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CORRESPONDENCE

Adenosine levels in the exhaled breath condensate: a potential surrogate marker of airway inflammation

To the Editor:

We would like to congratulate HUSZAR *et al.* [1] on their important and meticulous study demonstrating elevated adenosine levels in the exhaled breath condensate of atopic asthmatic subjects compared to nonatopic controls. Their findings are in agreement with and somewhat complementary to previous data obtained from bronchoalveolar lavage fluid of patients with asthma and chronic obstructive pulmonary disease [2], thus adding to the notion that adenosine may have a pathogenic role in chronic inflammatory disorders of the airways [3]. Unfortunately, our knowledge on the role of adenosine in physiological and pathological conditions remains limited by the availability of potent and selective adenosine-receptor antagonists for use in humans.

In relation to the findings of the present study, it is important to emphasise that these atopic asthmatics were all sensitised to grass pollen and all studied during the grass pollen season. Natural exposure to aeroallergens is likely to modulate the level of airway inflammation not only in asthma but also in hay fever patients. We have repeatedly shown that nonasthmatic individuals with allergic rhinitis also exhibit features of active inflammation in the lower airways which deteriorates during natural allergen exposure [4, 5].

It is therefore likely that the results of the study by HUSZAR *et al.* [1] could also be interpreted as a response to natural allergen exposure reflecting inflammatory changes occurring at airway levels. Indeed, the pioneering work by MANN *et al.* [6] clearly demonstrated a significant increase in the plasma levels of adenosine following allergen challenge in subjects with atopic asthma. Although the inclusion of an atopic control group would have enhanced the quality of the paper by HUSZAR *et al.* [6], an important implication of these findings is that adenosine levels in the exhaled breath condensate could be valuable in assessing disease activity in relation to airway inflammation. This will obviously require rigorous testing in future long-term studies where seasonal changes in exhaled breath condensate adenosine levels are clearly related to natural allergen exposure/avoidance.

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From the authors:

It is a pleasure to read the appreciation shown by L. Spicuzza and colleagues for our recent study on adenosine in exhaled breath condensate (EBC-adenosine).

We would like to comment on the possibility of using adenosine as a marker to assess the degree of airway inflammation. We agree with the comments made by L. Spicuzza and colleagues with regard to our results showing that EBC-adenosine levels are related to the degree of airway inflammation and are in line with previous findings, suggesting that adenosine may be a nonspecific marker of airway inflammation [1]. In particular, it is worth noting that in the study by DRIVER et al. [1], no chronic obstructive pulmonary disease patients were included, only asymptotic smokers along side asthmatic patients. In a preliminary study we have shown that EBC-adenosine is also elevated in patients with cystic fibrosis, confirming that elevated adenosine levels may be a nonspecific indicator for ongoing airway inflammation [2].

Interestingly, not only is the increase in airway adenosine concentration related to other markers of airway inflammation but airway hyperresponsiveness to adenosine monophosphate also reflects the intensity of airway inflammation. Because both the release and indirect action of adenosine have been shown to be related to the number and/or activation of "primed" mast cells and other inflammatory cells present in the airways this could explain the observed relationships [1–5]. It also seems to be obvious that the enhanced level of adenosine in the airways would lead to potentiated airway obstruction provoked by diverse bronchoconstrictor agents in asthma [6, 7].

Our results partly confirm the statement of the correspondents that exposure to aeroallergens may modulate airway inflammation in asthmatic patients. We found elevation in both EBC-adenosine concentrations and exhaled nitric oxide (eNO) levels in patients with worsening asthmatic symptoms. However, only eNO levels, not adenosine concentrations, were higher in patients in a stable condition than in healthy controls. This finding suggests that eNO may be a more sensitive marker of airway inflammation than EBC-adenosine in atopic asthmatics, showing even the hidden inflamed processes in the airways.

Furthermore, the notion concerning the potential effect of allergic rhinitis on mediator levels in the lower airways seems