antigens. The inflammatory cytokine IL-33 was elevated in Rac1-deficient lungs, which was associated with expansion of proallergenic innate lymphoid cells. Furthermore, suppression of Rac1 in human nasal epithelial cells resulted in enhanced production of IL-33, suggesting that Rac1 negatively regulates inflammatory signaling pathways. Finally, treatment with IL-10 was shown to mitigate the allergic inflammation seen in Rac1-deficient airways.

CONCLUSIONS. Clearance of apoptotic cells by airway epithelial cells is important for preventing allergen-induced airway inflammation.

REVIEWER COMMENTS. It is generally thought that traditional phagocytic cells in the lungs, such as alveolar macrophages, are primarily responsible for keeping the airways clean through removal of cellular debris and inhaled particulates. However, this study reveals that airway epithelial cells, which are not typically known for their phagocytic function, play a critical role in the clearance of apoptotic cells and in maintaining an antiinflammatory environment in the lungs. This study, along with others evaluating innate immune activity of epithelial cells, emphasizes the importance of the respiratory mucosal barrier in maintaining lung homeostasis. Therapies aimed at enhancing the immunosuppressive activity of airway epithelial cells, or blocking their release of proinflammatory cytokines such as IL-33, may prove beneficial for the treatment of asthma and other immune-mediated respiratory diseases.

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DIAGNOSIS AND MANAGEMENT

Outcomes of Stepping Down Asthma Medications in a Guideline-Based Pediatric Asthma Management Program

PURPOSE OF THE STUDY. Identifying strategies to adjust medications when managing chronic diseases poses a challenge to busy practitioners, and often the opportunity is lost to step down therapy. Clinical studies suggest that many patients currently treated with combination controller medications can be successfully stepped down. Use of a multidisciplinary care management team has also been a strategy associated with success in stepping down therapy. Nonadherence represents another method of step-down. This study was performed to identify predictive factors for success in stepping down therapy, the frequency of attempts to step down, and the relative success of guideline-eligible versus non-guideline-eligible step-down attempts.

STUDY POPULATION. The study included a retrospective, random sample of 477 participants in the Pediatric Asthma Management Program affiliated with the Mayo Clinic. The children were aged 5 to 8 years with asthma enrolled in a pediatric asthma management program in an integrated primary care practice. All children had persistent asthma, a history of emergency department or hospital visit for asthma during the past 12 months, or uncontrolled asthma symptoms.

METHODS. By using the National Asthma Education and Prevention Program Asthma Guidelines, participants were identified who were eligible, based on a defined control, to step down therapy. Other participants who did not meet the guidelines for step-down, but who attempted step-down anyway, were also analyzed. Age, gender, pulmonary function, smoking status, time of year, and type of step-down were analyzed for their predictive value.

RESULTS. Slightly more than 55% of the children in the study were eligible, based on the guidelines, to step down therapy, but only 33.7% did attempt to step down. A similar percentage of those who were not guideline eligible also attempted stepping down. Successful step-down occurred in 79.7% of guideline-eligible participants and in 61.7% of those who were non-guideline eligible. Time of year was the only predictive factor (success in any season except for fall), although guideline eligibility was significant in the univariate analysis.

CONCLUSIONS. Guideline-based stepping down of asthma medication is an option that should be frequently considered and will be frequently successful.

REVIEWER COMMENTS. The important finding in this study is that only a minority of children with asthma that is well controlled have attempted to step down therapy. Stepping down, regardless of whether guideline eligible or not, is often successful. It appears that stepping down in the fall is associated with less success. These findings underline the need for practitioners to regularly assess patients for eligibility to decrease asthma therapy.

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Factors Associated With Elevated Exhaled Nitric Oxide Fraction in Infants With Recurrent Respiratory Symptoms

PURPOSE OF THE STUDY. To evaluate the relationship between exhaled nitric oxide fraction (FeNO) and increased airway responsiveness, and to clarify whether there are any
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