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Problems with using exhaled nitric oxide to guide asthma treatment

To the Editor:

The editorial by Taylor¹ makes the important point that measurement of airway inflammation, specifically of the eosinophilic type, is needed to guide corticosteroid treatment in asthma. He illustrates that the use of exhaled nitric oxide (F_ENO) can provide better results than the use of symptoms and spirometry alone. However, he does not fully convey drawbacks of the use of F_ENO. These are overcome by the use of spontaneous or induced sputum quantitative cell counts.

The measurement of F_ENO is not, as incorrectly stated, specific for eosinophilic inflammation.² It also does not identify other types of inflammation such as neutrophilic inflammation caused by viral or bacterial infections, which are common in asthma.³ It does not identify when there is combined neutrophilic infective and eosinophilic inflammation. Furthermore, the normal range is wide and, as stated, the most appropriate cut-point between normal and abnormal is imprecise. When a cut-point of 35 ppb was used to guide the inhaled corticosteroid dose needed, the measurement was unable to control eosinophilic inflammation in 1/3 of the patients (which was no different from not using F_ENO), and it was unable to reduce exacerbations.⁴

In contrast, spontaneous or induced sputum cell counts are comprehensive in identifying different types of inflammation that require different treatment.^{3,5} The normal range for the percentage of eosinophils is narrow (<2%), and the abnormal range is wide. Hence, what is normal and abnormal is more precise. Sputum eosinophils $\geq 3\%$ predicts benefit from corticosteroid treatment. When sputum cell counts are used to guide corticosteroid treatment, exacerbations are reduced, and neutrophilic infective exacerbations have been shown to be common.³ Finally, the application of sputum cell counts to specialist clinical practice, as stated by Taylor,¹ is not impractical. They are currently available in 4 Canadian centers. Their introduction just requires the availability of a dedicated hematological or cytological trained technologist. A result, if urgently needed, can be available in an hour. An interpreted report usually can be provided within 24 hours, at a time practical for clinical decisions.

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Reply

To the Editor:

We are grateful to Drs Hargreave and Parameswaran¹ for their critical comments regarding our paper on the role of exhaled nitric oxide (F_ENO) measurements in asthma.² However, we believe that what they see as "problems with using exhaled nitric oxide" ought more fairly to be described as "limitations." As such, we would find ourselves in agreement with some but by no means all of their observations.