

## Elevated Carboxyhemoglobin in Active Asthma and Allergic Rhinitis as Measured by Pulse CO-Oximetry

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Elevated levels of exhaled carbon monoxide have been reported in patients with active or persistent asthma or allergic rhinitis. With the recent availability of a noninvasive pulse CO-Oximeter that measures carboxyhemoglobin, measurements were made on healthy clinic staff as well as children with controlled or active asthma and asymptomatic or active allergic rhinitis to assess whether this test might have applicability in these diseases. Carboxyhemoglobin (SpCO%) was measured by a pulse CO-Oximeter during an initial clinic assessment of patients by a single physician in a Pediatric Pulmonary Clinic. Fifty-one patients with uncontrolled asthma (average age 7.8 years) had an average SpCO% of 4.8%, and 87 patients with controlled asthma (average age 8.8 years) had an average SpCO% of 0.3%, a significant difference,  $P < 0.001$ . Seven patients with vocal cord dysfunction (average age 13.6 years) had an average SpCO% of 0.43%. In regard to allergic rhinitis, 122 symptomatic patients (average age 6.9 years) had an average SpCO% of 7.3%, while 40 asymptomatic patients (average age 7.4 years) had an average SpCO% of 1.5%,  $P < 0.001$ . These preliminary observations suggest that SpCO% may be a useful, noninvasive measure of asthma or allergic rhinitis activity.

### Introduction

IN ADDITION TO environmental carbon monoxide exposure, carbon monoxide may be endogenously produced by heme oxygenase, an inducible stress protein, which is activated in numerous inflammatory diseases, including pulmonary diseases.<sup>1–4</sup> In many respiratory diseases, the increase in carbon monoxide production is seen in elevated carboxyhemoglobin and in increased exhaled carbon monoxide, which may be useful markers of disease activity and severity.<sup>5–8</sup> Active asthma and allergic rhinitis are among the diseases in which exhaled carbon monoxide is elevated.<sup>9–16</sup> Recently, a noninvasive pulse CO-Oximeter that measures carboxyhemoglobin (SpCO%) has become commercially available. To become familiar with its use in a Pediatric Pulmonary and Cystic Fibrosis Center, measurements were made and retrospectively compared with the clinical status of patients with various pulmonary diseases: in this report, children with uncontrolled and controlled asthma and allergic rhinitis.

### Methods

Observations were made from March through October 2009 on consecutive patients of one physician (LEK). Carboxyhemoglobin (SpCO%) was measured by the Rainbow-SET Rad-57 Pulse CO-Oximeter, which allows for a range of  $\pm 2\%$  (Masimo, Inc., Irvine, CA).<sup>17</sup> A weight-appropriate sen-

sor was placed on a finger for 30 seconds to allow equilibration. A clinic nurse measured and recorded the value along with vital signs and pulse oximetry at the beginning of the visit. Asthma was diagnosed in patients, and the patients with asthma were treated in accordance with the recommendations of the Expert Panel Report 3.<sup>18</sup> Asthma control was assessed using the Asthma Control Test<sup>19</sup>: a score of  $>20$  was considered good control. Vocal cord dysfunction (VCD) was diagnosed by published criteria<sup>20</sup> and lack of response to asthma therapy. As VCD usually has a behavioral or neurological etiology rather than an inflammatory one,<sup>20</sup> it served as an control group with pulmonary symptoms. Allergic rhinitis diagnosis was based on nasal mucosa exam and positive allergy skin tests or elevated serum IgE RAST testing to environmental allergens. The clinical status was assessed by the published criteria.<sup>21</sup> Patients with a known history of passive smoke exposure were excluded. Statistical analysis of controlled versus uncontrolled asthma or allergic rhinitis patients was done with the Mann-Whitney  $U$  test. As this study presents data analyzed retrospectively, this study was submitted to and exempted from review by the Upstate Medical University Institutional Review Board.

