



## Editorial

## Breathing with COPD

## Respirar con EPOC

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### The patient

The patient enters the door of the doctor's office with difficulty, sweating, "dyspnoeic" and "blowing, more than breathing". He or she cannot even say good morning. Actually, he/she cannot say anything in this moment. He/she sits down and after 1-2 minutes starts conversing with their doctor. This is a patient with chronic obstructive pulmonary disease (COPD) in an advanced stage. The patient just had an episode of dyspnoea on exertion that we could compare with chest pain in patients with coronary insufficiency, or leg pain in intermittent claudication. The three processes share being associated with smoking, being set off by exertion and stopping with rest without needing medication.

### The editorial

"Dyspnoea" is the second word (the first is "pain") that generates more searches in PubMed and Google Scholar. In the *Archivos de Bronconeumología* searcher, there are 440 references of articles that have dealt with this issue in some way, including various special articles.<sup>1,2</sup> In this occasion, the objective of this editorial is to briefly review the most prevalent ideas about the mechanisms involved in the genesis of dyspnoea in patients with COPD, as well as to consider an integrative pathology-physiology model that makes it easier to understand the problem and its therapeutic focus for daily practice.

### The symptom

The most accepted definition of dyspnoea is the "uncomfortable sensation when breathing". In patients with COPD, the intensity of their condition closely determines their quality of life and the activities that they can carry out in their daily life. In addition to this, it precipitates the appearance of exacerbations and finally, it is an independent determinant of mortality.<sup>3</sup> It is clear that the presence and intensity of the dyspnoea and the limitation of exercise in COPD

have a multifactor origin, and there are excellent reviews for any interested readers.<sup>4,5</sup>

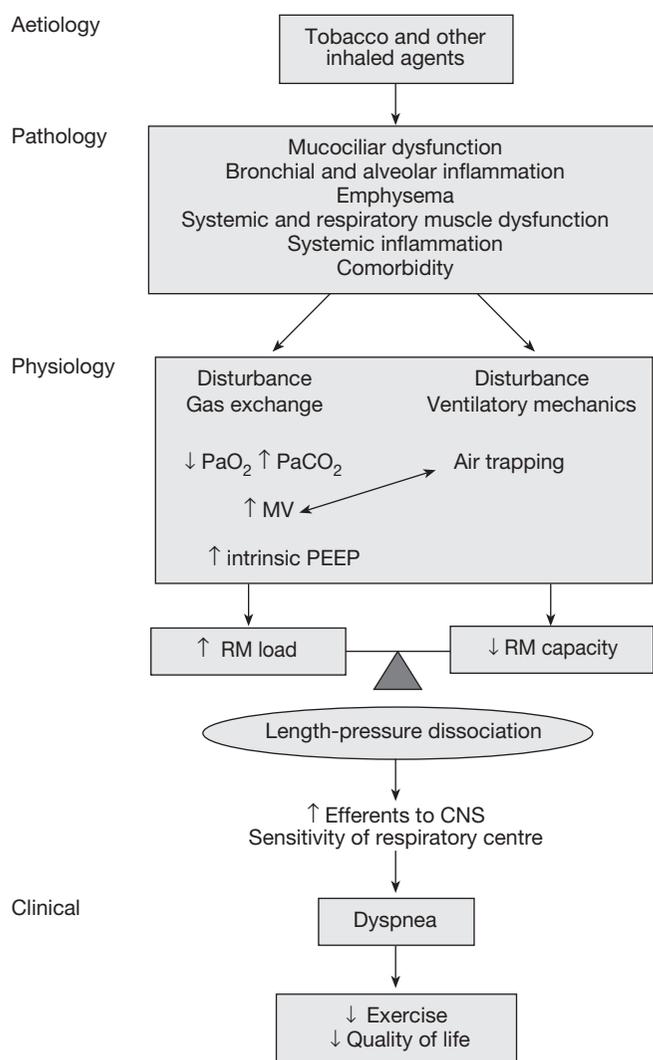
### Aetiology and pathology

The inhalation of harmful environmental agents, and especially of tobacco smoke, stimulates the process of damage to the lungs and airways, mucociliary dysfunction and local and systemic inflammation. In "predisposed" people, a constant state of inflammation is maintained and most likely, autoimmune phenomena are set off that perpetuate and accelerate the morphological alterations of the entire respiratory apparatus.<sup>6,7</sup> The disease, which may initially be constrained to the lungs, extends to other areas and ends up causing multi-organic damage. In this respect, some time ago, Killian et al<sup>8</sup> demonstrated that the tolerance to exercise in patients with COPD is not only limited by dyspnoea, but also by leg discomfort. Posterior morphological studies have found molecular and cellular anomalies in skeletal muscles. Specifically, they have demonstrated an excess in the production of substances that are reactive to oxygen and that block the transport of electrons in the mitochondria in respiratory muscles as well as in peripheral muscles.<sup>9,10</sup> Because of this, the aerobic capacity of the skeletal muscles of patients with COPD is reduced and the production of lactic acid is excessive; consequently, ventilation increases and the respiratory effort is greater (fig. 1).

