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Title: Relationship between phenotypic characteristics of children with sickle cell disease and airway nitric oxide levels

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Body: Background: Children with sickle cell disease (SCD) have evidence of airflow limitation on spirometry, and evidence for increased airway nitric oxide (NO) levels. Objective: To determine the relationship between phenotypic characteristics (atopy, asthma, acute chest syndrome (ACS), pulmonary function test abnormalities) and airway NO levels in children with SCD. Methods: Children with SCD were recruited during visits for routine annual pulmonary function testing. Subjects completed ISAAC/medical questionnaires, skin prick testing for aeroallergen sensitization, and pulmonary function testing. Nasal (NNO) and the fraction of exhaled NO (FENO) were measured. Subjects were classified by phenotypic characteristics, and NNO and FENO compared between groups, using Mann-Whitney tests. Results: 154 children participated. Seventy-six (49%) were male. Mean(±SD) age was 12.6±3.3 years. Hemoglobin levels were 96.0±18.3 g/L. FVC, FEV_1, and FEF_{25-75} were 86.7±14.0, 84.7±15.0, and 84.4±30.0 percent predicted, respectively. NNO and FENO were 890±387 and 17.9±15.9 ppb. Eighty (52%) subjects were atopic. Thirteen (8%) subjects taking asthma medication, and 38 (25%) with an asthma diagnosis or wheezing, were classified as asthmatic. Twenty (13%) subjects had a significant bronchodilator response (≥12%) in FEV_1 or FVC. Seventy-three (47%) subjects reported previous ACS or pneumonia. No significant differences were seen in NNO or FENO between any groups compared. Conclusions: Airway NO measurements did not correlate with any of the phenotypic characteristics evaluated in this cohort of children with SCD, and therefore may not be a meaningful tool in the assessment of SCD lung disease.