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The Bronchial Epithelial Secretory IgA System in Asthma

To the Editor:

I read the article by Ladjemi and colleagues with great interest (1). The authors examined components of the secretory IgA system in bronchial biopsies (1), reporting less intense immunostaining for pIgR (polymeric immunoglobulin receptor) in samples from people with asthma, relative to control subjects. Reduced pIgR immunostaining in asthma appeared to be independent of global asthma severity and atopic status. In contrast, pIgR gene expression was similar in control subjects and those with asthma (1), although the authors do not comment on the inconsistency between the immunostaining and gene expression data.

To better understand the significance of these observations, readers of the *Journal* need to know if the data might be confounded by corticosteroid treatment, especially as a large proportion of the asthmatic participants were using inhaled and oral steroids. Knowing if there is a relationship between inhaled steroid dose and the secretory IgA system is of great interest, given the links between high-dose inhaled steroids and the risk of pneumonia (2, 3). The article lacks important clinical information: the basis for the assessment of asthma severity is not stated, and it is not clear how asthma control was assessed, and whether this was based on a validated questionnaire.

The authors claim in the Introduction that a prior study showed decreased IgA content in BAL fluid from patients with severe asthma (4). However, Balzar and colleagues showed that BAL fluid secretory IgA concentrations were similar in severe asthma and mild asthma, and in normal subjects (4), although serum IgA was low in severe asthma (4). Finally, Reference 12 in their article is completely unrelated to the article's subject matter and appears to have been included by mistake. I would value comments from the authors on the issues raised herein. ■

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Reply to Upham

From the Authors:

We thank Dr. Upham for his interest and comments on our article about pIgR/SC (polymeric immunoglobulin receptor/secretory component) in asthma (1). First, although our data indeed show that bronchoepithelial pIgR immunostaining is reduced in asthma, irrespective of severity or its allergic phenotype, gene expression (pIgR mRNA levels) was not significantly affected. This apparent discrepancy was also observed in chronic obstructive pulmonary disease (COPD) (2), where pIgR immunostaining was reduced in COPD and correlated with disease severity, but pIgR mRNA was upregulated in mild COPD, probably in relation to a "direct" effect of smoking (independently of COPD). An imbalance between synthesis and post-transcriptional regulation, including proteolytic cleavage (3), could explain these observations and should be investigated. Second, the potential effect of corticosteroid treatment on bronchial pIgR expression remains unknown, as already pointed

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out previously in our first study in COPD (4). It is unlikely that treatment with inhaled corticosteroids (ICS) underlies pIgR downregulation in COPD, and no significant difference was observed in ICS-free patients compared with ICS-treated patients in a *post hoc* analysis of our COPD series (Figure 1). In contrast, in our asthma study (1), in which most patients were treated with ICS, our data could have been influenced by ICS. Considering that ICS inhibit expression of helper T-cell type 2 cytokines, now identified as "pIgR inhibitors" (1), one could expect that pIgR should be further reduced in ICS-naive patients. However, ICS could act through several other pathways, and therefore the effect of ICS is being prospectively explored in asthma. It should also be noticed that ICS use has been associated with an increased risk of pneumonia in COPD but not in asthma. Third, severe asthma was defined in our study according to the American Thoracic Society/European Respiratory Society guidelines (5) and uncontrolled, with at least two exacerbations during the previous year and an Asthma Control Questionnaire score greater than 1.5 during the 2 weeks before the endoscopy. Fourth, our statement was perhaps confusing about the results of the study by Balzar and colleagues (6), showing decreased serum IgA in patients with severe asthma compared with control subjects, whereas BAL secretory IgA also correlated (negatively) with asthma symptoms. Reference 12 in our study was indeed wrong (to be replaced by Reference 2), whereas another, previous study reported on reduced levels of BAL SC in asthma, irrespective of asthma severity (7). Altogether, we think our data convincingly show pIgR downregulation in asthma (irrespective of disease severity) and by IL-4 receptor activation, whereas potential regulation by inhaled corticosteroids and post-transcriptional mechanisms remains to be explored. ■

