



Guest Editorial

Understanding the biology of disease in underserved children with asthma

The missing piece of the health disparity puzzle



African American children are disproportionately affected by asthma compared with non-Hispanic white children. Recent data from the Centers for Disease Control and Prevention indicate that asthma prevalence rates (10.3% vs 7.8%) remain higher among non-Hispanic black children than non-Hispanic white children, and non-Hispanic black children are almost 3 times as likely to die of asthma as non-Hispanic white children.¹ Studies have also found that African American children have more frequent and burdensome asthma symptoms and use emergency department (ED) care more frequently than white children.² Socioeconomic factors (eg, family income, medical insurance type, parental educational level) have been associated with observed asthma-related disparities experienced by racial/ethnic minority groups. However, socioeconomic factors have not accounted for the entirety of gaps in asthma outcomes between racial groups.^{3,4} Even when numerous socioeconomic factors are taken into account, the disparity remains in African American children bearing more disease-related burden than white children.³ Intrinsic biological differences that may or may not be affected by socioeconomic factors differ among racial groups with asthma.⁵ For example, even among children of similar socioeconomic backgrounds, African American children with asthma tend to have more allergic disease.⁶ These data suggest that other factors related to actual disease pathophysiologic mechanisms may differ by race, which may be influenced by non-socioeconomic factors, such as genetic ancestry.

Asthma is now recognized as a heterogeneous disease composed of phenotypes that differ in pathophysiologic factors, natural history, and response to therapeutic interventions. Methods to better identify phenotype classifications that are meaningful in guiding management strategies are being explored. Recently, statistical cluster analysis techniques have been used to identify differences among patients with asthma in classification of asthma phenotypes. Statistical clustering has been described as “the process of partitioning individual items into successively smaller and smaller numbers of similar groups.”⁷ The purpose of cluster analysis techniques is to identify similarities within a group of a heterogeneous items or individuals to allow more homogeneous subgroups to be formed. Statistical clustering analyses among children and adults with asthma have used variables such as clinical symptoms (eg, symptom frequency), biomarkers (eg, eosinophil count, exhaled nitric oxide), disease trajectory (eg, age at onset,

duration of asthma), and comorbidities (eg, body mass index). Studies from large consortium-based studies, such as the Severe Asthma Research Program of the National Heart, Lung, and Blood Institute and the Childhood Asthma Management Program, have identified distinctions among children and adults with asthma that allow cluster phenotyping.^{8–11} In one study of the Severe Asthma Research Program child cohort, agglomerative cluster analysis was conducted among 161 children with asthma and identified 4 distinct clusters based on clinical and biological variables (eg, age at disease onset, allergen skin test results, eosinophil counts, lung function).⁸ Within this cohort, race was disproportionately represented among the 4 clusters. African American children comprised 51% of the entire cohort in this study but made up 83% of the “early onset atopic asthma with advanced airflow obstruction” cluster. This cluster was characterized by the highest exhaled nitric oxide levels, low lung flow with limited postbronchodilator reversibility, greater bronchial responsiveness to methacholine, highest daily inhaled corticosteroid use, and highest asthma-related health care use. A recent study conducted among children living in low-income urban environments as part of the National Institute of Allergy and Infectious Diseases Inner-City Asthma Consortium Asthma Phenotypes in the Inner City study also identified cluster phenotypes within a cohort of children with asthma. These investigators conducted hierarchical clustering analysis using 50 clinical and demographic variables along with asthma- and allergy-related biomarkers. Similarly, African American children were unequally distributed among the 5 phenotype clusters identified. African American children comprised 66% and 77% of clusters D and E, respectively. Cluster D was characterized by a higher degree of allergic sensitization, with the most participants with allergic rhinitis and highest rhinitis medication use despite intermediate rhinitis symptoms. Cluster E was characterized by the highest allergic inflammation, asthma, and rhinitis symptoms along with the highest asthma and allergy treatment levels and most impaired pulmonary physiologic findings.¹¹

In this issue of the *Annals of Allergy, Asthma, and Immunology*, Franklin et al¹² describe clinical features of African American children with asthma living in the Atlanta, Georgia, metropolitan area compared with white children in the same area in predicting ED use. In their study, children between the ages of 6 and 17 years who self-reported as non-Hispanic black or white with persistent asthma completed one “characterization” visit during which spirometry, allergy skin prick testing, medical history (including health care use in the previous 12 months), environmental

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exposure history, demographic, and residential geographic information was obtained. The investigators observed that African American children had higher markers of allergic disease burden (higher eosinophil percentages, higher total serum IgE, and more prevalent aeroallergen sensitization) and higher proportions of asthma-related ED use. After statistical adjustment for potential confounders, differences in predictors of ED use were identified between African American and white children. In white children, predictors of ED use included ED visit in the prior year, dust mite sensitization, and pet exposure; in African American children, predictors included ED visit in previous year, number of asthma controllers, forced expiratory volume in 1 second less than 80%, blood eosinophil counts, and mold sensitization. The lack of information on medication adherence, home environmental assessment, and nonspecific socioeconomic data in the study limited the ability of the investigators to fully adjust their findings for these important potential confounders. However, their results are in line with previous studies, including larger cluster analysis studies in which African Americans are disproportionately represented in clusters with a more significant atopic burden. Although ED use was associated with allergen sensitization in both racial groups in this study, type of allergen sensitization and markers of overall atopic disease burden differed between the 2 groups.

Overall, the current study adds to the increasing literature that suggests that intrinsic differences in asthma should be further explored within understudied racial groups, such as African American and Hispanic populations. Although these children are disproportionately affected by asthma, they are sorely underrepresented within clinical and translational studies of asthma.¹³ Few studies exist that aim to understand asthma pathophysiologic factors, genetic contributions to asthma, or therapeutic response specifically within African American or Hispanic populations. Unfortunately, analyses of racially specific characteristics of asthma, even when considered, are often performed post hoc and are underpowered to answer questions specific to understudied racial/ethnic groups. Therefore, asthma remains poorly understood in these neglected populations and disparity gaps persist. Future adequately powered and well-designed studies dedicated to fully characterizing asthma and relevant asthma phenotypes in African American and Hispanic children, genetic contributions to disease, and therapeutic response profiles are needed. To achieve this goal, funding from sources such as the National Institutes of Health must be dedicated to these types of studies. Researchers must also overcome perceived barriers to research within these populations, such as participant recruitment, because current data suggest that lack of inclusion of African American and Hispanic participants is less likely attributable to unwillingness to participate but more likely attributable to lack of inclusion and engagement by researchers.^{14,15} Along these same lines, researcher cultural competency or awareness and diversity of biomedical researchers are barriers to be addressed in conducting studies among underrepresented racial and ethnic groups. Considering recent US Census projections that 44% of children will belong to “minority” racial/ethnic groups by 2020, the lack of asthma-related knowledge among diverse populations is a critical and urgent public health concern.¹⁶ Until we devote adequate resources, engage underrepresented groups, and conduct well-designed studies among African American and Hispanic patients, the

scientific and medical communities cannot be satisfied that we have put forth full efforts to closing health disparity gaps and improving asthma outcomes in these heavily burdened and neglected populations.

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