



EDITORIAL

The scourge of chronic cough



Cough is a complex reflex aimed at clearing large airways from mucus or other material that may be on the mucosa.¹ It usually has a protective function, but sometimes cough can be excessive and useless, becoming a potentially harmful problem.² Chronic cough (CC) is defined as a pathologically excessive cough lasting more than 8 weeks,² it is a common condition, and the most reliable estimates place its prevalence between 5% and 10% of the adult population.³ Recently, it has been recognized that a substantial proportion of patients with CC have a definite clinical profile characterized by an exaggerated sensitivity to inhaled irritants, which easily trigger coughing, accompanied by a tingling sensation or irritation of the throat.^{2,4} In addition, these patients have common epidemiological features such as an age of presentation between fifty and sixty years, predominantly female and overweight.^{2,4} Provocation studies have shown that they have an objective augmented sensitivity to inhaled irritants.^{5,6} These observations, together with advances in our knowledge about the involvement of P2RX3 purinoreceptors of the airways in the generation of CC, have led to the concept of the “cough hypersensitivity syndrome”,^{4,7} which has two definite clinical expressions i.e. CC with no obvious (unexplained) cause, and excessive cough not remitting after the appropriate treatment of an underlying condition (refractory CC).² Little is known about the natural history of cough hypersensitivity, but the available evidence suggests that patients often suffer from it for many years.⁸ Regarding its possible prevalence, a study in UK primary care (PC) found no causal explanation in 1/3 of the patients with CC,⁹ while in another large study in southern California, unexplained CC accounted for 17% of the patients with CC visiting specialists.¹⁰ In this study 40.6% of patients with CC from different causes were still coughing one year after the index episode, a fact that suggests that in about half the patients, the “etiological” treatment does not control cough (refractory CC).¹⁰

In a recent report from the U.S. Department of Health and Human Services, cough ranked fifth as a cause of PC

physicians consultation,¹¹ in another similar report in Australia, cough accounted for 6.2% of PC visits,¹² in Sweden, cough is the third leading cause of PC visits¹³ and in the UK, a retrospective study of 2,109,430 visits to 350 PC physicians identified 43,453 (2%) visits because of CC.⁹ Interestingly, health costs in those with refractory CC increased significantly regardless of the diagnosis: asthma, gastro-esophageal reflux, COPD or smoking.⁹ In the already mentioned retrospective study, based on an administrative database in Southern California, 9.8% of patients with CC had been admitted to a hospital and 28.5% had visited the emergency room (ER) in the previous 3 years.¹⁰ Strikingly only 57% of these admissions and 46% of the ER visits could be attributed to exacerbations of respiratory diseases.¹⁰ This suggests that in many cases the presence of intense CC intimidates the attending physicians and causes a defensive approach. The study also helps us to understand the itinerary of these patients, 78% of the studied patients with unexplained CC had visited a pneumologist, 14% an otolaryngologist, 11% a gastroenterologist and 7% a urologist; moreover, 25% had visited two, and 3% at least three specialists.¹⁰ Compared to patients with the same underlying conditions, the overall health resources used by patients with refractory and unexplained CC was higher, as it also was in specific items such as visits to specialists, respiratory and non-respiratory medications (including proton pump inhibitors, “antitussives”, psychopharmaceuticals, oral corticosteroids and antibiotics).¹⁰ In a recent Spanish survey comprising 620 PC physicians, 92 pulmonologists, and 62 allergists, pulmonologists answered that they had seen 7 patients with CC the week prior to the survey and allergists and PC physicians 4.^{14,15} While 80% of the PC physicians follow these patients, they had also referred them at least once to a pneumologists (70%), an otorhinolaryngologist (48%), an allergist (37%), a gastroenterologist (2%) and a psychiatrist (2%).¹⁵ These data indicate that in Spain, as in California, patients with CC are often referred to one or more specialists.

Severe CC is a deleterious condition and in around 20% of the cases it produces incapacitating comorbidities such as sleep difficulties, urinary incontinence, syncope, or rib fractures.¹⁶ Reports from focus groups of patients show

Abbreviations: CC, Chronic cough; COPD, Chronic obstructive pulmonary disease; ER, Emergency room; PC, Primary care; UK, United Kingdom.

<https://doi.org/10.1016/j.pulmoe.2023.04.004>

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that many have a sense of frustration, anger, and anxiety. In addition, they complain about the frequent visits to their physicians and the numerous tests to which they are subjected without tangible results.¹⁷ In fact, physicians as well have a poor opinion of the effectiveness of the medicines they prescribe for the management of CC (bronchodilators, inhaled corticosteroids, and antitussives).¹⁴ Moreover, there is little correlation between perceived efficacy and prescription,¹⁴ suggesting that the factors prevailing in the pharmacological management of CC are safety, tolerability, or ease of use, that is, behaviors aimed at not doing any harm, rather than producing benefit. It is important, therefore, to integrate the patient's frustration regarding some of the tests performed and the lack of efficacy of current treatments in the care of CC, particularly in the light of the poor evidence supporting the accuracy of some test and the effectiveness of most treatments² into its management. In an online survey by the European Lung Foundation to explore the unmet needs of 1120 patients with CC in Europe, two issues worried patients the most: the lack of accurate and consistent information related to the causes and the treatment of CC and, in their view, the difficulty in reaching professionals with experience in CC.¹⁶ These results are similar to another study in Korea.¹⁸ It is difficult to determine the typical level of knowledge about CC by health professionals, but in a recent study in Spain while 87.0% of pulmonologists said that they follow CC guidelines, only 40.3% of allergists and 49.0% of primary care physicians answered positively.^{14,15} Available information, therefore, identifies three major unmet clinical needs: (1) accurate disease information, (2) competent care providers and (3) effective treatments.

The importance of CC for those suffering it and the expensive defensive approach it produces, makes it advisable for health care systems to implement specific programs of training, standardization, and coordination between the different providers to save costs in unnecessary tests and treatments (we have already mentioned the increase in ER visits or in the use of antibiotics in patients without signs of infection).¹⁰ Basic tests such as spirometry and bronchodilation test should be readily available in the PC settings and more complex tests used in CC diagnosis must be ordered judiciously since they are expensive and in quite a few instances unhelpful in solving the problem.²

Conflicts of interest

The author has participated as advisor for MSD.

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Received 5 April 2023; Accepted 13 April 2023

Available online 19 May 2023