of airway reversibility or a positive methacholine challenge. Homes were examined for mold damage, and floor dust samples were collected. A standardized and validated methodology for mold exposure called the Environmental Relative Moldiness Index (ERMI) was used. Children from homes with mold contamination were compared with those from homes without.

RESULTS. Thirty-two percent of the parents of the study children had asthma. Asthma at age 7 years was associated with parental history of asthma (odds ratio [OR] 3.9), allergic sensitization to dust mite (OR 3.3), African American race (OR 3.2), and high ERMI (OR 2.4) by multivariate analysis. Air-conditioning was associated with a decreased risk of asthma (OR 0.3). Mold exposure at age 7 years was not associated with an increased risk of asthma. There was no difference in mold sensitization between groups with high ERMI or low ERMI. The odds of having a home with a high ERMI was associated with African American race (OR 3.0) and negatively associated with air-conditioning use (OR 0.4).

CONCLUSIONS. High ERMI value in a home during infancy is associated with an asthma diagnosis at age 7 years.

REVIEWER COMMENTS. There are several interesting points from this study, the strength of which lies in the use of a standardized mold assessment technique. As we look for ways to prevent asthma, focusing on exposures in infancy and early childhood are likely to be important. This study identifies mold exposure as one of the risk factors for the development of asthma in at-risk children. It also demonstrates that the effect of exposure does not require allergic sensitization to molds, although the number of molds that were evaluated by skin testing was small and may have missed some sensitization. Regardless, remediation of mold damage in a home during infancy may result in the reduction of asthma, although this needs to be confirmed with prospective studies. This study also supports the association of early dust-mite sensitization and the development of asthma. Dampness in the home is associated with both mold and dust-mite growth; in this study, however, the dust-mite sensitization was not a confounder of the ERMI-asthma relationship, suggesting an independent effect. This study also sheds light on previous studies that have failed to confirm the relationship between mold exposure and asthma. Because the ERMI depends on the quantitative evaluation of mold DNA in floor dust samples, the authors were able to note that visual and olfactory assessment, even by inspectors, missed significant mold problems ~50% of the time.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2012-2183RR

Paul V. Williams, MD
Seattle, WA

Relationship Between Serum Vitamin D, Disease Severity, and Airway Remodeling in Children With Asthma

PURPOSE OF THE STUDY. To evaluate the relationship between serum vitamin D, lung function, and airway remodeling pathology in pediatric severe, therapy-resistant asthmatics (STRA).

STUDY POPULATION. Studied were 86 children, aged 6 to 16 years, 36 with STRA, 26 with moderate asthma (MA), and 24 without asthma (control). STRA was defined as those receiving at least 800 μg of inhaled steroids (beclomethasone equivalent) per day and additional controller medications. MA was defined as well-controlled asthma on <800 μg of beclomethasone equivalent per day.

METHODS. Serum 25-hydroxyvitamin D [25(OH)D3] was measured. Symptom control was assessed by the childhood asthma control test (ACT). Acute asthma exacerbations were defined as requiring high-dose oral steroids for at least 3 days in the past 6 months. Spirometry was performed in accordance with ATS guidelines. Bronchoscopy, bronchoalveolar lavage, and endobronchial biopsy was performed in 22 children with STRA, and nonasthmatic controls were included (bronchoscopy for other reasons). Differences between the 3 groups were assessed by using one-way analysis of variance or Kruskal-Wallis test.

RESULTS. Levels of 25(OH)D3 were significantly lower in STRA than in MA and control subjects (P < .001) and were positively associated with lung function, indicated by percent predicted forced expiratory volume in 1 second (P < .001) and forced vital capacity (P = .002), and with ACT scores (P < .001). An inverse relationship was noted between 25(OH)D3 levels and asthma-related exacerbation (P < .001), as well as inhaled steroid dose used (P = .001) in the MA and STRA groups. Finally, there was an inverse relationship between 25(OH)D3 and airway smooth muscle (ASM) mass (P = .008), although study did not indicate a relationship between 25(OH)D3 and tissue eosinophils, neutrophils, or mast cells. Additional assessment of ASM mass showed an inverse correlation with ACT score (P < .001) and a positive correlation with bronchodilator reversibility (P = .009).

