colleagues. With regard to the use of statins, in a previous study we reported on their potential role in decreasing pneumonia severity [3], and we agree that differences in statin and other drug use may have caused some unmeasured confounding in our study.

The issue of obesity and infection in general is complicated. A certain degree of mild obesity or being slightly overweight might even be beneficial to withstanding infection [4] or when admitted with critical disease to the intensive care unit [5]. Based on our own results and those of others, including those noted during the recent influenza A (H1N1) pandemic, we believe that severe obesity (perhaps in particular abdominal obesity) increases the risk of severe influenza and pneumonia, as also reflected in the current immunisation guidelines [6]. We believe there is less evidence that mild obesity or being slightly overweight predicts severe respiratory tract infections, particularly where it is not associated with obesity-related comorbidities such as cardiovascular disease or diabetes [1].

We wholeheartedly agree with the remarks by I. Schreter and colleagues that, given the globally rising prevalence of obesity, we need to improve our understanding of the biological association between obesity and infections. This task requires joint efforts from epidemiologists and clinical and laboratory researchers within endocrinology, infectious diseases, respiratory medicine and related specialties.

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The effect of nanoparticles on airway allergy in mice

To the Editors:

We read with great interest a recent experimental (*in vivo*) study by HUSSAIN *et al.* [1] and would like to comment on that article. First of all, we were very interested in the overall results that a single airway exposure to relatively low dose (16 μg·mouse^{-1}) of nanoparticles facilitates allergic airway inflammation. We have previously examined several types of nanoparticles/nanomaterials on ovalbumin-induced airway inflammation [2–5]. However, the doses were higher (25–100 μg·mouse^{-1} administered weekly a total of seven times) and provoked a more moderate increase in the number of inflammatory leukocytes into bronchoalveolar spaces in the absence of allergen than that in the present study by HUSSAIN *et al.* [1]. Thus, their study is valuable in terms of promoting the effect of relatively realistic dose of nanoparticles on allergic inflammation, although sensitivity against nanoparticles seems to depend on mouse strains (we used ICR mice). We have recently shown that single intratracheal instillation of carbon black nanoparticles (CBNPs) (14 nm) at a dose of 10 μg·mouse^{-1} aggravates bleomycin-induced pulmonary fibrosis (unpublished data); thus, taking these studies into consideration, it is confirmed at the animal model (*in vivo*) level that exposure to trace doses of some nanoparticles exacerbates several types of pulmonary inflammatory conditions.

Consistent with the study by HUSSAIN *et al.* [1], we have found that effects of nanoparticles/nanomaterials on airway hyperresposiveness depend on the characteristics of these materials: two sizes (14 and 56 nm) of carbon nanoparticles significantly enhanced airway resistance [2]; in contrast, two types (single- and multiwalled) of carbon nanotubes [3, 4] and two sizes (25 and 100 nm) of latex nanoparticles did not ([5] and unpublished data). Indeed, some previous reports have implicated the independency of airway hyperresponsiveness from airway inflammation [6, 7]; thus, the theory might be applied to the impacts of nanoparticles/nanomaterials on the allergic trait in the study by HUSSAIN *et al.* [1].

Regarding factors contributing to inflammatory cell infiltration in the airway, impacts of immune modulators on the T-helper cell (Th) milieu should be important to assess allergic reactions. In particular, Th2 (*e.g.* interleukin (IL)-5) and Th17 (*e.g.* IL-17A) cytokines are reportedly crucial for eosinophil

maturation, activation, survival and migration, and neutrophil invasion, respectively [8]. Measurement of the levels in the lung (brochoalveolar lavage supernatants and/or lung homogenates) warrants further information about the effects of nanoparticles on allergic pathophysiology. Alternatively, the nanoparticles may preferentially affect other chemotactic factors for leukocytes, such as eotaxin, RANTES (regulated on activation, normal T-cell expressed and secreted), anaphylatoxins and lipid mediators, and/or their producing cells.

Finally, as HUSSAIN *et al.* [1] described in their discussion, the effects of nanoparticles/nanomaterials on the phenotype and function of dendritic cells (DCs), as immune initiators, should be important for subsequent allergic pathology. Likewise, the degree of the effects appears to depend on the materials. We have also examined the effects of several environmental toxicants on bone marrow-derived DCs: CBNPs [9, 10], carbon nanotubes [3, 4], di-(2-ethylhexyl)-phthalate [11] and diisononyl-phthalate [12] activated DCs *in vitro* and *in vivo*, whereas latex nanoparticles did not (unpublished data). Interestingly, we have confirmed that the effects on DCs and antigen-presenting cells (APCs) parallel those on allergic pathology *in vivo* in their overall trend [12]. Therefore, we propose that the enhancing effects of nanoparticles on the allergic asthma examined by HUSSAIN *et al.* [1] are mediated *via* the inappropriate activation of APCs, including DCs.

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