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IT NEEDS MORE THAN JUST EOSINOPHILS TO CAUSE EMPHYSEMA IN COPD

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Asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases of the airways.

The role of inflammation and eosinophilia in lung function decline has been highlighted with high eosinophil sputum numbers [1], high variability in sputum eosinophils [2], and higher blood eosinophil numbers [3] linked to accelerated rate of lung function decline in asthma. Moreover asthma, which is known to be frequently associated with airway and blood eosinophilia [4], is a major risk factor for the development of COPD [5]. Lung function decline also occurs more frequently in COPD patients exhibiting increased eosinophilic inflammation [6]. One third of COPD patients indeed have airway eosinophilic inflammation [7, 8]. Accelerated lung function decline is not the only feature of COPD.

Most COPD patients also exhibit emphysema, which implies lung tissue destruction. In COPD, macrophages and neutrophils not only mediate airway remodelling but also destruction after exposure to pollutants [9, 10]. In the current issue of the *European Respiratory Journal,* DOYLE *et al* [11] found, *in vitro,* that eosinophil-derived interleukin (IL)-13 promoted alveolar macrophage-derived matrix metalloproteinase (MMP)-12 production, which has been shown to play a role in alveolar destruction [12]. They found that airspace enlargement is dependent on MMP-12, and that MMP-12 was increased in eosinophilic COPD patients exhibiting emphysema, while no differences were found between eosinophilic and non-eosinophilic subjects with asthma. In the study of CHAUDHURI *et al* [13], there was no significant association between asthma disease severity and sputum MMP-12 concentrations, but sputum MMP-12 in COPD patients was also directly associated with the extent of emphysema measured by computed tomography.

It is likely that eosinophils only play a role in the development of emphysema in patients inhaling pollutants. In this study, diffusing capacity of the lung for carbon dioxide was well preserved in nonsmokers with asthma, despite the higher frequency of eosinophilic inflammation in asthma [14, 15]. In asthma, the airspace enlargement is maybe more a sign of air trapping following airway remodelling than emphysema and destruction of the alveoli *per se* [16]. This suggests that additional mechanisms of eosinophilic inflammation are required to induce alveolar wall destruction. One can evoke oxidative stress induced following inhalation of pollutants or cigarette smoke and it has been shown that MMP-12 can also be produced by epithelial cells in response to cigarette smoke [17]. WOODRUFF *et al.* [18] also suggested that MMP-12, which was elevated in smokers but not in asthma patients, might produce emphysema more readily in smokers with lower levels of antiproteinase activity.

Anti-IL-5 has very modest clinical benefit in COPD patients [19, 20] in terms of reduction of exacerbations. It is not excluded that long-term treatment with anti-IL-5 or anti-IL-13 in COPD

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could have an effect in preventing the development of emphysema. Perhaps the clinical message derived from the study reported by DOYLE *et al.* [11] is that it is of utmost importance to obtain smoking cessation in these patients exhibiting eosinophilic inflammation.

Conflict of interest: None declared.

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