### Results

Fifty-one patients (31 boys) with uncontrolled asthma (average age  $7.8 \pm$  standard deviation 4.2 years) had an

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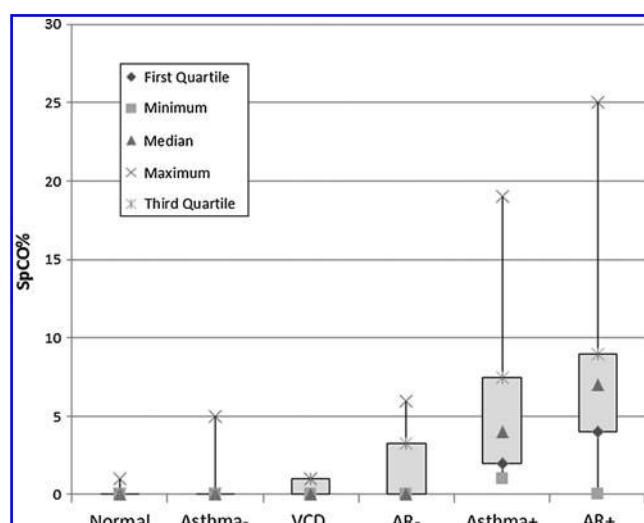


**FIG. 1.** Median SpCO% and interquartile range (IQR) for these patients: Normal: healthy control ( $n=23$ ); asthma: asymptomatic, controlled asthma ( $n=87$ ); VCD: vocal cord dysfunction ( $n=7$ ); rhinitis-: asymptomatic allergic rhinitis ( $n=40$ ); asthma+: symptomatic, uncontrolled asthma ( $n=51$ ); rhinitis+: symptomatic allergic rhinitis ( $n=122$ ). The difference between controlled and uncontrolled asthma and allergic rhinitis was significant at the  $P<0.001$  level.

average SpCO% of  $4.8\% \pm 3.5\%$  (median=4). Eighty-seven patients (56 boys) with controlled asthma ( $8.8 \pm 4.3$  years) had an average SpCO% of  $0.3\% \pm 0.8\%$  (median=0) ( $P<0.001$ ). Seven patients (1 boy) with VCD ( $13.6 \pm 2.2$  years) had an average SpCO% of  $0.4\% \pm 0.5\%$  (median=0). One hundred twenty-two patients (76 boys) with symptomatic allergic rhinitis ( $6.9 \pm 3.8$  years) had an average SpCO% of  $7.3\% \pm 4.2\%$  (median=7), whereas 40 patients (26 boys) with asymptomatic allergic rhinitis ( $7.4 \pm 4.3$  years) had an average SpCO% of  $1.5\% \pm 2\%$  (median=0) ( $P<0.001$ ). To make sure that there was no confounding environmental influence during clinic visits, 23 healthy clinic staff or pediatric residents in the clinic served as a control group with an average SpCO% of  $0.1 \pm 0.3$  (median=0). Results are described in Fig. 1, using the median and interquartile range.

## Discussion

Similar to studies of exhaled carbon monoxide, the observations reported herein suggest that endogenous carbon monoxide as measured by a noninvasive pulse CO-oximeter of carboxyhemoglobin is significantly elevated in children with symptomatic asthma and allergic rhinitis in comparison to their respective asymptomatic conditions and to controls. These initial findings are tentative and require prospective, controlled confirmation. One of the major limitations of these observations is that an insufficient number of repeat patient visits were available to assess changes in SpCO% in relationship to changes in clinical status. Nevertheless, these results seem tantalizingly enough to encourage further studies. Results, if confirmed, also suggest that the activity of endogenous heme oxygenase activity may be measured by an easy, noninvasive test, which may be useful in monitoring inflammatory diseases in which heme oxygenase may play a role.

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## Author Disclosure Statement

The author does not have any actual or potential financial or other conflict of interest.

