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EDITORIAL

Mars and Venus in the GP's office

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Discussions about the differences between men and women are age-old, but usually of great interest to both sexes and, despite our increasing understanding of gender psychology, likely to be prone to bias and misconstruction for centuries to come. The mix of gender differences in the pathogenesis, perception and presentation of disease is a potent brew for confusion, but needs further research if we are to completely understand the variety of ways in which nature and nurture interact in the development and manifestations of obstructive lung disease.

For some time, it has been known that men and women perceive and relate their symptoms differently [1]. For many diseases, it is also becoming clear that males and females develop different symptoms and clinical manifestations, at different stages of a disease, and respond differently to treatment [2, 3]. Traditionally, women have been considered to be more likely to report symptoms and to be more sensitive to changes in underlying disease [4, 5]. In relation to the presenting features of chronic obstructive pulmonary disease (COPD) in males and females, two papers published in the present issue of the *European Respiratory Journal* have some important contributions to make.

In the first of these papers, WATSON *et al.* [6] investigated predictors for the presence, development and remission of COPD symptoms in participants completing 3 yrs of the European Respiratory Society Study on Chronic Obstructive Pulmonary Disease (EUROSCOP). Over these 3 yrs similar proportions of males and females reported symptoms, although in males better lung function was associated with a reduction in new symptoms of wheeze and dyspnoea, and symptom prevalence reduced with annual improvement of forced expiratory volume in one second (FEV_1). The prevalence of phlegm was reduced with budesonide treatment, an effect seen only in males. An increase in the number of cigarettes smoked between visits increased the risk of developing phlegm and wheeze in males but not females. Therefore, symptom reporting by males in general appeared to reflect disease activity, either improvement or decline as measured by FEV_1 per cent predicted. Longitudinally, males showed a greater response based on their symptom reporting to cigarette exposure (worsening) and treatment (improvement), again suggesting that in males particularly, symptoms are a good predictor of disease status. Interestingly, females initially reported greater remission of symptoms in the first year of follow-up, but over the 3-yr period the symptom prevalence differences between males and females disappeared.

By contrast, DALES *et al.* [7] reported the clinical presentation and historical features in ever-smokers in a primary care setting in Canada. Respiratory symptom questionnaires and spirometry were administered in 1,034 (53% males) patients attending their general practitioner for any reason, but who had smoked at least 20 packs of cigarettes in their life. Males smoked significantly more than females and were more likely to have an abnormal FEV_1/vital capacity (VC) ratio, but more females than males reported breathlessness, a previous diagnosis compatible with airway obstruction, and were taking respiratory medications. Females reported more breathlessness and wheeze but significantly less sputum than males. Interestingly, when lower limit of normal cut-off points were used for airway obstruction, there was no difference in the prevalence of airway obstruction between males and females, but there were significant differences in diagnostic labelling.

These two studies add to the complexity of COPD symptom presentation and interpretation in males and females. The EUROSCOP study identifies cross-sectional and longitudinal differences between males and females in symptom prevalence, response to smoking and treatment, and highlights the closer relationship of symptom changes to disease status in males than females. The study by DALES *et al.* [7] suggests females are more likely than males to report breathlessness and to be prescribed respiratory medications, independent of differences in severity of airflow obstruction. Although there appear to be some contradictory findings in these studies, it must be remembered that the two populations are quite different, one being recruited primarily through mass media, workplace and public places and all having airway obstruction ($FEV_1/VC < 0.7$), and the other being from a primary care setting but presenting for any reason and with only 17% having airway obstruction.

Taken together, these studies are consistent with others suggesting that women may more frequently report some symptoms, such as dyspnoea and wheeze [8], but this increased reporting is not the case for all symptoms [9] and does not appear to be as sensitive to change as in men. This differential impact of gender on symptom reporting has been noted in other studies [10]. Although in some studies females have been less likely to report phlegm for a given level of airflow obstruction, they experience a greater impact on exercise capacity, breathlessness and quality of life [11–13]. In a Spanish study, in males and females matched for severity of airflow limitation, females tended to be younger, have smoked less in total pack-years and have better oxygenation.

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Despite this, they performed less well in walking distance and had worse quality-of-life scores and a higher degree of dyspnoea at iso-exercise [14].

