Factors in clinical expression of allergic airways disease
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CHAPTER 7

Similar levels of nitric oxide in exhaled air in non-asthmatic rhinitis and asthma after bronchial allergen challenge

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Allergy, in press
Summary

Background: Nitric oxide in exhaled air (eNO) is elevated in allergic asthma and to a lesser extent in allergic non-asthmatic rhinitis as well. eNO has been proposed as a mean of diagnosing and also monitoring asthmatics. Considering the different clinical appearances of both allergic diseases, differences either in the characteristics of the target organs or in the bronchial inflammatory process are expected.

Methods: Bronchial allergen challenge was performed in 52 patients sensitised to house dust mite (HDM), of whom 26 had non-asthmatic rhinitis and 26 had asthma. eNO was measured before, 1 day and 1 week after challenge.

Results: At baseline eNO was significantly lower in non-asthmatic rhinitis compared to asthma (geometric mean NO-output (SEM): 121 (1.1) in non-asthmatic rhinitis vs 197 (1.1) nl/min in asthma, p < 0.006). However, the increase in eNO after challenge in non-asthmatic rhinitis exceeded the increase in the asthma resulting in similar levels of eNO after allergen challenge (geometric mean NO-output (SEM) at 24 hours post-challenge 204 (1.1) in non-asthmatic rhinitis vs 244 (1.1) in asthma, p = 0.3).

Conclusion: The difference in eNO between non-asthmatic rhinitis and asthma is abolished after allergen exposure due to a significantly greater increase in eNO in non-asthmatic rhinitis. These findings may hamper the use of eNO as a diagnostic tool for asthma.
Introduction

Nitric oxide in exhaled air (eNO) is elevated in asthma\(^1\) and to a lesser extent in non-asthmatic rhinitis as well\(^2,3\). Measuring eNO is proposed as a diagnostic tool for in adults and in children\(^4\). In addition, eNO is advocated to be a valuable mean of monitoring asthmatic patients\(^5\), as eNO seems to be related to the degree of bronchial inflammation. On the one hand eNO decreases during treatment with inhaled steroids\(^6\), on the other hand eNO increases after allergen challenge\(^7\).

Apart from the potential clinical usefulness of eNO in asthma, nitric oxide (NO) is an interesting molecule in the pathophysiology of asthma and rhinitis because of its possible immunological effects. NO causes prolonged suppression of IFN-\(\gamma\) production by helper T (T helper) cells \textit{in vitro}\(^8\). IFN\(\gamma\) is one of the key cytokines in the differentiation of T helper cells into Th1 and Th2 subsets and inhibits the proliferation of the Th2 cells. Allergic diseases are assumed to be characterised by a shift in the balance between Th1 and Th2 cells towards Th2 cells. Thus, NO might enhance the Th2 mediated inflammatory response in allergic asthma and allergic rhinitis by the suppression of IFN-\(\gamma\).

The increased level of eNO is considered to be caused by upregulation of the inducible form of NO synthase (NOS) particularly in bronchial epithelial cells\(^9\). Recently, increase in the upregulation of inducible NOS (iNOS) within the airways was demonstrated after bronchial allergen challenge\(^10\), confirming the association between upregulation of iNOS and increase in bronchial inflammation. The inducible isoform of NOS is an enzyme that is capable of producing large amounts of NO and is expressed only after induction by immunologic and inflammatory stimuli\(^11\). By contrast, the constitutive isoform of NOS (cNOS) produces only small amounts of NO. The large quantities of NO that are produced by iNOS possibly are deleterious in allergic airway disease. In a study in ovalbumin sensitised iNOS-knock out mice there was less eosinophil accumulation in the lungs after ovalbumin challenge compared to controls\(^11\). However, the precise role of the different isoforms of NOS is still a matter of controversy.

The previously reported elevated levels of eNO in non-asthmatic rhinitics at baseline\(^3\) are in keeping with the finding that apart from the upper airways, the lower airways in non-asthmatic rhinitics are also characterised by some degree of bronchial eosinophilic inflammation\(^12\). However, considering the distinctive clinical appearances of allergic diseases, differences either in the allergic
inflammatory process or in characteristics of the target organs in these patients are expected. The late asthmatic response (LAR) that develops in some sensitised patients a few hours after bronchial allergen challenge is often used as a model for the bronchial allergic inflammation in chronic asthma. Although non-asthmatic rhinitics have isolated upper airway symptoms and no symptoms of the lower airways, an early asthmatic response (EAR) after bronchial allergen challenge can be elicited in these patients as well as in allergic asthmatics\textsuperscript{13}. Less frequently a LAR can also be found.

