Lack of utility of eNO?

To the editor:
We respectfully disagree with one paragraph in Dr. Kharitonov's comprehensive review of exhaled markers of inflammatory lung diseases [1]. The measurement of exhaled nitric oxide (eNO) seems to be a very useful diagnostic tool in the assessment of possible asthma [2, 3]. However, despite its proposed indication from Dr. Kharitonov [1], years of eNO research have failed to establish its clinical utility in the management and guidance of asthma. This seems strange in a disease which clearly needs surrogate markers to better aid physicians in treating asthma patients. Several studies have shown that eNO is increased in steroid naive asthmatic patients and that it can be decreased by inhaled corticosteroids (ICS) [4]. The differences in changes in lung function, airway hyperresponsiveness and eNO, however, do not really correlate with each other [5]. Exhaled NO increases while reducing the dose of ICS [6] and this even predicts loss of asthma control once the ICS have been completely stopped [7]. However, if, in accordance with clinical practice, the dose of ICS is decreased very gradually, eNO does not seem to have a predictive value for asthma exacerbations [8]. Outcome studies such as those of Green et al. [9], who used sputum induction as a marker despite the fact that eNO is far easier to perform than sputum induction, have suggested that aggressive control of inflammation leads to better outcomes. Surely this study must have been easy to do with eNO and perhaps the lack of published outcome studies of this type reflects the lack of utility of eNO.

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Reply to letter of Leuppi and Lim
From the Author:
I thank Dr Leuppi and Dr Lim for their comments on our publication. They agree that eNO is a very useful diagnostic tool in the assessment of severity, in monitoring the effect of corticosteroid treatment and in predicting loss of control in asthma [1]. Dr Leuppi and Dr Lim have stated, however, that "years of eNO research have failed to establish its clinical utility in the management and guidance of asthma".

There is no need to repeat the conclusion of our paper, but I would like to mention just one very interesting recent study. At the ERS 2003 congress the results of the first phase 1 clinical study investigating the results of optimizing the inhaled corticosteroids (ICS) dose using eNO were presented [2]. Interestingly, it has been shown that eNO measurements permit much lower maintenance of ICS doses than the use of a symptom-based algorithm without significant differences in airway inflammation.

Another statement by Dr Leuppi and Dr Lim that "the aggressive control of inflammation leads to better outcomes" and referring to the study by Green [3] may also be misleading. Dr Green's team themselves acknowledged several limitations of their study. Firstly, the study was not done in a true double-blind fashion. Secondly, the protocol for the sputum management group could have been biased to achieve more rapid control of airway inflammation, thus accounting for the improved outcomes in this group [3]. Finally, there are serious reservations about the feasibility of inducing sputum in clinical practice, including in the primary care setting. It needs to be mentioned that Green et al. have suggested that eNO would be more suitable and further studies will be needed to prospectively assess the use of this procedure in the management of asthma [3].

The aim of our paper was to review the evidence for the use of current non-invasive markers in exhaled breath for routine use in clinical practice. I think that in patients with pulmonary disease, the monitoring of exhaled breath, including eNO which is ready for use in clinical practice, has enormous potential as a non-invasive means of monitoring airway inflammation. It will be interesting to discuss these issues again, perhaps in 2–3 years, as only time will give us the answer.

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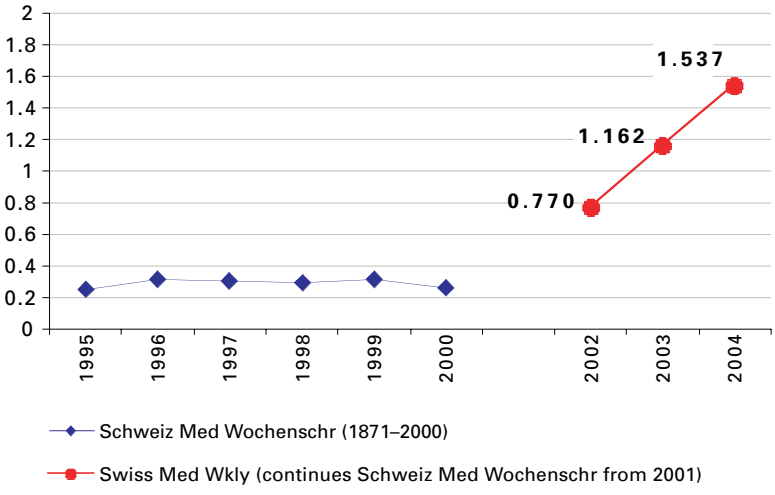

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