From the authors:

We are glad that our article [1], as we aimed, opened a new field of scientific discussion in asthma research. Furthermore, we are honoured that our paper has raised the interest of the group headed by P.J. Barnes, who also works in the field of exhaled air temperature in asthma [2] and who was an Associate Editor of the *American Journal of Respiratory and Critical Care Medicine* when we submitted the same manuscript with the title "Temperature of exhaled air is related to exhaled NO levels in allergic asthmatic children: a new marker for airway inflammation in asthma?" in autumn 2000. On that occasion, we could not reply to the comments of P.J. Barnes, since the manuscript, after a careful review lasting some months, was rejected. In addition, at that time and even when we submitted our article to the *European Respiratory Journal* in April 2001, we could not comment about the methods used in the study by PAREDI *et al.* [2], which was submitted to the *American Journal of Respiratory and Critical Care Medicine* in March 2001 and published at the beginning of 2002, and not, as erroneously reported in reference 2 of their comment letter, in 2001.

As we clearly state in our article, from the very first to the published version of the manuscript, this was a preliminary study testing the hypothesis that the temperature of exhaled air could be increased in asthmatic patients as one of the Celsus′ cardinal signs of inflammation, which has also been mentioned by PAREDI *et al.* [2].

We deliberately employed this experimental design because we wanted to start this research from the less advantageous but the more natural condition, which meant measuring the temperature of the air exhaled during a slow expiratory act and evaluating the correlation of this rough value with the level of exhaled nitric oxide (NO) obtained by a standardised measurement.

We agree that we failed to recognise the fact that exhaled breath temperature and plateau are dependent on the exhalation flow rate, but it should be considered that the study by PAREDI *et al.* [2] was only published at the beginning of this year and, therefore, we had no opportunity to learn from their report at the time of our study.

We feel that our results are not unreliable, as stated by P. Paredi and colleagues in their comment letter, as the within subject coefficient of variation was <3%. However, we agree that the relationships between exhaled air temperature and both flow and pressure need to be investigated further, as we repeatedly stated in our paper. In addition, we also commented on the necessity of exploring the influence of environmental factors to obtain more conclusive results. Nevertheless, in our opinion, when excluding the disturbing factors in our study, *i.e.* the lack of a standardised flow, the observed results should be expected to be even more consistent. It is indeed hard to imagine that the lack of flow standardisation could be advantageous to either the reproducibility of the measurement or the correlation with other markers of inflammation, as it was observed in 52 asthmatic children.

Conversely, a possible reason for the failure to observe a correlation between plateau temperature (PLET) and exhaled NO in the study by PAREDI *et al.* [2] could be due to the low number of patients they evaluated (18), which could be responsible for a type II statistic error, a fact that was not considered by the authors.

Furthermore, we still believe that PLET can have a more physiological significance than exhaled breath temperature increase (Δe° T), which is a mathematic extrapolation predominately reflecting the changes in temperature of exhaled air during the first part of the expiratory manoeuvre (~3 s over an exhalation period of 12 s) [2]. At an exhalation flow rate of 10–11 $L \cdot min^{-1}$, approximately one-third of the air exhaled in the first 3 s comes from the anatomical dead space, and although this could be the more reproducible parameter to characterise the curve, it is hard for us to understand why this value should be clinically related to the exhaled NO values that are representative for the end of the expiratory manoeuvre.

A further point raised by P. Paredi and colleagues in their comment letter was that the lack of standardisation of the method may explain some of the unexpected findings in our paper, such as the failure of steroids to decrease exhaled breath temperature. However, PAREDI *et al.* [2] were unable to show any difference in Δe°T in corticosteroid-treated compared with untreated asthmatic patients and therefore, we cannot understand why our results, in this regard consistent with theirs, should represent an unexpected finding.

In conclusion, we would like to stress again that our study was a very preliminary one, aimed to open a new field of research rather than to be conclusive. When we performed the study, and, to the best of our knowledge, even today, no standardised method for the measurement of exhaled air temperature to evaluate airway inflammation in asthma has been approved. We hope that the observation by two independent groups that exhaled air temperature is somehow related to the degree of airway inflammation in asthma will encourage other research groups to further investigate our hypothesis so that more conclusive results can be obtained and, eventually, standardisation of the method can be proposed.

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