The present prospective, experimental study was designed to investigate differences in allergen induced bronchial inflammation, including changes in eNO, between house dust mite (HDM) \textit{(D. pteronyssinus)} allergic asthmatics and HDM allergic perennial rhinitics without any clinical evidence of asthma (results considering other markers of inflammation submitted elsewhere). So far, eNO has not been studied in non-asthmatic rhinitis after bronchial allergen challenge, but only at baseline. In addition, no comparative challenge studies between asthma and non-asthmatic rhinitis, with respect to eNO, have been done. Here we describe the measurements of changes in level eNO in allergic non-asthmatic rhinitis and allergic asthma after a standardised bronchial allergen challenge.

\textbf{Materials and methods}

\textit{Patients}

The study population existing of fifty-two subjects sensitised to HDM \textit{(D. Pteronyssinus)} as determined by skin prick test (SPT) and Radio Allergosorbent Test (RAST) were investigated, of whom 26 had asthma and 26 had perennial rhinitis without asthma. Asthma was diagnosed according to the American Thoracic Society (ATS) criteria and included a documented history of recurrent episodes of wheezing, chest tightness and dyspnoea and a normal lung function between asthmatic attacks\textsuperscript{14}. Perennial non-asthmatic rhinitis was characterised by episodes of sneezing, watery rhinorrhoea, pruritus in the nose and nasal obstruction without any current or past asthmatic symptoms\textsuperscript{15}. The participating patients were recruited via the outpatient departments of Pulmonology and Otorhinolaryngology at the Academic Medical Center.
The following inclusion criteria were used for all: a) FEV₁ ≥ 70% of predicted value b) IgE to *D. pteronyssinus* > 0.5 IU/ml c) able to stop short acting β₂-adrenoceptor agonists for at least 8 hours, oral anti-histamines for 2 weeks and inhaled corticosteroids for 6 weeks prior to the start of the study d) no significant change in allergen exposure due to allergen avoidance during at least 6 months. Whenever co-sensitisation to pollen was present the study was performed outside the relevant pollen season. Exclusion criteria were: a) immunotherapy in the history b) respiratory tract infection within 6 weeks prior to the study c) immunosuppressive medication d) smoking. The AMC Medical Ethical Committee approved the study, and all subjects gave written informed consent.

**Study design**
The study had a prospective experimental design. Prior to the inclusion all subjects were screened for inhalant allergies by Radio Allergosorbent Test (RAST) and skin prick test (SPT) with a standard panel of allergens. Medication by corticosteroids and anti-histamines was ceased 6 weeks and 2 weeks prior to the study period, respectively. Baseline levels of NO-output and NO expiratory plateau concentration, forced expiratory volume in one second (FEV₁) and histamine threshold (PC₂₀ histamine) were determined on day one. In addition diurnal change in FEV₁ was recorded after a control inhalation challenge with diluent. Bronchial allergen challenge was performed on the second day of the study period. Twenty-four hours and one week after bronchial allergen challenge NO output and NO expiratory plateau concentration, FEV₁ and PC₂₀ histamine were repeated. Moreover, NO was measured 1 hour after allergen challenge.

**Allergen extract**
A standardized *D. pteronyssinus* extract (1 mg/ml) (ALK, Houten, The Netherlands) containing 10⁷ 6 SQ units/ml (representing 50,000 BU/ml) was kept at -20°C in small aliquots. This allergen batch was used for all assays, and contained 85,1 μg Der p1 and 9.7 μg Der p2 per mg protein. Two-fold dilutions were made freshly from the stock immediately before allergen challenge in phosphate buffered saline, 0.03% human serum albumin, 0.5% phenol (ALK).
**Bronchial allergen challenge**

