

AIRWAY INFLAMMATION STUDIES

Nitric Oxide -A Diagnostic Tool?

by Susan Blonshine, BS, RRT, RPFT

Research has shown that the exhaled nitric oxide (NO) in an asthma population is higher than from the lower airways of a control group. The NO levels are also higher after allergen challenges in sensitized animals. When compared with a normal population, the exhaled NO concentration is not significantly different from those asthmatics receiving inhaled corticosteroids. Multiple studies have documented increased levels of NO with airway inflammation and a decrease in NO levels with anti-inflammatory therapies. Several studies have addressed varying questions related to the applicability of exhaled NO. The use of inhaled NO as a diagnostic tool is also under investigation.

Inhaled corticosteroids and exhaled NO levels

In a double-blind, cross-over study published in January of this year, S. Lim and colleagues examined the effect of inhaled budesonide (800 micrograms twice daily via Turbohaler) on lung function.¹ The authors also studied various markers of airway inflammation including airway responsiveness to methacholine (PC₂₀), exhaled NO, eosinophils in induced sputum, bronchoalveolar lavage (BAL), and airway biopsies.

The patients studied were mild asthmatics requiring only beta-2 agonist therapy. After inhaled steroids, there was a significant increase in FEV₁ and provocative concentration, resulting in a 20 percent decrease in FEV₁ (PC₂₀) and a

reduction in exhaled NO. The relationship between FEV₁, PC₂₀, and exhaled NO correlate with a decrease in airway inflammation. The study group was small but continues to support exhaled NO as a marker of changes in airway inflammation.

Inhaled antigens and exhaled NO

Another recently published study investigated the longitudinal changes of exhaled NO outside and during the pollen season in pollen-allergic asthmatic children.² The population studied included children known to have a seasonal allergic asthma sensitive to grass pollen. Measurements of exhaled NO and pulmonary function were made during the course of a year — before, during, and after the

pollen season. Exhaled NO was measured by a tidal breathing method. The exhaled NO values of the asthmatic children were compared with those of healthy children matched for age. Spirometry and asthma symptoms were also evaluated at each visit. The FEV₁ did not change significantly before and during the pollen season.

The study revealed a significant change in the exhaled NO in grass pollen-allergic children. The authors speculated

that measurement of exhaled NO could be a sensitive non-invasive marker of asthma disease activity.

Standardizing the technique

The methods for measuring exhaled NO include single-breath (SB) and tidal-breathing (TB). A European Respiratory Society task force recently reported guide-

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lines for standardization of both methods in order to compare results from various laboratories.³ The task force studied NO values measured with SB and TB methods in subjects with asthma or chronic obstructive pulmonary disease (COPD) and in healthy subjects. The influence of smoking in asthma was also assessed, as well as the differences

between groups. NO concentrations differed substantially between both methods and between study groups. The nitric oxide values of the single-breath and tidal-breathing methods are not interchangeable. Although the data are not interchangeable, both methods can be used to measure differences between groups.

In addition to differences in methods, there may also be measurement conditions that potentially influence the exhaled NO levels. One of these conditions is ambient NO.

Exhaled NO levels were measured in 47 stable asthmatic children matched for gender and age

