Title: "Non-Invasive Markers of Lung Disease in Exhaled Breath"

Christopher H. Fanta, M.D.

Analysis of chemicals in exhaled breath has the potential to diagnose diseases of the airways and lung parenchyma without tissue biopsy. On-going investigations are exploring the value of exhaled breath analysis in asthma, pneumonia, and lung cancer. In this presentation, the value of measurement of exhaled nitric oxide gas in the diagnosis and assessment of asthma will be considered.

Airway narrowing in asthma is caused by constriction of airway smooth muscles and swelling/inflammation of the airway walls. Traditional assessment of asthma relies on measurement of expiratory airflow as an indicator of airway narrowing, without the ability to estimate the contribution of untreated airway inflammation. A marker of on-going airway inflammation in asthma would be clinically useful. Nitric oxide is generated from arginine and oxygen by the action of nitric oxide synthase. Inducible nitric oxide synthase is upregulated in the presence of airway inflammation, in particular eosinophilic airway inflammation as occurs in asthma (and eosinophilic bronchitis). Using real-time electrochemical analysis, clinically available nitric oxide analyzers (using scrubbers to remove ambient nitric oxide) can measure the nitric oxide concentration in the exhaled breath of humans in parts per billion. Healthy individuals typically have values of fractional exhaled nitric oxide (FeNO) of less than 40 ppb. An FeNO >40 ppb suggests abnormal airway eosinophilic inflammation. Inhalation of anti-inflammatory corticosteroids reduces airway eosinophilia and suppresses FeNO. Measurement of FeNO is useful in the diagnosis of asthma; predicting a favorable response to treatment with inhaled steroids; monitoring airway inflammation over time in asthma; detecting medication non-compliance; and identifying patients who may benefit from targeted anti-eosinophilic biologic therapies. Important limitations of the test include a broad overlap in FeNO values between healthy and asthmatic individuals; and the rapid suppression of FeNO by inhaled corticosteroid drugs in the absence of full control of airway inflammation.