Bronchial allergen challenge was performed by using a reservoir aerosol delivery system according to the method described by Sterk et al.\(^\text{16}\) with modifications\(^\text{17}\). A collapsible reservoir of approximately 30 litre, made of static field dissipative material (RCAS 1206, Richmond Redlands, CA, USA) and filled with dry air, was connected to a nebulizer (Mallinckrodt Diagnostica, Petten, The Netherlands) producing allergen aerosols from a 0.5 ml sample. The entire volume of the reservoir was inhaled by tidal breathing through a 3-way valve system with the nose clipped. Previous studies demonstrated a 70% recovery of nebulised allergen. The starting allergen dose was calculated from the SPT threshold and the PC\(_{20}\)histamine according to the method of Cockcroft et al.\(^\text{18}\). FEV\(_1\) was measured on a dry rolling-seal spirometer (SensorMedics BV, Bilthoven, The Netherlands). Drop in FEV\(_1\) (mean of two measurements) relative to baseline values (median of three measurements within 5%) was measured 0.5 and 10 minutes after inhalation of allergen. With intervals of 10 minutes doubling doses of allergen were inhaled from the reservoir, until a decline of 20% in FEV\(_1\) was reached. Subsequently, FEV\(_1\) was measured hourly for at least 10 hours. The bronchial response to allergen was expressed as the percentage change from baseline. FEV\(_1\) was corrected for the diurnal variation in. Both the early asthmatic response (EAR) and late asthmatic response (LAR) were defined as \(\geq 20\%\) drop in FEV\(_1\) relative to the baseline value.

**Bronchial histamine challenge**

Bronchial histamine challenge was performed according to the two-minute tidal breathing method as described by Sterk et al.\(^\text{16}\). Non-specific bronchial hyperresponsiveness to histamine (PC\(_{20}\)histamine) was defined as the concentration of histamine diphosphate in PBS (range: 0.015 to 32 mg/ml) causing a drop of 20% in FEV\(_1\) as calculated by log-linear interpolation.

**NO measurements**

The NO concentration was measured in exhaled air using a chemiluminescence NO/NOx analyser (CLD 700 AL med ECO Physics, Durnten, Switzerland, range 1-100 ppb, update frequency 100 msec, T-90 1 sec). The subjects inhaled NO-free air through a mouthpiece in a sitting position with the nose clipped. During tidal breathing the expired air was collected for 2
minutes in a NO-inert Douglas bag via a T-valve with an expiratory resistance. Simultaneously, respiratory flow and volume data were collected via a pneumotachograph. NO concentration in the sample bag was measured immediately after this procedure. NO output per minute was calculated from NO-concentration in the sample bag and expiratory volume. In addition to the NO-output measurements, real time NO concentrations were measured during two minutes of tidal breathing by direct sampling from the mouthpiece via a Teflon tube. The mean plateau expiratory NO concentration was then calculated. There were no significant differences in tidal volume and frequency of breathing, neither between non-asthmatic rhinitis and asthma nor before and after allergen challenge (results not shown). Significant correlations between NO-output and NO expiratory values were found at all time points (at baseline: R_s = 0.54 p < 0.0001, after EAR: R_s = 0.55 p < 0.0001, 24 hours after allergen challenge: R_s = 0.50 p < 0.0001 and 1 week after allergen challenge: R_s = 0.34 p < 0.03).

Statistical methods

SPSS version 8.0.2 Statistics U.K. (Chicago, IL, USA) was used for statistical analyses. Within group comparisons were done with Wilcoxon test, between group differences were analysed with Mann-Whitney test. The Spearman rank test was used to determine correlations. All p-values were two-tailed and p-levels of less than 0.05 were considered significant.

Results

Baseline characteristics, lung function and bronchial allergen challenge
Baseline characteristics and lung function parameters in non-asthmatic rhinitis and asthma patients are shown in table 1. All patients tolerated the bronchial allergen challenge without complications. Short acting β2-agonists were not used during 12 hours after allergen challenge. All of the 26 asthmatic patients had an EAR, of whom 19 had a dual response, i.e. both an EAR and LAR, and 7 a single response, i.e. an isolated EAR. Twenty-one of the non-asthmatic rhinitis
patients experienced an EAR, 11 had a LAR. The early asthmatic reaction was similar in non-asthmatic rhinitis and asthma (median maximal decrease in FEV$_1$ –29% in non-asthmatic rhinitis vs –32% in asthma, p = 0.1), but the late asthmatic reaction was more pronounced in asthmatics (–21% in non-asthmatic rhinitis vs –34% in asthma, p = 0.02).

