

Correspondence

Airway inflammation: An important marker of control for asthma guidelines?

To the Editor:

Dr Bjermer,¹ in his December Rostrum article, urges us to consider a novel paradigm in asthma management by considering asthma as a constitutional inflammatory disease. This thinking, however, swims against the tide of recent studies but is a call that requires further consideration.

Recently, a series of large studies have been completed that have explored the concept of asthma control in patients with mild-to-moderate asthma. In these studies control was largely defined by outcomes that reflect airway function, such as symptom scores, functional variables, reliever use, lung function, and exacerbation frequency, and captured by tools such as the Asthma Control Questionnaire.²⁻⁵ The authors of such studies reasonably argue that asthma control is a laudable objective, yet in these and similar study designs, the use of inflammatory markers within the definition of control have been assiduously avoided, presumably because of the logistic complexity and cost that such inclusion would require.

This could prove to be a significant oversight. There is now mounting evidence to suggest that the dose-response curves for inhaled corticosteroids on outcomes such as asthma death, asthma symptoms, reliever use, lung function, inflammatory markers, and airway remodeling have different dose sensitivities and response profiles. Thus the selection of an appropriate inhaled corticosteroid dose for asthma control will be determined by the outcome marker chosen. If indeed inflammatory markers require higher doses of corticosteroids for longer periods of time, then these outcome measures will not be adequately met by the use of control tools, such as the Asthma Control Questionnaire.

Dr Bjermer further asserts that many changes of airway remodeling can result from chronic airway inflammation but nihilistically and perhaps falsely asserts that “these changes are irreversible.” Indeed, remodeling changes of airway vascularity, subepithelial collagen deposition, and basement membrane thickening can all be partially reversed by inhaled corticosteroid therapy, although these changes might take longer to accrue than the improvement in inflammatory cell profiles⁶ and might require higher doses of inhaled corticosteroids.⁷

Currently, there are few trials with long-term data based on the control/suppression of inflammatory markers and the potential

benefits for airway remodeling. However, there are accumulating data to support the use of control strategies in which corticosteroid dose adjustment is based on the use of inflammatory markers (eg, induced sputum⁸ and exhaled nitric oxide⁹), and these might further reduce exacerbation rates with similar or reduced inhaled corticosteroid requirements compared with conventional guideline-adjusted corticosteroid dosing.

Asthma control guidelines continue to evolve, and it seems prudent that we heed Dr Bjermer's call to better understand the significance of control of inflammation within these guidelines.

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REFERENCES

1. Bjermer L. Time for a paradigm shift in asthma treatment: from relieving bronchospasm to controlling systemic inflammation. *J Allergy Clin Immunol* 2007;120:1269-75.
2. Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study. *Am J Respir Crit Care Med* 2004;170:836-44.
3. O'Byrne PM, Bisgaard H, Godard P, Pistolesi M, Palmqvist M, Zhu Y, et al. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *Am J Respir Crit Care Med* 2005;171:129-36.
4. Boushey HA, Sorkness CA, King TS, Sullivan SD, Fahy JV, Lazarus SC, et al. Daily versus as-needed corticosteroids for mild persistent asthma. *N Engl J Med* 2005;14:1519-28.
5. Papi A, Canonica GW, Maestrelli P, Paggiaro P, Olivieri D, Pozzi E, et al. Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma. *N Engl J Med* 2007;356:2040-52.
6. Ward C, Pais M, Bish R, Reid D, Feltis D, Johns D, et al. Airway inflammation, basement membrane thickening and bronchial hyperresponsiveness in asthma. *Thorax* 2002;57:309-16.
7. Chetta A, Zanini A, Foresi A, Del Donno M, Castagnaro M, Raffaele D'Ippolito R, et al. Vascular component of airway remodeling in asthma is reduced by high dose of fluticasone. *Am J Respir Crit Care Med* 2003;167:751-7.
8. Green RH, Brightling CE, McKenna S, Harradine B, Parker D, Bradding P, et al. Asthma exacerbations and sputum eosinophil counts: a randomised controlled trial. *Lancet* 2002;360:1715-21.
9. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005;352:2163-73.

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