RESULTS. The rate of pertussis immunization was the same in both groups (65.2% cases versus 68.9% controls, \( P = .172 \)). Nearly 80% of cases were younger than 18 years old (mean = 13.9 years). Sixty-two (38%) patients with pertussis and 85 (26%) controls had asthma before the date of pertussis testing (odds ratio [OR] 1.83, \( P = .005 \)). On the basis of the adjusted OR, the population attributable risk percentage of asthma for the risk of pertussis was 17% for all subjects. Antibiotic use and family history of asthma approached, but did not reach, statistical significance between groups. After adjusting for those variables, a history of asthma before the index date of pertussis PCR was still significantly associated with the risk of pertussis (OR 1.73, \( P = .013 \)). Age stratification analysis showed that the association between asthma and increased risk of pertussis was present only in children and adolescents. The use of oral or inhaled corticosteroids did not affect pertussis risk.

CONCLUSIONS. Asthma is associated with an increased risk of pertussis. Given the high incidence of asthma, relatively low pertussis immunization rates, and the increased attributable risk of asthma for pertussis infection, patients with asthma should be a target group for primary pertussis vaccination and for appropriate boosters.

REVIEWER COMMENTS. It is possible that altered innate or acquired immunity and/or altered airway epithelium increase the risk of pertussis infection in patients with asthma. The authors were not able to assess asthma control, so they were unable to correlate asthma control with risk of pertussis infection. One can speculate that poorly controlled asthma with greater airway inflammation increases the risk of pertussis (and other airway infections). This study does not change the need to enhance overall immunization rates or the need to monitor and maintain asthma control carefully. It does, however, provide a little more incentive to do both.

Kit BK, Simon AE, Ogden CL, Akinbami LJ. Pediatrics 2012;129:62–69


STUDY POPULATION. Asthmatic individuals aged 1 to 19 years with current asthma as part of the National Health and Nutrition Examination Survey during 3 time periods: 1988 to 1994, 1999 to 2002, and 2005 to 2008.

METHODS. Cross-sectional analysis of the study population for use of preventive asthma medication (PAM), including inhaled corticosteroids, leukotriene receptor antagonists, long-acting \( \beta \)-agonists, mast-cell stabilizers, and methylxanthines.

RESULTS. In children with current asthma, there was an increase in the use of PAMs from 17.8% (SE: 3.3) in 1988 to 1994, to 34.9% (SE: 3.3) in 2005 to 2008 \( (P < .001) \). Adjusting for age, gender, race/ethnicity, and health insurance status, the odds of PAM use were higher in 2005 to 2008 compared with 1988 to 1994 (adjusted odds ratio \( [aOR] = 2.6, 95\% \) confidence interval \( [CI] \): 1.5–4.5). A multivariate analysis over all 3 time periods showed lower use of PAMs among non-Hispanic black \( (aOR = 0.5, 95\% \) CI: 0.4–0.7) and Mexican American \( (aOR = 0.6, 95\% \) CI: 0.4–0.9) children compared with non-Hispanic white children. PAM use was lower in 12- to 19-year-olds compared with 1- to 5-year-olds and also in children who did not have health insurance compared with those who did have health insurance.

CONCLUSIONS. Between 1988 and 2008, the use of PAM increased among children with current asthma. Non-Hispanic black and Mexican American adolescents aged 12 to 19 years, and uninsured children with current asthma had lower use of PAM.

REVIEWER COMMENTS. This study demonstrates an increased use of PAMs in asthmatic children in 2008 vs 1988. Although several factors are likely at work, it seems likely that the National Asthma Education and Prevention Program asthma treatment guidelines, initially released in 1991, are a major reason for this result. These guidelines, and subsequent updates in 1997 and 2007, emphasize the importance of inflammation in the pathophysiology of asthma and the value of preventive medications in reducing adverse outcomes (eg, emergency room visits, hospitalizations, and the use of systemic corticosteroids). It is plausible that the growth of direct-to-consumer pharmaceutical advertising may also have augmented the use of PAMs. The authors also point out that the lower use of PAMs in non-Hispanic black and Mexican American asthmatic children may partially explain the increased risk for adverse outcomes in these patient groups.

MEDICAL THERAPIES

Daily or Intermittent Budesonide in Preschool Children With Recurrent Wheezing

PURPOSE OF THE STUDY. To compare the efficacy of daily low-dose inhaled glucocorticoids versus intermittent high-dose
inhaled glucocorticoids in children at risk for asthma exacerbations.