### Table 1 Baseline characteristics and lung function parameters.

<table>
<thead>
<tr>
<th></th>
<th>Non-asthmatic rhinitis (n = 26)</th>
<th>Asthma (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr.)</strong></td>
<td>27 (5)</td>
<td>27 (6)</td>
</tr>
<tr>
<td><strong>Sex (m/f)</strong></td>
<td>6/20</td>
<td>6/20</td>
</tr>
<tr>
<td><strong>spIgE (KU/l)</strong></td>
<td>13 (3.4)†</td>
<td>27 (2.8)†</td>
</tr>
<tr>
<td><strong>total IgE (KU/l)</strong></td>
<td>126 (3.8)</td>
<td>243 (3.8)</td>
</tr>
<tr>
<td><strong>FEV$_1$ (%pred)</strong></td>
<td>103 (13)†</td>
<td>95 (15)†</td>
</tr>
<tr>
<td><strong>PC$_{20}$hist (mg/ml)</strong></td>
<td>9.6 (2.7)††</td>
<td>1.2 (4.0)††</td>
</tr>
<tr>
<td><strong>PC$_{20}$hist,24hrs (mg/ml)</strong></td>
<td>2.1 (1.5)††</td>
<td>0.4 (1.4)††</td>
</tr>
<tr>
<td><strong>Perennial rhinitis (%)</strong></td>
<td>100</td>
<td>73</td>
</tr>
<tr>
<td><strong>EAR ΔFEV$_{1,max}$ (%)</strong></td>
<td>-29.1 (12.0)††</td>
<td>-31.7 (11.5)</td>
</tr>
<tr>
<td><strong>LAR ΔFEV$_{1,max}$ (%)</strong></td>
<td>-18.9 (21.1)††</td>
<td>-27.6 (34.1)†</td>
</tr>
</tbody>
</table>

*mean and SD, †† geometric mean and GSD, ††† median value and IQR, spIgE: specific Immunoglobulin E, PC$_{20}$hist,24hrs: PC$_{20}$histamine at 24 hours after allergen challenge, EAR: early asthmatic reaction, LAR: late asthmatic reaction, ΔFEV$_{1,max}$: maximal decline in FEV$_1$ after allergen challenge non-asthmatic rhinitis vs asthma: ††† p < 0.0001, †† p = 0.001, † p < 0.04.
Table 2 shows baseline characteristics and lung function parameters of non-asthmatic rhinitic and asthmatic single and dual responders. Two non-asthmatic rhinitics had a LAR, in the absence of a definitive EAR, but with an early decrease in FEV\textsubscript{1} between 15 – 20%. They were included in the group of dual responders. Changes in FEV\textsubscript{1} after allergen challenge in asthmatic and non-asthmatic single and dual responders are depicted in figure 1. In non-asthmatic rhinitics there were no significant differences in baseline FEV\textsubscript{1}, PC\textsubscript{20} histamine and EAR between single and dual responders (p > 0.1). In asthmatics there were no significant differences in baseline FEV\textsubscript{1} and EAR between single and dual responders (p > 0.1), but baseline PC\textsubscript{20} histamine was significantly lower in dual responders as compared to single responders (p < 0.05).

Table 2 Baseline characteristics and lung function parameters in rhinitic and asthmatic single and dual responders.

<table>
<thead>
<tr>
<th></th>
<th>Non-asthmatic rhinitis</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>dual responders</td>
<td>single responders</td>
</tr>
<tr>
<td>spIgE (KU/l)##</td>
<td>20.2 (2.1)</td>
<td>9.47 (4.1)</td>
</tr>
<tr>
<td>total IgE (KU/l)##</td>
<td>160 (3.1)</td>
<td>106 (4.4)</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (%pred)#</td>
<td>103 (15)</td>
<td>103 (11)</td>
</tr>
<tr>
<td>PC\textsubscript{20} hist (mg/ml)##</td>
<td>6.4 (3.2)†</td>
<td>12.9 (2.1)†</td>
</tr>
<tr>
<td>PC\textsubscript{20} hist,24hrs (mg/ml)##</td>
<td>1.0 (1.7)++</td>
<td>3.7 (1.6)++</td>
</tr>
<tr>
<td>EAR ΔFEV\textsubscript{1, max} (%)###</td>
<td>-29.1 (9)</td>
<td>-29.1 (13)</td>
</tr>
<tr>
<td>LAR ΔFEV\textsubscript{1, max} (%)###</td>
<td>-31.5 (15)+++</td>
<td>-11.1 (10)</td>
</tr>
</tbody>
</table>

