

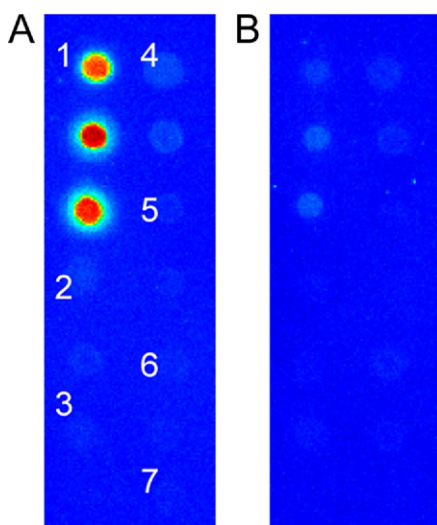


Figure 1. A, IgE to gluten hydrolysate (1) in the serum sample of a patient with anaphylactic reaction to doughnuts. There is no binding to gluten (2), gliadin (3), raw or cooked wheat (4-6), or timothy (7). B, Nonatopic serum was used as a control in the Immunospot assay.

serum was used as a control. A distinct IgE binding to 1 ingredient of doughnut (Berlinermix 20 SF), used as an enhancer, was seen in the Immunospot test. One of the components of Berlinermix 20 SF was palm oil, in which partially acid hydrolyzed gluten (Meripro 711; Syral, Aalst, Belgium) was used as an emulsifier. The SPT wheal size with hydrolyzed gluten was 10 mm, and a specific IgE binding in Immunospot was found to gluten hydrolysate but not to pure palm oil. There was no specific binding to other food allergens tested. In open food challenge, mild urticaria appeared after ingestion of 10 mg of hydrolyzed gluten and anaphylaxis after 100 mg. The result of the control test with wheat bread not containing hydrolyzed gluten was negative.

The other patient was a 14-year-old boy with a history of asthma and allergic rhinitis for many years. On the basis of SPT, he was sensitized to timothy, cat, and dog and had negative SPT reactions to wheat and gliadin. He had no food restrictions in his diet. During the last 2 years he had experienced 3 episodes of urticaria-angioedema after ingestion of doughnuts. The SPT wheal size for hydrolyzed gluten was 15 mm, and distinct, very strong IgE binding was detected in Immunospot to hydrolyzed gluten. In open food challenge, mild pharyngeal discomfort appeared after ingestion of 10 mg and 100 mg of hydrolyzed gluten and urticaria-angioedema after a dose of 150 mg.

Gluten-derived products are used in the food industry, especially in bakery products as emulsifiers.² The peptides produced by partial hydrolysis may contain highly IgE-reacting high-molecular-weight entities different from gluten-binding epitopes, likely resulting in a rearrangement of peptides issued from gluten processes.³ Hydrolyzed wheat proteins can induce unexpected immediate hypersensitivity through food ingestion.⁴ In our cases ingestion of hydrolyzed gluten was the source of severe allergic reactions in children without reaction to native wheat flour (Fig 1). The possibility of allergic reactions caused by “new” unexpected allergens, in our case allergy to jelly doughnut, needs to be kept in mind. It is important to perform a wide diagnostic setup with all individual ingredients. In addition, once confirmed as potential allergens, proper labeling of the products is warranted. In these cases

gluten hydrolysate-sensitive patients did not react to wheat or gluten, the labeling of which is mandatory in the European Union.

Our findings and results, together with preliminarily reported cases from several countries in Europe, suggest that acid gluten hydrolysate is a novel allergen that should be included in mandatory labeling of foods.

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ACCESSORY MUSCLE USE IN PEDIATRIC PATIENTS WITH ACUTE ASTHMA EXACERBATIONS

Physicians have few objective methods with which to assess the severity of acute asthma exacerbations in pediatric patients. Percent predicted forced expiratory volume in 1 second (%FEV₁) by spirometry is the accepted criterion standard but is frequently not available in acute care settings. Prior pediatric investigations have noted modest correlation of accessory muscle use with lower %FEV₁ but have not reported severity-dependent associations of accessory muscle use by muscle groups in use with %FEV₁ or hospitalization decisions.^{1,2} Because this is an easily identifiable physical finding, we sought to examine associations of individual accessory muscle groups with both %FEV₁ and hospitalization in pediatric patients with acute asthma exacerbations.

Disclosures: Dr Arnold holds 2 patents with Precision Pulsus Inc (Apnea Detection System and Method and apparatus for measuring pulsus paradoxus). Dr Hartert has received lecture fees from Merck and has received industry-sponsored grants from MedImmune.

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We prospectively enrolled participants ages 5 to 17 years with physician-diagnosed asthma and signs or symptoms of an acute exacerbation who presented to our urban, tertiary care pediatric emergency department. We defined accessory muscle use as any visible use of the scalene, sternocleidomastoid-suprasternal, intercostal, or subcostal muscles.³ Accessory muscle use was further quantified for analyses as none, 1 group, or 2 or more muscle groups to examine severity-response relationships. The clinical team determined need for hospitalization and was masked to our assessment of accessory muscle use and %FEV₁ values.

