zones for gravitational reasons; the resulting inhomogeneity in blood flow and blood volume would reduce the measured *K*CO. All published data on changes with age are derived from cross-sectional studies. The only cohort study of >8 yrs of *T*L,CO and *K*CO is that of WATSON *et al.* [20] who followed up, among others, 29 male never-smokers (mean age 37 yrs at start) over a 22-yr period. They found no change in the *K*CO.

We understand that a joint working party of the American Thoracic Society and the European Respiratory Society is currently reviewing reference values for spirometry, lung volumes and the transfer factor. We hope the carbon monoxide transfer coefficient will not be neglected, since the current recommendations are unsatisfactory. Ideally, values for total lung capacity should be obtained from the same individuals used to obtain reference values for the single breath transfer factor of the lung for carbon monoxide and the carbon monoxide transfer coefficient, so that the effects of poor inflation and/or true differences in total lung capacity at a given height and age can be allowed for [17].

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Exhaled breath condensate contains more than only volatiles

To the Editors:

I read with interest the review of WOOD *et al.* [1] on biomarkers of lipid peroxidation. I would like to congratulate the authors on this well-detailed overview of the topic. At the same time I would also like to point out that their statement saying "breath condensate samples…rely on the volatility of the substances being measured" is false. If, by this, the authors mean that only volatile substances can be captured in condensate samples they are misunderstanding this sampling method. The authors may not be familiar with this technique, which may be why they make this comment and also mention that exhaled ethane and penthane are materials being measured in condensate several times in their review. The latter two are present in the gas phase of exhaled breath and are measured directly in the breath and not in the cooled (condensed) sample [2].

The principle of exhaled breath condensate (EBC) collection is cooling the exhaled breath, resulting in a fluid sample that contains evaporated and condensed particles (water, ammonia, *etc.*) plus some droplets from the airway lining fluid. These droplets are released by turbulent airflow, and possibly by other currently not completely understood mechanisms, and can be added to the water vapour from anywhere

between the alveoli and the mouth. Therefore, in EBC samples, not only volatiles, but also several other mediators with no volatile characteristics can be found and have been reported, including adenosine, different interleukins (-4, -5, -8), interferon-γ, *etc.* [3–5]. Regarding markers of lipid peroxidation, EBC contains isoprostanes and thiobarbituric acid-reactive substances [2].

The authors are right in saying that there are methodological limitations to this type of sampling. However, this is mainly due to the limited understanding of solute formation and dilution of samples, and the accuracy of some of the currently available methods for measuring mediators in EBC. I agree that ambient air may influence the levels of exhaled biomarkers in EBC and this is shown for hydrogen peroxide [6]. Volatility may be a problem when measuring mediators from EBC, not because the sampling relies on this characteristic, but because if a molecule is volatile it is very hard to figure out the result of its equilibration between the gas and the fluid phase while breath condensation is ongoing. A good example is the ammonia measurement [7, 8].

Despite the misinterpretation of exhaled breath condensate, I believe that this review is a valuable source of knowledge and references on lipid peroxidation, with detailed information on the limitations and advantages of the current measuring methods.

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From the authors:

We thank I. Horváth for his kind comments on our review "Biomarkers of lipid peroxidation, airway inflammation and asthma" [1], and agree that we have been imprecise with the use of the term "breath condensate". The paper would be improved by replacing this term with "exhaled breath" in relation to ethane, pentane and nitric oxide measurements.

While there is an intuitive explanation for the presence of volatile substances in exhaled breath, the mechanisms by which nonvolatile substances enter expired breath are poorly understood and need to be further investigated. 8-iso-prostaglandin $F_{2\alpha}$ and malondialdehyde have been measured in breath condensate as markers of lipid peroxidation [2]; however, it is, as yet, unknown whether this medium can be used for reliable measurement of antioxidant defences. Analysis of total and oxidised glutathione concentrations in induced sputum indicates that sputum supernatant is suitable for this purpose [3]. Hence, we stand by our conclusions in this area.

At the moment both sputum induction and breath condensate collection are promising techniques. The most useful sampling technique remains to be determined and this is an important area of future research. Comparison of both sampling methods in a head-to-head study is needed to resolve this issue.

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Noneosinophilic asthma

To the Editors:

We read with interest the article by BUIST [1] on similarities and differences between asthma and chronic obstructive pulmonary disease. We would like to make some comments on the nature of inflammation in asthma, which the author has mentioned to be predominantly eosinophilic. Patients have been noted to have severe asthma or suffer an exacerbation without an increase in the eosinophil population in the airways [2]. Based on several studies from 1995 onwards with data on eosinophil levels (cut-off values 2–4%) on bronchial biopsy specimens, bronchoalveolar lavage fluid and sputum of asthmatic