## References

- Wu L, Wang R. Carbon monoxide: endogenous production, physiological functions, and pharmacological applications. *Pharmacol Rev* 2005; 57:585–630.
- Otterbein LE, Choi, AMK. Heme oxygenase: colors of defense against cellular stress. *Am J Physiol Lung Cell Mol Physiol* 2000; 279:L1029–L1037.
- Ryter SW, Choi AMK. Heme oxygenase-1/carbon monoxide. From metabolism to molecular therapy. *Am J Respir Cell Mol Biol* 2009; 41:251–260.
- Ghosh S, Gal J, Marczin N. Carbon monoxide: endogenous mediator, potential diagnostic and therapeutic target. *Ann Med* 2010; 42:1–12.
- Yasuda H, Yamaya M, Yanai M, Ohru T, Sasaki H. Increased blood carboxyhaemoglobin concentrations in inflammatory pulmonary diseases. *Thorax* 2002; 57:779–783.
- Fredenburgh LE, Perrella MA, Mitsialis SA. Heme oxygenase-1: a multifaceted triple-threat molecule. The role of heme oxygenase-1 in pulmonary disease. *Am J Respir Cell Mol Biol* 2007; 36:158–165.
- Gajdócsy R, Horváth I. Exhaled carbon monoxide in airway diseases: from research to clinical relevance. *J Breath Res* 2010; 4:047102.
- Babusikova E, Jesenak M, Durdik P, Dobrota D, Banovcin P. Exhaled carbon monoxide as a new marker of respiratory diseases in children. *J Physiol and Pharmacol* 2008; 59:Suppl 6, 9–17.
- Yamara M, Sekizawa K, Ishizuka S, Monma M, Sasaki H. Exhaled carbon monoxide levels during treatment of acute asthma. *Eur Respir J* 1999; 13:757–760.
- Yilmaz O, Ozturk F, Bakirtas A, Cengizlier R, Turkas I. Exhaled carbon monoxide levels in children with bronchial asthma. *Pediatr Asthma Allergy Immunol* 2003; 16: 155–162.
- Grover RS, Kumar R. Exhaled carbon monoxide levels: as a marker of clinical severity and control of asthma. *J Asthma* 2008; 45:677–680.
- Zhang J, Yao X, Yu R, Bai J, Sun Y, Huang M, Adcock IM, Barnes PJ. Exhaled carbon monoxide in asthmatics: a meta-analysis. *Respir Res* 2010; 11:50.
- Ohara Y, Ohara T, Ohru T, Morikawa T, Asamura T, Sasaki H, Arai H. Exhaled carbon monoxide levels in preschool-age children with episodic asthma. *Pediatr Int* 2012; 54: 227–232.
- Shaoqing Y, Ruxin Z, Yingjian C, Jianqiu C, Yanshen W, Genhong L. A meta-analysis of the association of exhaled carbon monoxide on asthma and allergic rhinitis. *Clin Rev Allergy Immunol* 2011; 41:67–75.
- Monma M, Yamaya M, Sekizawa K, Ikeda K, Suzuki N, Kikuchi T, Takasaka T, Sasaki H. Increased carbon monoxide in exhaled air of patients with seasonal allergic rhinitis. *Clin Exp Allergy* 1999; 29:1537–1541.
- Andersson JA, Uddman R, Cardell LO. Increased carbon monoxide levels in the nasal airways of subjects with a history of

- seasonal allergic rhinitis and in patients with upper respiratory tract infection. *Clin Exp All* 2002; 31:224–227.
17. Barker SJ, Curry J, Redford D, Morgan S. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry. A human volunteer study. *Anesthesiology* 2006; 105:892–897.
  18. EPR-3. Expert Panel Report 3: guidelines for the diagnosis and management of asthma (EPR-3 2007). Bethesda: US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program; 2007. NIH publication no. 08–5846.
  19. Liu AH, Zeiger R, Sorkness C, Mahr T, Ostrom N, Burgess S, Rosenzweig JC, Manjunath R. Development and cross-sectional validation of the childhood asthma control test. *J Allergy Clin Immunol* 2007; 119:817–825.
  20. Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. *Pediatrics* 2007; 120:855–864.
  21. Spector SL, Nicklas RA, Chapman JA, Bernstein IL, Berger WE, Blessing-Moore J, Dykewicz MS, Fineman SM et al. Symptom severity assessment of allergic rhinitis: part 1. *Ann Allergy Asthma Immunol* 2003; 91:105–110.

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