

patients need treatment with steroids, antihistamines, fluid resuscitation, possibly epinephrine, oxygen, and antithrombotics before being transferred to the cardiac catheterization laboratory.⁶

Recently, Ridella et al⁷ reviewed the literature and demonstrated that most cases have been treated with steroids (76%), histamine₁-blockers (70%), nitroglycerin (47%), and histamine₂-blockers (35%). Epinephrine was used only in 23% of the cases. Aspirin was used in 18% of the cases.

Desensitization is the only treatment that significantly decreases the risk of life-threatening allergic reaction in the case of a further sting. In stinging insect-induced anaphylaxis, the diagnosis should be confirmed because desensitization is indicated for its high probability of success (approximately 98%).⁶ Heart failure is a commonly accepted contraindication to immunotherapy, but in these patients another anaphylaxis may be fatal. Some administered specific immunotherapy to patients with postmyocardial ventricular systolic dysfunction, without any circulatory adverse effects.⁸

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Measurement of exhaled nitric oxide in the evaluation for eosinophilic esophagitis in children

Eosinophilic esophagitis (EoE) is a chronic immune-/antigen-mediated disease consisting of eosinophilic-predominant infiltration of the esophagus.¹ Symptoms are related to esophageal dysfunction and can include dysphagia, chest pain, food impaction, feeding dysfunction, anorexia, and early satiety. Some patients do not have these symptoms, and instead have gastroesophageal reflux disease–like symptoms of abdominal pain and vomiting. Most are recalcitrant to proton pump inhibitor medical treatment, but others can be proton pump inhibitor (PPI)-responsive. The histologic characteristics found in the esophageal biopsy are mucosal eosinophilia, eosinophilia microabscesses, superficial layering of eosinophils, and extracellular eosinophil granule deposition.² Thus, EoE is a clinicopathologic disease. Multiple esophageal biopsies during upper endoscopy are required to help in diagnosis, but it is an invasive procedure performed under anesthesia. The availability of a rapid, real-time, noninvasive, clinical marker for EoE would be mutually beneficial to the physician and the patient.³

Exhaled nitric oxide (eNO) is a non-invasive marker of airway inflammation used clinically to monitor asthma inflammation. It is obtained from the patient during oral exhalation using an Food and Drug Administration-approved nitric oxide analyzer. It has been shown in multiple studies to be indicative of inflammation of the airways specifically from the eosinophil and epithelium.^{4,5}

The use of eNO as a marker of inflammation for EoE has not been reported in the literature. We proposed to measure eNO in patients undergoing upper endoscopy by their pediatric gastroenterologist because of chronic upper gastrointestinal (GI) symptoms. The comparison of each upper endoscopy biopsy result with the corresponding eNO level measured at our allergy clinic was performed.

Our aim was to measure eNO in patients with biopsy-proven EoE, biopsy-proven gastroesophageal reflux (non-EoE), and normal GI biopsy (control). Each specialist was blinded to the other specialist's test result.

Fifty-five patients (mean age, 12 ± 5 years, 30 male) who were to have an upper endoscopy performed for chronic GI symptoms suspicious for EoE were selected. Patients selected had no dietary changes and no steroid use 4 weeks before any measurements. Patients with history or current symptoms of persistent asthma were excluded from the study because of a possible increase in eNO from the lower airways. Patients who were taking allergy or asthma medications, including inhaled or nasal steroids, leukotriene modifiers, and bronchodilators, were excluded as well. All patients performed eNO, measured in parts per billion, on an MINO portable analyzer (Aerocrine, Sweden). All measurements of eNO were performed as per ATS Guidelines for pediatric patients.⁶ The normal eNO cutoff of <15 ppb that was used in our study has been already established and is based on age and height of the patient.⁷ Results of eNO were compared with the endoscopy biopsy results. Additionally, spirometry measurements were performed to evaluate any possible underlying reactive airways. The spirometry results of forced expiratory volume in 1 second (FEV₁), FEV₁/forced vital capacity, and peak expiratory flow rate were collected.