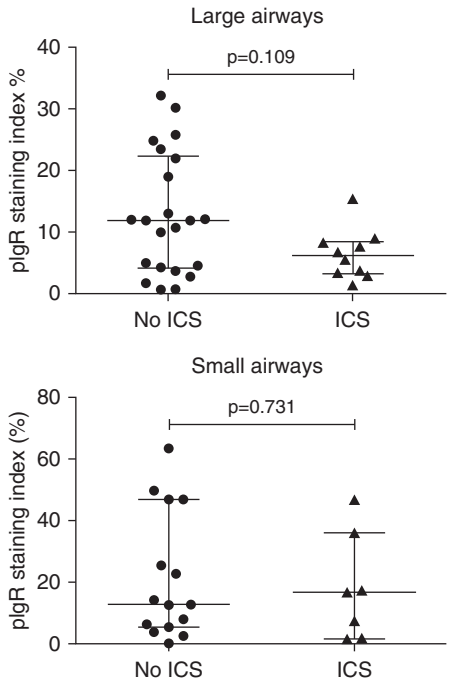

Figure 1. *Post hoc* analysis of pIgR (polymeric immunoglobulin receptor) immunostaining data in large and small airways from our chronic obstructive pulmonary disease study (1) according to the presence or not of therapy with inhaled corticosteroids (ICS). Mann-Whitney *U* test was used.

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How to Determine the Patient's Head and Neck Posture during Computed Tomography Scanning?

To the Editor:

We have read with great interest the article by Kirby and colleagues published in the January 1, 2018, issue of the *Journal* (1), and we would like to thank the authors for their contributions to the study of chronic obstructive pulmonary disease (COPD). However, as we were attempting to replicate their study, an issue arose related to the computed tomography examinations: how to determine what the patient's head and neck posture should be during computed tomography scanning.

In previous retrospective studies, respiratory mechanics in patients with COPD have been proven to be closely related to head and body position (2–4). Even with static exhalation pressure held constant, the airway morphology of a given subject may vary with different head and body positions. Therefore, it may be necessary to standardize the head and body position of patients with COPD during scanning.

In their article (1), the authors state that all images were acquired "in the supine position," and imply that the head and neck position of the study participants during imaging is adequately described. However, was a pillow used? In the cited study by Ingimarsson and colleagues, the supine child had its head supported by a small pillow (2). Was this the case with adults in the current study? Moreover, in the cited article by Schwab and colleagues (5), the use of a "neutral position" is mentioned, which implies there was no significant flexion or extension of the neck. We believe that the details of the head and neck posture adjustment are not fully described in the article by Kirby and colleagues (1); this information is crucial for readers who want to repeat their experiments.

Congratulations on the publication of this wonderful article! We would greatly appreciate if the authors could clear up our confusion about the positioning of patients during their study. ■

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Reply to Hu *et al.*

From the Authors:

We appreciate Hu and colleagues' letter regarding our article (1) and are grateful for the opportunity to provide a more detailed description of our image acquisition protocol related to head positioning, and to highlight the importance of standardizing computed tomography (CT) image acquisition.

The importance of standardizing image acquisition parameters with scanner-specific protocols, breath-hold coaching, and image analysis software is well known (2). The standardization is thought to be so important that working groups, such as the Quantitative Imaging Biomarkers Alliance (QIBA) (3), have been established to quantify the effect of these sources of variability and provide guidelines for standardizing quantitative CT imaging.

Hu and colleagues raise an important issue regarding the need for standardization of head positioning during image acquisition. There is ample evidence that body (4) and head (5, 6) positioning during image acquisition may influence airway dimensions. In our study, CT was performed with the participants supine, their hands raised above their head, and a small pillow placed under the head to position the head in the neutral position. A larger pillow, or two small pillows, were occasionally used for participants who reported discomfort because of severe kyphosis, shortness of breath, or difficulties keeping their arms above their heads to give the participants comfort and maintain

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