Inhaled corticosteroid dose-response on blood eosinophils in asthma

We read with interest the article by David Price and colleagues (Oct 19, p 849)[1] showing a clear association between asthma control and a spot measurement of blood eosinophils. The mean beclomethasone-equivalent inhaled corticosteroid (ICS) dose in their cohort was 219 µg/day. The dose-response relationship between ICS and blood eosinophils is important to consider. Evidence exists of a dose-response effect of ICS on the reduction of blood eosinophils and eosinophilic cationic protein (ECP) for beclomethasone-equivalent ICS doses of up to 800 µg/day.[2] In terms of mechanism, dose-related reduction in blood eosinophils and ECP by ICS seems to be disconnected from commensurate adrenal suppression,[2] suggesting that systemic bioavailability of ICS might not be the principal cause of suppressing blood eosinophils.

The data from Price and colleagues[1] were somewhat contradictory, showing that patients on step 4 treatment with high dose ICS had a 13% increased likelihood of having a blood eosinophil count of more than 400 cells/µL, which was not reported for patients on step 3 treatment who were also taking 800 µg/day or more of beclomethasone-equivalent ICS dose, although step 2 patients on low dose ICS were 8% less likely to have a raised blood eosinophil counts. However, we appreciate that differentiation would be difficult between the suppressive effects of ICS on eosinophils per se and the ICS dose being a proxy for associated asthma severity.

Titration of ICS dose over 1 year against mannitol airway hyper-responsiveness results in reduced exacerbations, improved symptom control, and reduced reliever use, accompanied by a 34% fall in ECP.[3] The relative suppression in response to 400 µg/day beclomethasone-equivalent ICS dose of blood is 23% in eosinophils and 17% in ECP and of sputum is 76% in eosinophils and 55% in ECP.[4] These findings suggest that sputum is a more sensitive measure, although it is less practical than blood. In this regard, titration of ICS against sputum eosinophils results in reduced exacerbations and associated airway hyper-responsiveness.[5] Therefore, use of serial blood eosinophils to adjust ICS dose might result in reduced exacerbations, especially in patients who already have an Asthma Control Questionnaire score of less than 0·75,[6] indicative of optimum asthma control, at the time when the eosinophil count is measured.

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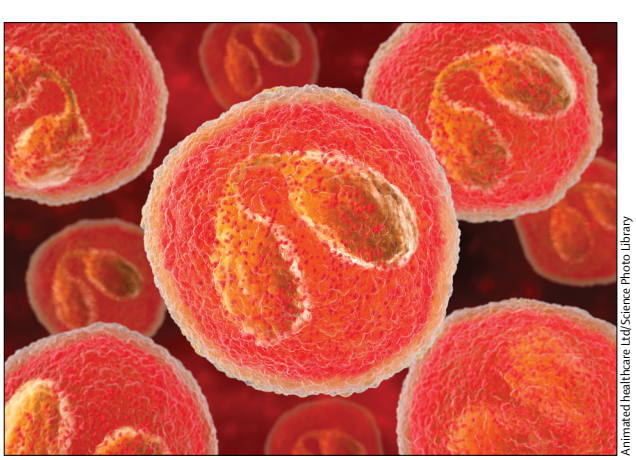
Authors' reply

We thank Brian Lipworth and colleagues for their comments on our Article[1] and agree it would be of interest to know if use of serial blood eosinophil counts to adjust ICS dose might result in reduced exacerbations. Some older data suggest that this approach might work well,[2] but new studies are needed.

This question is likely to be partially answerable with observational data to see if blood eosinophil counts are responsive to increases in ICS in clinical practice. Alternatively, the answer might come from mining of old clinical trial datasets. A definitive answer could come from a randomised controlled clinical trial in which ICS are titrated according to blood eosinophils in an intervention arm only, while the other arm is in routine care, and asthma exacerbations and other related outcomes are prospectively assessed.

We also agree that, unlike the consistent relations of blood eosinophils with other outcomes, the reported non-linear association with British Thoracic Society steps 2–5 deserves further research. The lower odds of eosinophilia at step 5 is probably due to use of oral corticosteroids in this group. Assuming that systemic availability is not the primary cause of ICS-induced suppression of blood



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