### Physiology

The limitation of air flow defines the COPD. In greater or lesser degree, both the increase in the resistance of the airways (from "obstructive" pathological changes) as well as the loss elastic retraction pressure (from the elastolytic destruction of the parenchyma) are responsible for the obstruction. As a consequence, the process of emptying the lungs during exhaling is slower. If the respiratory frequency increases, like what happens during exercise or exacerbations, the time of the exhaling will be reduced and air will remain "trapped" in the alveolus at the end of the exhaling: dynamic overinflation (DH).<sup>11</sup> As the functional residual capacity increases, the inspiratory capacity decreases, the thoracic cavity is

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**Figure 1.** Physiopathologic model of dyspnoea and limitation in the capacity to exercise in the COPD. RM: respiratory muscles; CO<sub>2</sub>BP: carbon dioxide blood pressure; O<sub>2</sub>BP: oxygen blood pressure; PEEP: positive end-expiratory pressure; CNS: central nervous system; VM: ventilation minute.

deformed (to a barrel chest), the inspiratory muscles alter their geometry and their sarcomeres are shortened. As the tension that a muscle is capable of producing depends on its initial length, the overinflation reduces the capacity to generate muscular strength by shortening the length of the inspiratory muscles when they are relaxed. However, the diaphragm becomes flatter (with a greater radius) and, according to Laplace's law, it is capable of producing less tension. The final result of the process is an increase in the use of the inspiratory muscles and a lower capacity to carry out its functions.

The role of the expiratory muscles in the affected ventilation of the COPD has not been studied very deeply. Far off are the studies carried out by the Jere Mead group that demonstrated the existence of the recruitment of these muscles during exercise in patients with severe COPD.<sup>12</sup> Later it was demonstrated that the excess of activity of the expiratory muscles not only contributed to increasing the air flow, but also in generating dynamic compression in the airways, positive end-expiratory pressure and an additional increase of the DH. Recently, in patients with severe COPD, it has been demonstrated that even when resting, the muscles of the abdominal press are active during exhaling, and that they frequently present a dysfunction that reduces their strength and resistance.<sup>13</sup> Continuing on this line of work, it is described in the current number of *Archivos de*

*Bronconeumologia* how this type of patients shows a reduction of the resistance of the expiratory muscles to exercise. This deficit is associated with a greater development of DH and dyspnoea during exercise and lower quality of life. The patients studied by the authors are a very specific subgroup. Underweight people, those with other associated co-morbidities and those with a positive response to inhalatory bronchodilators have been excluded. In spite of the fact that the results of this study cannot be generalised, the findings are relevant and support the idea to introduce specific programs for strengthening expiratory muscle in the context of respiratory rehabilitation.

The disproportion between the capacity of the muscles to generate movement and the load that is carried by them (simplifying: length-tension disproportion) is transmitted to the central nervous system, which at the same time increases the nervous respiratory impulse towards the thorax. This central discharge can be measured by electromyography of the respiratory muscles and specifically, the diaphragm. The respiratory nerve impulse is greater in patients with COPD than in healthy people, and it is related with a greater intensity of the obstruction and the DH.

### Practice

The process by which the patient perceives a certain degree of dyspnoea when carrying out his/her daily activities is far from being completely understood. In any case, according to the diagram found in figure 1, and at least in patients with COPD, the dyspnoea could be explained by a group of alterations of the respiratory function, that include the obstruction of the air flow, the pulmonary overinflation and the mechanical and biological dysfunction of the muscles. The feeling of difficulty breathing restrains the patient when exercising or requires him/her to finish before he/she would have. The result is a progressive detraining and loss of quality of life.

### The message

The patient described above is common in pneumology consultations and it will become more and more frequent given the previsions for the prevalence of COPD in our society. Articles such as the one published in this number of *Archivos de Bronconeumología* by Mota et al demonstrate that the research on the physiopathological mechanisms of the COPD is actively being carried out and with beneficial results for clinical practice. The information provided by this article and other recent studies should be applied as soon as possible to our patients with severe COPD. Available evidence points to the need to develop specific care units whose priority is to improve health results. The design of each intervention should be necessarily individualised given the amount of different "phenotypes" of COPD, but in any regard, the objective will be the same: make our patients "breath better".

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