevalence of COPD is 13.1 %, with disparities ranging from 11.6 % to 13.9 % across different regions of the world. These indicators are crucial in recognizing the importance of COPD as a global public health issue and essential to identify effective prevention and treatment measures. Since the studies by Oswald and Fletcher, certainly the prevalence of COPD is strictly related to smoking, which is acknowledged as the main evolutionary predisposing factor of the disease in 55-75 % of cases.<sup>7-9</sup>

## COSTS RELATED TO HEALTHCARE SYSTEMS

COPD constitutes a significant burden on the healthcare system, but precise costs are difficult to estimate. Herse et al calculated the COPD-related costs in Finland during 1996-2006, and, based on changes in smoking behavior and the projected

population, they estimated costs for 2007-2030 using a mathematical model.

Between 1996-2006, annual costs related to COPD were €100-110 million, with a decrease in direct costs and an increase in indirect costs. The model predicted a 60 % increase (up to €166 million/year by 2030), attributed to healthcare expenses due to the aging of the population, which leads to an increased need for hospitalization. They conclude by reporting that, unless strategies change, there will be a significant rise in direct costs by 2030.<sup>10</sup>

In economic terms, COPD is also a disease of great importance. According to Gibson et al, direct healthcare costs per year for COPD amount to approximately €23.3 billion in the European Union. Exacerbations, which may require hospitalization, as well as comorbidities, contribute significantly to this cost.<sup>11</sup>

## COPD AND BIOMASS

Salvi and Barnes published a review on the evidence of COPD related to biomass fuel, occupational exposure to gases and dust, chronic asthma, respiratory infections in childhood, pulmonary tuberculosis, ambient air pollution, and low socioeconomic status.

The study suggests that there is a significant number of non-tobacco-related risk agents capable of causing COPD. It is estimated that the burden of non-smoking-related COPD is much higher than previously thought: around 3 billion people are exposed to biomass fuel smoke compared to 1 billion smokers. This suggests that exposure to biomass smoke could be the largest universal risk factor for COPD.<sup>12</sup>

The understanding of biomass exposure-induced COPD is still a not well-defined subject of debate. Meneghini et al compared 2 groups: 16 non-smoking COPD patients exposed to biomass (mean time 133 hours/year) and 15 smoking COPD patients (mean 48 packs/year). Patients underwent spirometry, chest CT scan, a 6-minute walk test, and induced sputum.

The results showed that non-smokers with COPD exposed to biomass had functional values analogous to the smoking COPD group but exhibited more hypoxemia and dyspnea, lower blood pressure, and lower oxygen saturation. Smoking COPD patients exhibited more emphysema in the CT scan, thicker bronchial walls, and lympho-

mononuclear cells as well as Interleukins 6 and 8 in sputum.

This phenotype may be associated with a ventilation-t

perfusion mismatch leading to hypoxemia, with less visible damage to the pulmonary parenchyma and the bronchial compartment as evaluated by tomography. The conclusion suggests the need for further studies on this phenotype to understand hypoxemia and its consequences, to assess the prognosis and therapeutics.<sup>13</sup>

Exposure to these pollutants can cause lung inflammation and lead to chronic respiratory symptoms. The study of Chen et al reported that those who cooked 21 times a week had a higher risk of suffering from chronic bronchitis than those who did it 9 times in the same period.<sup>14</sup>

In Thailand, information on biomass household cooking and the effects of smoke is limited. Juntarawijit explored risk factors and respiratory symptoms in subjects who were in charge of cooking. They randomly selected 1,134 households and collected data on their activities for the following 30 days through a questionnaire. Rhinitis, chronic cough, and dyspnea were the most common symptoms associated with the number of hours spent cooking in the kitchen and the number of dishes prepared. Even cooking with clean fuel can quantitatively increase the risk of respiratory difficulties and symptoms.<sup>15</sup>

Finally, Li et al investigated the use of "solid fuels" for cooking and heating (coal, wood) compared to "clean fuels" (gas, electricity) and the risk of developing COPD. They monitored 475,827 adults (30-79 years) without COPD for 9 years. In this prospective cohort study, they reported 9,835 cases of COPD associated with the use of coal and wood, limited to women and smokers.<sup>16</sup>

## COPD AND OCCUPATIONAL EXPOSURE

Regarding COPD, in many countries, especially those in the third world, there is a significant number of non-tobacco-related risk agents capable of causing COPD. Publications from 50 years ago already mentioned the possibility that occupational factors could cause COPD.

Around 2003, the American Thoracic Society assessed the accumulated evidence regarding the role of occupational factors in the pathogenesis of COPD, establishing that approximately 15 % of cases could be attributed to occupational exposure.<sup>17,18</sup>

Subsequently, several publications arrived at similar conclusions associating COPD with workplace exposure. However, a comprehensive national study conducted in the United States from 1994 to 1998 estimated the prevalence of COPD and its relationship with jobs in the industry. Investigating a cohort of 9,823 subjects aged 30-75, adjusted by age, smoking status, pack-years, body mass index, and socioeconomic status, cases of COPD attributed to work were estimated at 19.2 %, rising to 31.1 % in non-smokers.<sup>19- 21</sup>

In their publication, Fishwick et al list a lengthy catalog of occupations that can induce occupational COPD, including: construction workers, individuals exposed to silicon carbide foundries, coke ovens, railway workers, and those in the wood industry using paint or welding.<sup>22</sup>

In the United States, railway workers have been exposed to diesel exhaust gases since diesel locomotives were introduced after World War II. By 1959, 95 % of their locomotives were diesel. Diesel exhaust gases are a mixture of extra-fine particles covered in organic substances and vapors. Limited information exists about whether this exposure can cause or worsen obstructive lung diseases.