We assessed associations of pretreatment accessory muscle use with simultaneous %FEV₁ for participants meeting all American Thoracic Society (ATS) spirometry criteria and with hospitalization for the entire cohort.^{4,5} We used the Kruskal-Wallis and χ^2 tests, respectively, for these analyses and a multivariable model that adjusted for age, sex, and race. The study protocol was approved by our institutional Human Research Protection Program.

Between April 2008 and August 2010, 672 eligible patients were enrolled and 604 unique participants were included for analysis. Median (interquartile range [IQR]) age was 8.75 (6.8-11.3) years, 61% of participants were male, and 57% were African American. Global Initiative for Asthma chronic control levels for the preceding 3-month period were as follows: controlled, 104 (17%); partially controlled, 198 (33%); and uncontrolled, 302 (50%). Disposition included 77.5% discharged to home, 16% admitted to the floor, and 6.5% admitted to the pediatric intensive care unit. Of the entire cohort (n = 604), accessory muscle use was noted in 318 (53%).

All participants attempted spirometry, and 350 (58%) met all ATS acceptability criteria. These participants were less likely to be hospitalized (19% vs 28%; $P = .01$) and, if hospitalized, were less likely to be admitted to the pediatric intensive care units (4% vs 10%; $P = .007$). There was no increase in the odds of obtaining spirometry meeting ATS criteria vs not meeting ATS criteria with use of any (odds ratio [OR], 1.18; 95% confidence interval [CI], 0.84-1.65) or 2 or more groups of accessory muscles vs none (OR, 1.25; 95% CI, 0.83-1.90). Median (IQR) %FEV₁ for this group (n = 350) was 52% (38%-74%). Median (IQR) %FEV₁ was 71% (56%-86%) in those without use of any, 48% (37%-63%) in those with use of 1, and 35% (25%-44%) in those with use of 2 or more accessory muscle groups ($P = .001$, Kruskal-Wallis; Fig 1). The association of any accessory muscle use with decreased %FEV₁ remained after controlling for age, sex, and race in multivariable linear regression ($\beta = -28$, 95% CI, -32 to -24; $P = .0001$).

Hospitalization occurred in 33 (12%) of those without, 44 (27%) of those with use of 1 group, and 59 (38%) of those with use of more than 1 accessory muscle group ($P = .001$, Pearson test). Accessory muscle use (any vs none) remained associated with increased odds of hospitalization when adjusted for age, sex, and race in the multivariable model (OR, 4.2; 95% CI, 2.6-6.6; $P < .001$).

Accessory muscle use in pediatric patients with acute asthma exacerbations is associated with statistically significant and clinically important decreases of %FEV₁ and with greater likelihood of hospitalization. These associations are strengthened by their severity-dependent nature. Accurate accessory muscle use assessment is of value to physicians because it is simple, low cost, relatively objective, and physiologically plausible because it is indicative of increased work of breathing. In addition, participants with accessory muscle use are as likely to undergo ATS criteria spirometry as those without accessory muscle use, suggesting that efforts to obtain this test of lung function are warranted.

Limitations include that 42% of participants could not perform spirometry due to young age or severity of illness. This may have

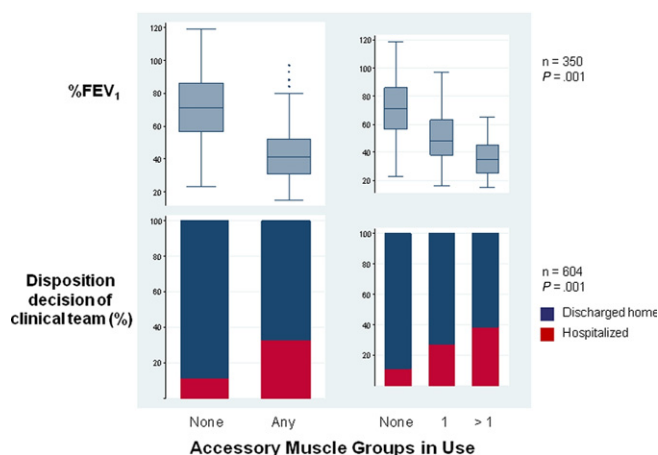


Figure 1. Percent predicted FEV₁ (%FEV₁) and emergency department disposition according to use of none, one, or more than one group of accessory muscles before treatment. Top: Box comprise IQR with median lines across boxes. Fences are 1.5 value of IQR beyond IQR bounds. Bottom: Disposition of entire study cohort according to accessory muscle use.

introduced bias, but had these studies been available, the values of %FEV₁ with accessory muscle use would likely have been lower.

Concern has long been expressed that new imaging and laboratory technology may replace physicians' use of and skill in the physical examination.^{6,7} Indeed, Sir William Osler's teaching maxim "The whole art of medicine is in observation" is relevant to the findings of our study.⁸ Observation for use of accessory muscles has clinical value, should be made during the care of patients with acute asthma exacerbations, and is associated with significant physiologic and clinical outcomes.

