Reviewer's report

Title: Use of interrupter technique in assessment of bronchial responsiveness in normal subjects.

Version: 1 Date: 21 September 2004

Reviewer: Nicole Beydon

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Results
The authors should clearly state if there was or not a significant difference in baseline PFT according to gender. Particularly, for the FEV1 in %pred which seems lower in female; and for the RintEI (does normalization by height erase the difference between male and female RintEI measurement at baseline?).
The second sentence of the result section has to be rewrite. There is no contrast in higher RintEI values in those who have lower FEV1 and if an interpretation has to be given it should be done in the discussion section.
The end point of the challenge was an at least 20% fall in FEV1; we would like to know if, at this endpoint, all the subjects had an at least 100% increase in RintEI or not. And if not how was interpreted the test in these discordant subjects. A figure showing the % of changes in FEV1 and RintEI might response to this question too.
The relevance of Rint measurement during bronchial challenge in children cannot be extrapolated from studies in adults. Children have narrow baseline airways compare to that of adults. During bronchoconstriction the assumption of the pressure equilibration in the airways may be false and specific studies in children have to validate Rint method.

Figure
The Bland Altman figure has to include +/- 2 SD of the mean difference lines to allow a good visualization of the values outside the 95% CI.

Discussion
The RintEI was found less sensitive than RintL (using the SI index as Phagoo et al) in a study conducted in children with unspecific respiratory symptoms (Beydon Pediatr Pulmonol 2001). Healthy subject may have different Rint changes during bronchial challenge, according to the algorithm used to calculate the Rint, because of their larger airways that facilitates the pressure equilibration. This may be different in the smaller airways of children. These conflicting results have to be comment.

Conclusion
As in the abstract the term useful does not seem appropriate since healthy subjects do not need bronchial challenge. Moreover, before using Rint method as the only marker of bronchoconstriction during bronchial challenge, studies like the present one, has to be conducted in asthmatic subjects. As state by the authors, differences in healthy and asthmatic smooth muscle contraction could indeed influence the relationship between RintEI and FEV1 measurements.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The conclusion of the abstract relies on the clinically relevance to perform bronchial challenge in
normal subjects. The term useful does not seem appropriate since healthy subjects do not need bronchial challenge and the reliability of Rint measurement during bronchial challenge is not studied in sick patients in the study.

Material and methods
The exclusion of the subject who increased his resistance of 30% of baseline after diluent inhalation has to be cleared. We would like to know if the FEV1 of this subject had changed or not. In the absence of FEV1 changes and in real life, if Rint had not be measured this subject would have undergone the bronchial challenge. 

27 subjects = 14% of the data were said to be “non evaluable”. The authors should give an explanation to what was the problem with all these tests, since we do not expect bronchial challenge to be unsuccessful in young normal adults.

Discussion
It is hard to understand the sentence about FRC and RintEI (p 9 line 5-8)
Authors meant a 30% INCREASE in RintEI p 9 line 9-10, In the same sentence the SD is a data not shown in the result section.

Discretionary Revisions (which the author can choose to ignore)
The background section of the abstract does not fit too well with the methods section, since the study subjects are neither very young nor old subjects.

Introduction
The use of the interrupter technique in nasal resistance measurement does not rely on the physiologic assumption of Pmo equilibrating with Palv, that is used for airway resistance assessment. This reference is out of the subject.

Result
It would be easier if usual abbreviations for PFT parameters were used (FEV1/CVF FEF50,IC... instead of FEV%, Vmax50, VCin.
The intra individual coefficient of variation for RintEI at baseline could be of interest in order to have an idea of the reproducibility of this technique, so we can more appreciate the relevance of a 100% increase.

Discussion
There are no references to support that the plethysmograph method is more time consuming in young adults, does the authors have additional data ?
The authors showed a better sensitivity of DRR for RintEI measurements but no differences in the PD100RintEI and PD20FEV1. The discussion could discuss alternative ways to express bronchial reactivity using the more sensitive parameter (DRR).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests: None