Hart et al conducted a study of cases and causes of death in railway workers between 1981-1982, and found 536 cases of COPD and 1,525 controls whose death wasn't related to diesel gases. Adjusted by age, smoking status, and race, locomotive engineers and conductors exposed to diesel gases had a higher risk of mortality from COPD, which increased proportionally to years of work. They conclude by stating that more studies are needed to evaluate whether the risk is apparent with new-generation engines (which emit much less gas).<sup>23</sup>

### 1. COPD and coke

Coke is produced by mixing and heating coal at 1000-1400°C in the absence of oxygen. Its manufacturing is one of the most environmentally polluting industrial processes, as it involves the distillation of tar and light oils during the procedure. In China alone, there are 1,900 coke plants producing 180 million tons and employing 300,000 workers in their furnaces, who are exposed to emissions containing polycyclic aromatic hydrocarbons and volatile organic compounds. Epidemiology has revealed that workers with prolonged exposure have a significantly higher risk of lung cancer, as these emissions have adverse health effects.<sup>24</sup>

Hu et al investigated 712 coke oven workers and 211 controls in China, measuring concentrations of benzene-soluble fraction and quantitatively estimating individual cumulative exposure. They gathered information on smoking and respiratory symptoms, and performed a spirometry.

The authors found that benzene-soluble fraction levels exceeded legal limits and that coke workers had a higher risk of experiencing cough, chronic expectoration, and functional impairment. In smokers, the risk of COPD was 58 times higher than in non-smokers not exposed to coke.<sup>25</sup>

## **2. COPD related to livestock and agricultural activities**

In agriculture and livestock farming, there is a risk of respiratory morbidity and mortality. In a 2007 publication, Lamprecht et al reported studies conducted on 1,258 adults engaged in agricultural and livestock activities. They included a spirometry and a questionnaire on work activities, smoking habits, and previous lung conditions. 30.2 % of farmers suffered from airway obstruction. In this population, the risk of irreversible obstruction attributable to rural tasks was 7.7 %, thus agriculture was considered a risk factor.<sup>26</sup>

In a study involving 4,735 Norwegian farmers, Eduard et al measured exposure to dust, spores, endotoxins, bacteria, mites,  $\beta$ -D glucans, fungal antigens, organic and inorganic dust, silica, ammonia, and hydrogen sulfide. They also evaluated lung function and symptoms.

Exposure to most agents predicted respiratory morbidity, with significant associations found for ammonia, hydrogen sulfide, and inorganic dust.

Livestock farmers were more likely to have chronic bronchitis. Farmers with atopy had a significantly lower FEV1 (forced expiratory volume in one second). In the latter group, the effects of agriculture and specific exposure were substantially higher, and they were more susceptible to developing COPD.<sup>26</sup>

## **3. COPD and automotive work**

In automobiles, combustion gases constitute a substantial source of pollution and a health hazard. Traffic police are exposed to these gases, and the pulmonary involvement can be asymptomatic. Naik et al conducted a spirometry study on 136 traffic police officers who worked for more than 6 months in the Kashmir Valley (India), as well as

140 unexposed controls of the same age and gender. Among the 136 traffic police officers, 11.2 % had abnormal lung function tests compared to 3.6 % of the 140 controls. Both the FEV1 and the forced vital capacity (FVC) showed a marked decrease, with 5.8 % exhibiting an obstructive pattern and 5.1 % a restrictive pattern. Exposure to exhaust gases for more than 10 years was notably associated with lung function abnormalities ( $p = 0.038$ ). The authors suggest that, in addition to protective measures, personnel should undergo a periodic evaluation of their lung functions.<sup>27</sup>

In highly industrialized countries, occupational lung diseases, especially asthma, have surpassed pneumoconiosis (caused by inadequate mineral extraction in mining deposits) as the most significant cause of work-related respiratory conditions.<sup>28-30</sup>

## **4. COPD related to excavation and formwork activities**

As a complement to a publication from 2001, Oliver et al conducted an 18-month investigation on 343 workers engaged in tunnel excavation and formwork exposed to respirable silica concentrations exceeding legal limits. This investigation involved questionnaires, clinical-radiographic examinations, and an examination of the relationship between these factors and work activities, including breaking cement walls, spillage from formwork chipping, and tunnel excavation/mining. No cases of silicosis were found in X-rays performed.