STUDY POPULATION. Children (n = 278) in the study were between the ages of 12 and 53 months with positive values on the modified asthma predictive index (API), recurrent wheezing episodes, and at least 1 exacerbation in the previous year, but a low degree of impairment. Children were excluded from the study if they had received more than 6 courses of oral glucocorticoids or had been hospitalized more than 2 times for wheezing during the previous year.

METHODS. The subjects were randomly assigned to receive budesonide inhalation suspension for 1 year as either an intermittent high-dose regimen (1 mg twice daily for 7 days, starting early during a predefined respiratory tract illness) or a daily low-dose regimen (0.5 mg nightly) with corresponding placebos. The primary outcome measure was the frequency of exacerbations requiring oral glucocorticoids.

RESULTS. The daily regimen of budesonide did not differ significantly from the intermittent regimen with respect to the frequency of exacerbations, with a rate per patient-year for the daily regimen of 0.97 versus a rate of 0.95 for the intermittent regimen. There were also no significant differences between the groups in other measures, including the time to the first exacerbation, quality of life, and adverse events; however, the mean exposure to budesonide was 104 mg less with the intermittent regimen than with the daily regimen.

CONCLUSIONS. A daily low-dose regimen of budesonide was not superior to an intermittent high-dose regimen in reducing asthma exacerbations. Daily administration led to greater exposure to the drug at 1 year.

REVIEWER COMMENTS. This well-designed and interesting study will help to change how we treat asthma in children; however, it is important to understand that these results are applicable only to children who fulfill the strictly defined criteria of this trial. For example, these results do not apply to children whose asthma is more severe or children who do not have positive values on the API. Another important consideration is that the intermittent regimen used in this trial (with the secondary result of reduced exposure to budesonide) involved treating with high-dose budesonide only at the onset of predefined respiratory tract illnesses on the basis of individualized symptoms that historically had occurred before the onset of wheezing. This reduced the exposure to budesonide to once every 3.5 months on average, in contrast to the approximately monthly exposure that would be anticipated to be required when such therapy would be started indiscriminately with each upper respiratory tract infection. This approach demands careful, individualized instruction. With these caveats taken into account, physicians may have 2 reasonable approaches to treatment to consider in treating this group of pediatric patients.


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Linear Growth and Bone Maturation Are Unaffected by 1 Year of Therapy With Inhaled Flunisolide Hydrofluoroalkane in Prepubescent Children With Mild Persistent Asthma: A Randomized, Double-Blind, Placebo-Controlled Trial

PURPOSE OF THE STUDY. To determine the effect of flunisolide hydrofluoroalkane (HFA) on growth velocity and bone maturation in prepubescent children with mild persistent asthma.

STUDY POPULATION. A total of 249 children (Tanner stage ≤1) aged 4 to 10 years, with mild intermittent asthma, were randomized to flunisolide hydrofluoroalkane (HFA) (n = 122) or to placebo (n = 127). At study completion, 218 met criteria for inclusion in efficacy analysis (at least 3 measurements of post-baseline height).

METHODS. This was a multicenter, randomized, double-blind, parallel-group, placebo-controlled study. During a 2-week run-in period, during which albuterol was allowed for symptoms, compliance with study procedures, baseline symptom scores, and need for inhaled corticosteroids was obtained. Subjects were randomized 1:1 to 2 puffs flunisolide HFA (85 μg/puff) twice daily or 2 puffs placebo twice daily. The primary end point was growth velocity assessed by regression analysis estimated for each eligible subject by the slope of the linear regression of stadiometric height over time, expressed as cm/52 weeks. The secondary end point was change from baseline to week 53 in radiographic bone age based on bone maturation in the hand and wrist.

RESULTS. Flunisolide HFA 2 puffs twice daily for 1 year compared with placebo did not affect growth velocity (6.01 ± 1.84 cm/52 weeks versus 6.19 ± 1.30 cm/52 weeks, P = .425), mean change in height (6.14 ± 2.12 cm versus 6.31 ± 1.26 cm, P = .343), or bone maturation (0.93 ± 0.46 vs 1.01 ± 0.41, P = .128) in children with mild persistent asthma.

CONCLUSIONS. One year of chronic use of flunisolide HFA (85 μg/puff) for the treatment of mild persistent asthma did not suppress growth or bone maturation at the highest approved dose.

REVIEWER COMMENTS. The topic of growth suppression with inhaled corticosteroids is an important concern for
Daily or Intermittent Budesonide in Preschool Children With Recurrent Wheezing

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