It should be remembered that the EUROSCOP population had relatively mild airway obstruction, and were continuing smokers. It is possible these symptom-reporting trends may not be generalisable to more severe COPD, but if primary care physicians are engaged in case finding on the basis of symptoms, these reporting differences between males and females may be important in the early detection of COPD and the likelihood of subsequent performance of spirometry for confirmation. Some studies have not shown that phlegm is an under-reported symptom, but do confirm a high symptom prevalence for females with COPD [15], which is consistent with the observation from the EUROSCOP that females had greater prevalence at baseline of all symptoms apart from the presence of phlegm. However, over the 3 yrs of the EUROSCOP, symptom prevalence was similar by gender, a distinctly different outcome to several other studies suggesting that women are more likely than men to report symptoms of COPD, particularly breathlessness, for a given degree of airway obstruction.

The implications of these differences in symptom reporting may be significant not only in relation to detection and diagnosis of COPD, but also in management and the accuracy of clinical prognosis. Differences in diagnostic sensitivity and management were highlighted in a North American study [16] where the response of primary care physicians to a hypothetical case history was assessed. COPD was given as a more probable diagnosis in males than females, suggesting that physicians may be biased towards diagnosing COPD in males, and towards diagnosing asthma in females with airway obstruction. In the clinicians' response to this hypothetical scenario, spirometry was performed infrequently, increasing the possibility that COPD will neither be suspected or confirmed as readily in females. This is supported by the findings of WATSON *et al.* [11] in the Confronting COPD International Survey, which showed that after adjusting for age, pack-years and severe breathlessness, females were less likely to have had spirometry. Despite this, they were more likely to receive smoking cessation advice than males, indicating these diagnostic and reporting biases can adversely affect management for both sexes. The findings by DALES *et al.* [7] also suggest that females may sometimes be prescribed respiratory medication inappropriately, without a relationship to airway obstruction or a clear diagnostic ''label'', increasing the possibility of side-effects without definite efficacy. Conversely, males may receive medication less often for milder airway obstruction, with potential detrimental effect, although the consequences of this are less clear for COPD than asthma.

The differential effects of smoking in males and females have now been described in a large number of studies [17, 18] and, although there are some conflicting data, it generally appears that females are more severely affected by similar levels of exposure (pack-years) than males, both in terms of symptoms and severity of airway obstruction. Many studies have shown that the prevalence of airway hyperresponsiveness is higher in females than males, even when lung function and smoking habits are taken into account, and this is known to be an important risk factor for the development of airway obstruction in continuing smokers. In the study by WATSON *et al.* [11], despite significantly lower pack-years of smoking, females were more likely to report severe dyspnoea but have similar levels of cough and less sputum. From cross-sectional data in the Copenhagen City Heart Study, females had a greater loss of lung function per pack-year of smoking than males, and the risk of hospitalisation was greater in relation to pack-years in females than males [13], although this has not been reproduced in all studies. After adjusting for smoking, females may subsequently suffer greater levels of impact of COPD, including effects on health status, exercise tolerance, breathlessness and risk of hospital admission [14].

Along with the observed sex differences in relation to the damaging effects of cigarette smoke, there also appear to be differences between males and females in their response to treatment, although traditionally clinical trials have not examined these differences in detail. Smokers have poorer responses to inhaled corticosteroids and, in a Dutch study of the effect of inhaled corticosteroids on lung function decline in asthma, males had significantly less decline in FEV_1 over a 23-yr follow-up than females, in whom any effect on decline was negligible [19]. In the EUROSCOP, the effects on phlegm in males suggest that there may be differential effects for males and females in mild COPD. Responses to nondrug interventions, such as pulmonary rehabilitation, may also differ, with females reporting greater benefits than males in dyspnoea and fatigue; symptoms which have important prognostic implications in COPD. In the Lung Health Study, males had higher sustained quit rates at 12 and 36 months than females, although amongst participants who ceased smoking in the first year, females were more likely to experience improvement in FEV_1 % pred [20].

Whilst the full extent of gender differences in treatment response and prognosis is still poorly understood, studies such as those reported in the present issue of the *European Respiratory Journal* contribute to our understanding of the impact of gender on symptom reporting and its impact on diagnosis, management and outcomes. This field is still in its infancy, but studies that enlighten this debate and help clinicians to tailor their practice to patients' individual characteristics, gender included, are to be welcomed. Vive la difference!

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