The overall prevalence of chronic bronchitis, asthma, dyspnea, and medically diagnosed asthma was 10.7 %, 25 %, 29 %, and 6.6 %, respectively. Breaking cement walls was associated with chronic bronchitis and asthma. Those involved in tunnel construction exposed to silica and cement dust have a higher risk of suffering from respiratory diseases, which varies according to the different work activities. The authors emphasize the importance of exposure and suggest that tunnel construction with formwork could be associated with a higher risk, compared to traditional methods.<sup>31</sup>

## **5. COPD in non-smoking and passive smoking at work**

Passive smoking is associated with a higher risk of coronary heart disease and lung cancer, with an unknown risk-free exposure level. Findings suggest that the prevalence rate of passive smoking exposure among non-smoking workers is 10 %.

Though relatively low, this represents 12.5 million workers exposed 2-3 times per week in the United States.

As of late 2010, 26 states in the U.S. had comprehensive smoke-free workplace laws, except for southern states, possibly contributing to the 11.6 % of non-smoking workers exposed to passive smoking.

A study by Calvert et al investigated the national prevalence of workplace exposure to potential skin hazards, passive smoking, and outdoor work in several industries and occupations, along with the national prevalence of chronic exposure to vapors, gas, dust, and fumes.

Among 17,524 adults who worked during the 12 months prior to the interview, the highest prevalence was recorded in construction, mining, and agriculture. For outdoor work, occupational exposure was more common in agriculture (85 %), construction (73 %), and mining (65 %). Finally, exposure to vapors, gas, dust, and fumes was more common among mining workers (67 %), agriculture (53 %), and construction (51 %).

They identified the industries and occupations with the highest prevalence of potentially hazardous workplace exposure and provided goals for intervention and research activities.<sup>32</sup>

COPD has always been considered a condition predominantly affecting males, due to its strong association with smoking. However, the increase in smoking habits among women has led to COPD becoming increasingly prevalent in this gender.

A study published in the U.S. comparing two cohorts from different periods revealed that the prevalence of COPD in women, confirmed by spirometry, had increased from 50.8 to 58.2 per 1000, while in men, it had decreased from 108.1 to 74.3 per 1000 in the same period. Similar trends were observed in Australia, the Netherlands, and Canada, but in third-world countries, it is still higher in males. Morbidity has remained stable since 1995, but mortality, which was always higher in men, showed similar risks for both genders from 2000 to 2010.

According to Aryal et al, women with COPD may exhibit a different pattern of comorbidities compared to men: a higher tendency for chronic bronchitis, osteoporosis, and depression symptoms but better survival after exacerbation episodes.<sup>33-35</sup>

## 6. COPD and disinfectant agents

Exposure to disinfectants has been associated with pulmonary conditions, including asthma, in healthcare workers. Despite the biological evidence of the association between antiseptics and the risk of COPD, data on this association are scarce. In 2019, Dumas et al investigated and published in a prospective cohort study of nurses their findings on the relationship between exposure to disinfectants and the incidence of COPD. They conducted biennial questionnaires tracking 116,429 nurses, including those without a history of COPD, using data collected from 2009 to 2015.

Over nearly 369,000 person-years of follow-up, 582 nurses reported having COPD. The periodic use of disinfectants solely for cleaning medical instruments and surfaces was associated with the incidence of the condition. Exposure to several disinfectants at high concentrations (hydrogen peroxide, glutaraldehyde, chlorine, alcohol, and quaternary ammonium compounds) showed a significant relationship with the incidence of COPD, and this association did not vary based on smoking habits or prior asthma status.

The results suggest that the regular use of chemical disinfectants among nurses may be a risk factor for developing COPD. If confirmed, strategies should be developed to reduce exposure while remaining compatible with infection control in medical environments.<sup>36</sup>

## 7. Occupational COPD and gender differences

The study by Eng examined gender differences in occupational exposure models to investigate whether the identified discrepancies were due to gender disparities in employment and/or gender-specific objections within tasks.

To do so, they selected 1,431 men and 1,572 women adjusted by age through telephone interviews. *Women:* women had 30 % higher probabilities of engaging in monotonous tasks and high-speed jobs, as well as exposure to disinfectants, textile dust, and hair dyes. *Men:* men had 2-4 times higher possibilities of exposure to irregular schedules, loud noises, night shifts, vibrating tools, gases, and dust.

Even within the same occupation, significant differences existed in occupational exposure patterns. Therefore, gender should be taken into account in the research of occupational health.<sup>37</sup>

In conclusion, it is important to consider the following:

1. There is a constant correlation between COPD and occupational exposure to noxious substances, regardless of the age of the worker and tobacco consumption.
2. The pathogenesis of COPD and its relationship with occupational exposure to dust, gases, and fumes is not fully understood. Further experimental and epidemiological research on a larger scale is needed to confirm the relationship between these two variables.
3. A thorough literature review revealed that approximately 15 % of COPD is related to work, and aggravated by smoking. New agents causing COPD continue to be reported and published.
4. Women exhibit a different clinical manifestation of COPD and, under similar exposures, are more prone to developing the disease compared to men.
5. Personal protection for workers is of particular importance since it is challenging to assess the nature of dust, smoke, or gases, their ambient concentration, and the duration of the exposure.

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