*mean and SD, ## geometric mean and GSD, ### median value and IQR, spIgE: specific Immunoglobulin E, PC\textsubscript{20} hist,24hrs: PC\textsubscript{20} histamine at 24 hours after allergen challenge, EAR: early asthmatic reaction, LAR: late asthmatic reaction, ΔFEV\textsubscript{1, max}: maximal decline in FEV\textsubscript{1} after allergen challenge non-asthmatic rhinitic dual vs non-asthmatic rhinitic single responders: + p = 0.07, ++ p = 0.08, +++ p < 0.0001
asthmatic dual vs asthmatic single responders: † p < 0.05, ‡‡ p < 0.01, ‡‡‡ p < 0.0001

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Figure 1 Changes in FEV$_1$ after bronchial allergen challenge.

a. in non-asthmatic rhinitic single responders (n = 15) and non-asthmatic rhinitic dual responders (n = 11)
b. in asthmatic single responders (n = 7) and asthmatic dual responders (n = 19).
Figure 2

![Graph](image)

**Figure 2**

2a. NO-output after bronchial allergen challenge. Geometric mean values ± SEM are shown. Asthma *vs* non-asthmatic rhinitis: p < 0.006 at baseline, p = 0.31 at 24 hours, p = 0.39 1 week after challenge.

2b. NO-output after bronchial allergen challenge in asthmatic single and dual responders and non-asthmatic rhinitic single and dual responders.

- asthmatic dual responders *vs* asthmatic single responders: p = 0.013 at baseline
- asthmatic dual responders *vs* rhinitic dual responders: p = 0.004 at baseline, p > 0.2 at the time points after challenge
- asthmatic single responders *vs* rhinitic single responders: p > 0.25 at all time points
NO-output
NO-output before and after bronchial allergen challenge in non-asthmatic rhinitis and asthma is shown in figure 2a. NO-output in asthmatic and rhinitic single and dual responders before and after allergen challenge is depicted in figure 2b.

Allergen induced changes in NO-output: non-asthmatic rhinitis vs asthma
In both non-asthmatic rhinitis and asthma there was an increase in NO-output at 24 hours after allergen challenge which was highly significant in non-asthmatic rhinitis (p < 0.0001), but also significant in asthma (p < 0.05). One week after challenge there was still a significant increase in NO-output in non-asthmatic rhinitics (p < 0.05 relative to baseline), but not in asthmatics. The relative change in eNO at 24 hours after allergen challenge, was significantly greater in non-asthmatic rhinitis (p < 0.05).

Allergen induced changes in NO-output in single and dual responders
The relative increase in NO output from baseline was significant in rhinitic dual responders (p < 0.01), in rhinitic single responders (p < 0.01) and in asthmatic dual responders (p < 0.05), but not in asthmatic single responders. The increases in NO-output in the 4 subgroups were significantly different (Kruskal-Wallis p = 0.01). The increase in NO-output relative to baseline was most pronounced in rhinitic dual responders (p < 0.01 as compared to rhinitic single responders or to asthmatic dual responders).

Correlations with changes in lung function
Overall, there was a significant correlation at baseline between NO-output and PC_{20 histamine} \( R_s = -0.31, p = 0.03 \), however this correlation was absent when non-asthmatic rhinitics or asthmatics were considered separately (\( R_s = -0.06, p = 0.8 \) for non-asthmatic rhinitics and \( R_s = -0.18, p = 0.4 \) for asthmatics).
NO-output at baseline correlated significantly with the magnitude of the LAR (\( R_s = -0.31, p < 0.05 \)). This correlation was still present considering the asthmatic patients (\( R_s = -0.40, p = 0.042 \)), but not in non-asthmatic rhinitics (\( R_s = 0.02, p = 0.9 \)). There was also a significant correlation between NO-output at 24 hours after challenge and the magnitude of the LAR (\( R_s = -0.46, p = \))
Again, this association was only present in asthmatic patients ($R_s = -0.61, p = 0.001$), but not in non-asthmatic rhinitic patients ($R_s = -0.24, p = 0.23$).

**Discussion**

This is the first study to demonstrate an increase in eNO after bronchial allergen challenge in non-asthmatic rhinitics. Strikingly, the increase in eNO in this group exceeded the increase in eNO in asthma, resulting in similar levels in non-asthmatic rhinitis and asthma after allergen challenge. This finding underlines the similarities in bronchial changes between asthma and non-asthmatic rhinitis and confirms that increased eNO is not specific for asthma.