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TOBACCO EXPOSURE AND ASTHMA MORBIDITY IN PUERTO RICANS AND MEXICAN AMERICANS

Puerto Ricans on both the island and mainland experience the highest asthma morbidity rates of any race and ethnicity, whereas Mexican Americans have the lowest.^{1–3} Using a biologic measure of tobacco exposure, we attempted to determine whether the differences in asthma morbidity between these 2 ethnic groups were due to cigarette smoke exposure. The study protocol was approved by the Chicago public and Catholic schools and the institutional review boards at *Censored for Review*.

This exploratory, cross-sectional analysis was based on the English-only inception cohort established by the Chicago Initiative to Raise Asthma Health Equity study.⁴ Pulmonary obstruction was assessed using prebronchodilator forced expiratory volume in 1 second/functional vital capacity using the SpiroPro spirometer (Jaeger a subsidiary of VIASYS Healthcare/Cardinal-Health, Conshohocken, Pennsylvania).^{4,5} Saliva was collected using a collection pad (Quantisal; Immunalysis, Pomona, California). The cotinine concentration was extracted using an enzyme-linked immunosorbent assay (Salimetrics, State College, Pennsylvania) with a lower limit of detection of 0.05 ng/mL. Exclusions included participants reporting mixed ethnicity (15 children and 6 adults), those missing cotinine measurements (9 children and 13 adults), and children with cotinine levels greater than 8 mg/mL (1 child).

We defined a severe asthma exacerbation in the past year as experiencing an asthma episode that required spending 1 or more nights in the hospital, going to an emergency department, or requiring urgent medical care at the physician's office. Asthma symptom frequency was measured as the sum of days and nights in the past 2 weeks that the participant experienced wheezing, chest tightness, cough, or shortness of breath. Child quality of life was measured using a modification of the Children's Health Survey for Asthma.^{4,6,7}

The sample of 101 children and 70 adults is described in the Table 1. Half of the Puerto Rican and Mexican American children had cotinine levels between 1 and 8 ng/mL, suggesting recent environmental tobacco smoke exposure.⁸ All of the adults reporting that they did not smoke had cotinine levels less than 1 ng/mL; 16 of the 17 adults reporting that they currently smoked had

salivary cotinine levels greater than 8 ng/mL. Bivariate analyses were conducted between the descriptive variables and asthma morbidity outcomes. For children, asthma symptoms were associated with caregiver age ($P = .004$). Caregiver quality of lifewas associated with caregiver age, home ownership, and ethnicity ($P = .02$, $P = .01$, and $P = .006$, respectively). For adults, severe asthma exacerbations were associated with home ownership, self-reported smoking, and cotinine levels ($P = .02$, $P = .04$, and $P = .046$, respectively).

Independent predictors of the asthma outcomes were determined using backward stepwise elimination, retaining variables in the final models with $P < .05$. (Stata/IC 10.1 for Windows; StataCorp, College Station, Texas) Logistic regression was used for severe asthma exacerbations, negative binomial regression for asthma symptoms, and linear regression for caregiver asthma quality of life. For children, we looked at 3 outcomes. Both Puerto Rican ethnicity (odds ratio [OR], 2.61; 95% confidence interval [CI], 1.07–6.33) and private insurance (OR, 2.49; 95% CI, 1.02–6.12) independently predicted increased severe asthma exacerbations. Increased caregiver age predicted fewer asthma symptoms (incidence rate ratio [IRR], 0.92; 95% CI, 0.89–0.96). Puerto Rican ethnicity predicted lower caregiver asthma quality-of-life score (IRR, -0.32 ; 95% CI, -0.63 to -0.01), whereas increased caregiver age predicted a higher score (IRR, 0.03; 95% CI, 0.01–0.05). An interaction term for ethnicity $\times$ cotinine was not significant. For adults, 2 outcomes were analyzed. Severe asthma exacerbations were associated with Puerto Rican ethnicity (OR, 5.18; 95% CI, 1.29–20.84) and pulmonary obstruction (OR, 0.22; 95% CI, 0.05–0.94). Cotinine levels greater than 8 ng/mL, compared with levels less than 1 ng/mL, predicted increased severe asthma exacerbations (OR, 6.86; 95% CI, 1.43–32.85). No characteristics were independently associated with symptom frequency in adults.

In other analyses, we replaced cotinine with reported household smoking (child models) or current smoking (adult models). For children, the association with Puerto Rican ethnicity diminished and home ownership became a significant predictor of increased asthma symptoms. Other models did not change.

To our knowledge, this is the first study to report multiple indicators of asthma morbidity and objective markers of tobacco exposure for both Puerto Rican and Mexican American children and adults. In children, ethnicity remained a strong predictor of caregiver quality of life and severe asthma exacerbations despite controlling for environmental tobacco smoke and sociodemographics. In adults, ethnicity remained a strong predictor of severe asthma exacerbations after controlling for cotinine, pulmonary obstruction, and other sociodemographic characteristics. These analyses, although limited by the small sample size and exclusion of Spanish-speaking individuals, suggest that the disparities in asthma morbidity between Puerto Ricans and Mexican Americans cannot be fully explained by smoking behaviors. Other behavioral or biological factors should be investigated to explain adverse asthma outcomes in these populations.

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