Author's response to Persson letter

Dr Persson raises excellent points regarding the potential for epithelial cells to contribute to the clearance of eosinophils from tissue. We are in agreement that eosinophils can migrate from bone marrow to blood to submucosa to epithelium to lumen. However, the speed of the process, the role and response of each compartment, the stimulus for it and its overall control remain poorly understood. Dr Persson suggests that previous reports show an inverse relationship of tissue compared with luminal/epithelial eosinophils following allergen challenge such that the accumulation of eosinophils in the lumen equates to resolution of inflammation. This suggests to him that the epithelium plays a resolving role.[1 2] We agree that at certain timepoints following an acute stimulus, this relationship may exist. However, chronic asthma represents a more dynamic and ongoing process, with the level of control and severity related to the intensity and chronicity of the cellular migration. In fact, unlike the allergen challenge studies alluded to, the relation of submucosal to epithelial/luminal eosinophils is almost always positive.[3] But importantly, perhaps because sputum samples are an integration of multiple airway samples over time and not a tiny (often $<1\ mm^3$) static piece of tissue, there are consistently stronger relationships of asthma severity and control to sputum/luminal eosinophils than to those in tissue especially in those patients treated with inhaled steroids (3 and personal unpublished data).

Thus, in contrast to Dr Persson's assertion, the finding of luminal eosinophils does not appear to relate to resolution of inflammation, rather to uncontrolled disease, which requires and responds to treatment with increased anti-inflammatory therapies.[4] The ongoing expression of epithelial eotaxin-2 and eotaxin-3, their relation to sputum eosinophils, and importantly to severe poorly controlled asthma observed in our recent study, implies that this migration initiates a process associated with luminal migration, and with epithelial damage as well.[5] In fact, this is consistent with multiple studies that report a deleterious effect of eosinophils and their products on epithelial function.[6 7]

Although definitive evidence that epithelial and luminal eosinophils have negative rather than positive effects in chronic asthma requires inhibition of epithelial migration through inhaled CCR3 antagonists, we believe that the bulk of the data support a negative impact of epithelial-eosinophil migration on asthma control.

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