It seems unlikely that methodological aspects of the NO measurement can explain the findings in the present study. Baseline levels of eNO were different between non-asthmatic rhinitis and asthma as reported earlier, with levels similar to those reported in literature. All patients underwent the same reproducible procedure. The significant increase in eNO in asthmatic dual responders in the present study is in concordance with the results published by Kharitonov et al. To exclude nasal contamination the patients exhaled against a resistance. The low value of eNO in non-asthmatic rhinitics at baseline, in spite of the tenfold higher nasal eNO concentrations that have been reported previously, also strongly argues against nasal contamination. Moreover, 73% of the asthmatics also suffered from perennial rhinitis. Possibly, the existence of a plateau in the expression of iNOS explains the smaller increase in eNO in asthmatics as compared to non-asthmatic rhinitics.

NO in exhaled air has been proposed as a marker of bronchial inflammation. Monitoring the inflammatory process might be important in the management of asthma. Some studies on associations between eNO and other markers of inflammation and disease severity report correlations between eNO and bronchial hyperresponsiveness and sputum eosinophil numbers, however this was not confirmed in other studies. Moreover, no relationship between eNO and mucosal eosinophils measured in bronchial biopsies could be demonstrated. Therefore, it has been hypothesised that eNO complements other markers of inflammation for determining the severity of asthmatic bronchial inflammation. The absence of correlations between steroid-
induced changes in levels of eNO and changes in eosinophils in sputum is in keeping with this hypothesis. Likewise, we did not find correlations at baseline between eNO and parameters for bronchial inflammation, \textit{i.e.} sputum eosinophils, neutrophils and concentration of eosinophil cationic protein (ECP) and myeloperoxidase (MPO) in induced sputum (results not shown).

Comparison of inflammatory parameters between asthma and non-asthmatic rhinitis at baseline did not show significant differences in percentages and numbers of sputum eosinophils between both groups. By contrast a significant difference in eNO at baseline was found between asthma and non-asthmatic rhinitis. These findings suggest that eNO surpasses sputum eosinophils in discriminating between non-asthmatic rhinitis and asthma. However, in this respect non-specific bronchial hyperreactivity, as measured with PC$_{20}$histamine, appears to be superior. Moreover, the difference in PC$_{20}$histamine between non-asthmatic rhinitis and asthma remained significant after allergen challenge in contrast to the difference in eNO at baseline, which disappeared after allergen challenge. The absence of correlations between changes in eNO and changes in PC$_{20}$histamine in this and previous studies add further support to the above-mentioned hypothesis that these parameters reflect different aspects of the bronchial inflammatory process.

We divided asthmatics and non-asthmatic rhinitics on the basis of their late bronchial responsiveness to allergen into single responders and dual responders. Single responders were defined as patients that exhibited an EAR but no LAR after allergen challenge, dual responders were defined as patients that did have a LAR. Thereby it was elucidated that the larger increase in eNO in non-asthmatic rhinitis as compared to asthma was mainly due to a significantly larger increase in eNO in rhinitic dual responders as opposed to the other subgroups. Non-asthmatic rhinitic dual responders apparently can be triggered more easily to produce large amounts of NO. Therefore it is tempting to assume that these patients are more prone to develop bronchial inflammation as compared to rhinitic single responders, and might be at risk to develop asthmatic symptoms. It has been suggested previously that elevated levels of eNO in atopic asymptomatic subjects, or in atopic asthmatics in clinical remission, are predictive for the onset or relapse of asthmatic symptoms. On the other hand, eNO in asthmatic single responders, patients with clinical evidence of asthma, was similar to the levels of eNO in non-asthmatic rhinitics at
baseline. This finding indicates that relatively low values of eNO at baseline do not exclude the presence of asthmatic symptoms.

We conclude that the difference in eNO between non-asthmatic rhinitis and asthma at baseline, was abolished after bronchial allergen challenge. The increase in eNO after allergen challenge was most pronounced in the subgroup of rhinitics that exhibited a dual asthmatic response after challenge. These findings underline the similarities in bronchial changes in non-asthmatic rhinitis and asthma and may hamper the use of eNO as a diagnostic tool for asthma.
References