CONCLUSIONS. This study demonstrates that lower serum 25(OH)D3 levels are associated with increased asthma severity, increased asthma-related exacerbations, and higher inhaled glucocorticoid requirements. Furthermore, decreased serum 25(OH)D3 levels resulted in worse lung function and poorer asthma control. Within the STRA group, low serum 25(OH)D3 levels were associated with increased ASM mass but not with other parameters of airway remodeling or airway inflammation.

REVIEWER COMMENTS. This study provides additional data to support the association between vitamin D status and
Steroid Requirements and Immune Associations With Vitamin D Are Stronger in Children Than Adults With Asthma


PURPOSE OF THE STUDY. To compare the age-specific relationship between serum vitamin D (25-OH-D) levels and allergic sensitization, vitamin D receptor (VDR) activation pathways, peripheral blood mononuclear cell (PBMC) steroid responsiveness, and inhaled corticosteroid (ICS) requirements in children and adults with asthma.

STUDY POPULATION. One hundred three patients with asthma (53 children, 50 adults) and 102 healthy control subjects (51 children, 51 adults) were matched for age, gender, race, and BMI.

METHODS. Serum 25-OH-D levels were checked during the winter in all subjects. Inducible markers of VDR activation (cytochrome P450 family 24 [cyp24a] mRNA and plasma cathelicidin [LL-37]) were measured. Tumor necrosis factor (TNF)-α and interleukin (IL)-13 were measured after in vitro stimulation of PBMC with dexamethasone.

RESULTS. Although there was great overlap in 25-OH-D levels between groups, asthma had a higher rate of vitamin D deficiency (<20 ng/mL) than healthy control subjects (56.8% vs 47.6%). The level of vitamin D-regulated targets (cyp24a and LL-37) correlated with 25-OH-D level in children, but only cyp24a had a similar correlation in adults. There was a significant inverse correlation between 25-OH-D and serum immunoglobulin (Ig) E in children but not adults. Dust mite–specific IgE was associated with lower 25-OH-D levels, but there was no such association in adults or to specific IgE levels for other aeroallergens. In children, but not adults, 25-OH-D levels had a significant inverse correlation with ICS requirement in the patients with asthma. A similar inverse correlation between 25-OH-D level and cyp24a and LL-37 was seen only in children. Cyp24a expression by PBMC correlated with the degree of TNF-α and IL-13 suppression by dexamethasone only in children. All of these associations were stronger in children aged 6 to 12 years than those aged 13 to 17 years. In the older children, the associations did not reach statistical significance.

CONCLUSIONS. There are significant associations between serum vitamin D level, inhaled corticosteroid requirement for asthma, and in vitro responsiveness to corticosteroids in children (particularly 6- to 12-year-olds) but not in adults.

REVIEWER COMMENTS. There has been a surge of interest in vitamin D and its effects on numerous biological functions. Many associations are based on epidemiologic studies, including the role of vitamin D in atopic diseases. It is not clear if the rate of vitamin D deficiency and insufficiency has increased or if there is just greater awareness of the problem. This study demonstrates the association of 25-OH-D levels with biologic function, particularly in school-age children. Because the study was done in the winter, it is not clear if the same associations would be found in the summer when endogenous 25-OH-D levels are likely to be higher. It is also not clear why the associations were strongest in the youngest subjects. Finally, it is not clear if vitamin D supplementation would change the results or improve asthma outcomes in the study population. Nonetheless, this study suggests the opportunity for early intervention in young children with asthma. At the very least, it is another reason to recommend that children “turn off the screens” and go outside to play.

Sleep-Disordered Breathing Is Associated With Asthma Severity in Children


PURPOSE OF THE STUDY. To examine the association between obesity, sleep-disordered breathing, and asthma severity in children.

STUDY POPULATION. The study included 108 asthmatic children, aged 4 to 18 years, 45.4% African American and 67.6% male subjects, enrolled in an asthma specialty clinic at Rainbow Babies and Children’s Hospital, Cleveland, Ohio.
Relationship Between Serum Vitamin D, Disease Severity, and Airway Remodeling in Children With Asthma
Todd A. Mahr and Jennilee Mumm
*Pediatrics* 2012;130;S28
DOI: 10.1542/peds.2012-2183SS

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