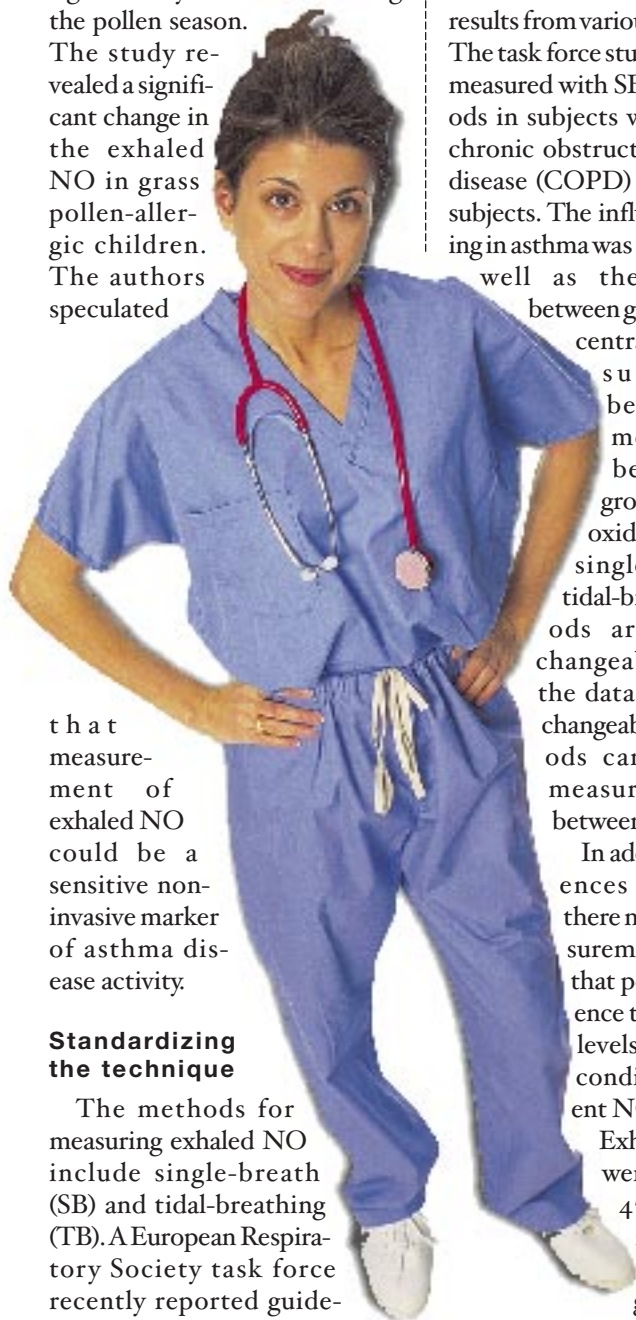
to healthy children.⁴ The tidal breathing method was used with sampling at the expiratory side of the mouthpiece. The steady-state NO levels were recorded. Measurements were randomly performed breathing ambient air or NO-free air from a closed circuit.

The study confirmed that exhaled NO values of asthmatic children are significantly higher than in healthy controls. When breathing ambient air, the NO levels were significantly affected. The authors recommend using a tidal breathing method with the inhalation of NO-free air.

Diffusing capacity and inhaled NO

Dean Hess, PhD, RRT, FAARC, discussed another diagnostic application of inhaled NO at the 1998 AARC International Respiratory Congress. Dr. Hess outlined a study currently underway at Massachusetts General. The intent of the study is to evaluate inhaled NO in place of carbon monoxide as a diagnostic agent for diffusing capacity studies. The patient population they chose to study is mechanically ventilated patients with acute respiratory distress syndrome (ARDS).

The hemoglobin affinity for NO is approximately 1,000 times that of carbon monoxide. The study poses the question: "Can the measurement of



DLNO be useful in mechanically ventilated patients with ARDS?" Therapists measure inspiratory and expiratory flow with a flow sensor at the airway and measure NO concentration on inspiration, expiration, and end-tidal. At the time of Dr. Hess's lecture last November, studies had been completed on five patients. This study is an excellent example of how therapists can apply the knowledge gained concerning inhaled NO in ARDS to investigate another application.

Further study needed

Exhaled NO levels appear to be an index of airway inflammation and a marker of a therapeutic response in bronchial asthma.^{5,6,7} These studies support the monitoring of exhaled NO in acute and chronic lung inflammation. The application of this tool related to current methodologies and outcomes needs further study before it can be recommended as a standard noninvasive monitor of pulmonary inflammation.

Respiratory therapists must continue to investigate the tools available to diagnose and monitor asthma and other chronic respiratory diseases. They must also be able to apply the knowledge gained in inhaled NO studies to other applications. Pulmonary diagnostics will continue to span new horizons as different applications of nitric oxide are investigated. 🐾

Exhaled NO levels appear to be an **index** of **airway inflammation**

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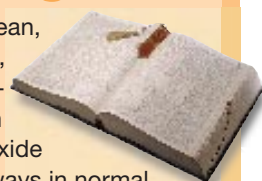
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additional reading

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Inhaled NO

See the February and March 1999 issues of **RESPIRATORY CARE Journal** for in-depth coverage of the September 1998 AARC Journal Conference on inhaled nitric oxide.