

Furthermore, it has been shown that in asthmatics treated with budesonide in a dose-escalation study, AMP was more sensitive than methacholine in detecting differences in AHR by approximately one doubling dilution [5].

Despite improvements in airway hyperresponsiveness, clarithromycin conferred no worthwhile improvement upon lung function. Therefore, the study by KOSTADIMA *et al.* [1] provides a timely reminder that monitoring the effects of asthma pharmacotherapy based solely on lung function can miss potentially beneficial effects upon airway hyperresponsiveness and underlying inflammation [6]. Further long-term studies are needed to assess whether effects upon airway hyperresponsiveness with clarithromycin translate into clinically meaningful reductions in exacerbations. Moreover, whether macrolides confer benefit upon inflammatory biomarkers, such as airway hyperresponsiveness to adenosine monophosphate and sputum eosinophilia, requires investigation.

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From the authors:

In our study [1], an 8-week treatment with clarithromycin was associated with a significant improvement in airway hyperresponsiveness to methacholine in asthmatic patients. As G.P. Currie and D.K.C. Lee correctly point out, this significant change was not accompanied by a clinically important increase in indices of expiratory flow function. We agree that further long-term clinical trials are necessary to identify any beneficial effects of clarithromycin on symptoms of asthma and on markers of airway inflammation.

We chose inhalation of methacholine, a direct stimulus, to detect changes in airway hyperresponsiveness in asthmatics treated with clarithromycin. Provocation with AMP (indirect bronchial challenge) could have also been used. Provocative concentration causing a 20% fall in forced expiratory volume in one second AMP reflects the extent of airway inflammation due to asthma more closely than provocative concentration causing a 20% fall in forced expiratory volume in one second methacholine [2]. In addition, as G.P. Currie and D.K.C. Lee appropriately emphasise in their letter, provocation with AMP is more sensitive than provocation with methacholine in detecting changes in airway hyperresponsiveness following anti-inflammatory treatment [3]. The fact that we were able to detect improvement in airway hyperresponsiveness using the less sensitive direct bronchial challenge further supports a potentially important role of clarithromycin in the treatment of asthmatic airway disease.

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"Chronic obstructive pulmonary disease": the diagnostic last refuge of the intellectually challenged?

To the Editor:

SUISSA [1] makes an important contribution to the debate on inhaled steroids and chronic obstructive pulmonary disease (COPD) in identifying, in an observational study, an artificial increase in death rate of the reference group leading to a spurious appearance of effectiveness. SUISSA [1] refers, in

discussion, to what I believe to be an equally important and curiously neglected source of bias, the unintended inclusion of asthma patients when selecting patients for studies from administrative databases using only age and bronchodilator use to define the disease entity. The term COPD is a too-convenient shorthand label for a group of conditions that can be shown, even with standard investigative tools, to be of