Biopsy results showed that 18 of the 55 total patients had EoE, 23 patients had gastritis, and 14 patients had no inflammation. The range of eosinophils found on biopsy in the EoE-positive group ranged from 15 to 100/high-power field. Nine of the 18 EoE biopsy-proven patients had normal eNO levels, whereas the remaining 9 had elevated eNO, ranging from 16 to 80 ppb. Thirty-two patients had normal eNO and no EoE on biopsy. These results show a high specificity (>87%) and negative predictive value (78%) (Fig 1). Eleven of the 14 total patients (with and without EoE) with elevated eNO had decreased FEV₁ or bronchodilator reversibility on spirometry.

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		ESOPHAGEAL BIOPSY		Total
		EoE-bx Positive (≥ 15/hpf)	EoE-bx Negative (< 15/hpf)	
FRACTIONAL EXHALED NITRIC OXIDE (parts per billion)	Elevated eNO (≥ 15ppb)	9 (9/18= 50%) Sensitivity	5	14
	Normal eNO (< 15ppb)	9	32 (32/37= 87%) Specificity	41 (32/41= 78%) Negative PV
Total		18	37	55

Bx = Biopsy; EoE = Eosinophilic Esophagitis; eNO = Exhaled Nitric Oxide; hpf = high power field; PV = Predictive Value; ppb = parts per billion

Fig 1. Sensitivity and specificity table of esophageal biopsy for eosinophilic esophagitis and exhaled nitric oxide.

We have shown that measurement of eNO in the normal range has a good specificity for screening out children for EoE, however, eNO is poor at identifying EoE. Testing with eNO may have clinical utility during the evaluation of EoE. When the eNO level was normal, this correctly identified more than 86% of those who did not have EoE. The measurement of eNO does not replace the required diagnostic test of an upper endoscopy with biopsy of the esophagus. Nevertheless, a normal eNO could be helpful in the approach of those EoE-suspicious children that do not have asthma, but elevated measurements were not sensitive for EoE in children. Elevated eNO levels corresponded more with respiratory airway inflammation and not with esophageal inflammation.

Limitations to our results are that this was a small pilot study in only children with suspected EoE that were referred to an allergy/immunology clinic. No children with asthma or those on PPI therapy were studied due to the confounding effect this would have on eNO. Future directions for use of eNO in EoE should be targeted to those with elevated measurements during treatment interventions.

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A case of difficult-to-treat eosinophilic asthma controlled with clarithromycin

Difficult-to-treat asthma is a major health problem that has been intensively researched. Patients with difficult-to-treat asthma have the highest incidence of hospitalizations and emergency department visits,¹ have the greatest risk of fatal asthma attacks,² and use up to 3 times more resources.³ Previous studies of patients using macrolides for 6 to 16 weeks have reported lung function and symptom improvement in asthma patients with evidence of *Chlamydia pneumoniae* or *Mycoplasma pneumoniae* infection in the upper or lower airways.⁴ Besides antibiotic effects, macrolides have anti-inflammatory and immunomodulating properties. For instance, macrolides regulate the production

of the proinflammatory cytokines tumor necrosis factor α and interleukin 8 (IL-8) by decreasing the binding of transcription factors NF- κ B and AP-1.⁵ Macrolides effectively inhibit IL-8 release and induce apoptosis in eosinophils.^{6,7} Long-term treatment with macrolides is recommended in a few lung diseases, such as diffuse panbronchiolitis, cystic fibrosis, posttransplantation bronchiolitis obliterans, and chronic obstructive pulmonary disease.^{4,8} Results from a recent randomized controlled trial demonstrated that azithromycin taken for 1 year decreased exacerbations of chronic obstructive pulmonary disease.⁸ The authors attributed these results to the antibacterial properties of this antibiotic; however, one must assume that the immunomodulatory effects of macrolides played an important role as