16.3% improvement as compared with placebo). In the 2 ragweed SLIT studies, overall improvement relative to placebo was 17.1%. These treatment effects were numerically greater than those for montelukast (0.65% to 10.3%, overall 5.4% improvement compared with placebo) and desloratadine (1.7% to 12.5%, overall 8.5% improvement compared with placebo). In contrast, MFNS had a numerically greater effect than did SLIT (13.1% to 28.1%, overall 22.2% improvement compared with placebo). In 2 studies of HDM SLIT for PAR, overall TNSS improvement was 16.1% higher than with placebo. This effect was greater than that seen for montelukast, desloratadine, and MFNS (3.7%, 4.8%, and 11.2% improvement compared with placebo, respectively).

CONCLUSIONS. As compared with placebo, grass and ragweed SLIT are more effective at lowering TNSS than montelukast and desloratadine but somewhat less effective than MFNS. HDM SLIT had a greater effect on TNSS than the pharmacologic treatments.

REVIEWER COMMENTS. Currently, the FDA has approved SLIT tablets for grass and house dust mite allergies. The currently available preparations are very expensive and often not covered by insurance. A great weakness in the study and marketing of new products is that they are usually not compared with existing products in head-to-head studies. Subcutaneous allergen immunotherapy (SCIT) has been proven effective (and more effective than pharmacotherapy) for numerous (but not all) aeroallergens. SLIT tablet doses are not easily compared with SCIT doses, but data indicate that significantly higher monthly doses of SLIT than SCIT are necessary for efficacy. At this point, if a patient has isolated allergies to grass, ragweed, or dust mites, SLIT tablets are an option, but cost and other factors (such as the potential for long-lasting therapeutic benefit with SLIT) must be considered in the discussion between patients and their allergists.

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Asthma

PATHOPHYSIOLOGY, DIAGNOSIS, AND MANAGEMENT

Early Life Rhinovirus Wheezing, Allergic Sensitization, and Asthma Risk at Adolescence

Rubner FJ, Jackson DJ, Evans MD, et al. *J Allergy Clin Immunol*. 2017;129(2):501–507

PURPOSE OF THE STUDY. To define the relationships among specific viral illnesses and the type and timing of aeroallergen sensitization with the persistence of asthma into adolescence.

STUDY POPULATION. This is a prospective cohort study that enrolled 289 newborns who had a parental history of respiratory allergies and/or asthma and were followed to age 13 years (n = 213).

METHODS. After enrollment, the infants had scheduled visits at ages 2, 4, 6, 9, and 12 months and annually thereafter. They were also seen during periods of acute illness. At these visits, nasal lavage was collected and analyzed for respiratory viruses. The viral panel included RSV, RV, influenza types A and B, parainfluenza virus types 1 to 4, adenovirus, coronavirus, and enterovirus. Allergen-specific IgE levels were determined at ages 1, 2, and 3 years for *Dermatophagoides pteronyssinus*, *Dermatophagoides farina*, *Alternaria alternata*, and dog and cat allergens and were repeated at ages 5, 6, 9, 11, and 13 years with the addition of ragweed, silver birch, timothy grass, and cockroach. Wheezing during the first 3 years of life and asthma during school age were determined by physician diagnosis, the use of β agonists, daily asthma controller medications, or the use of oral steroids for exacerbation.

RESULTS. A total of 454 wheezing illnesses were documented during the first 3 years of life. Viruses detected included the following: RV (48%), RSV (21%), parainfluenza viruses (12%), metapneumovirus (7%), coronaviruses (5%), adenovirus (4%), influenza types A and B (4%), and enteroviruses (2%). RSV-induced wheezing accounted for an increased risk of asthma during school ages 6, 8, and 11 years; however, the association was lost by age 13 years. On the other hand, RV-associated wheezing during early childhood was associated with asthma that persisted to age 13 years (OR +3.3; 95% CI, 1.5–7.1). Additionally, 65% of children who were sensitized by age 1 year had asthma that persisted to age 13 years; children who were not sensitized by 1 year of age but were sensitized by age 5 years had a 40% rate of asthma in adolescence, and the remaining children who were not sensitized by age 5 years had an asthma rate of 17%. Subsequently, those with both early-life, RV-associated wheezing and aeroallergen sensitization by age 3 years had the highest risk of persistent asthma. Protective factors that reduced asthma risk at age 13 years included the presence of a cat in the home at the time of birth, while the protective impact of a dog in the home waned by age 13 years.

CONCLUSIONS. This study found that high-risk children with a parental history of allergies and/or asthma were more likely to develop asthma that persisted into adolescence when they had RV and aeroallergen sensitization in early childhood.

REVIEWER COMMENTS. This study highlights that the timing of wheezing illness, the type of viral infection causing the illness, and aeroallergen sensitization are all important influences on the development of persistent asthma. This study demonstrated that RV-associated wheezing correlates with longer-lasting asthma than RSV-associated wheezing in

early childhood and suggests that prevention strategies are needed to impact long-term outcomes.

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Diagnostic Value of Serum Baseline Tryptase Levels in Childhood Asthma and Its Correlation With Disease Severity

Gao S, Fan J, Wang Z. *Int Arch Allergy Immunol*. 2016;171 (3–4):194–202

PURPOSE OF THE STUDY. To determine if the measurement of serum baseline tryptase (sBT) levels can accurately diagnose pediatric asthma and predict asthma severity.

STUDY POPULATION. The study included 114 asthmatic children between the ages of 5 and 12 years. Within the cohort, 36 children had mild intermittent asthma, 38 had mild persistent asthma, and 40 had moderate to severe persistent asthma. In addition, 34 age-matched healthy children were included as controls.

METHODS. Serum baseline tryptase levels were measured in all asthmatic children and healthy controls. Asthma severity was assessed for asthmatic children using asthma serum markers (total IgE, interleukin-13, interferon-γ), childhood asthma control tests (C-ACT), GINA guideline–based severity evaluations, and pulmonary function tests. The diagnostic accuracy of sBT levels was assessed by receiver operating characteristic (ROC) analysis. The correlation between sBT levels and asthma severity was assessed by Pearson and Spearman correlation tests.

RESULTS. Median sBT levels were significantly greater in the mild persistent (4.2 μg; range 1.6–6.0) and severe persistent (4.7 μg; range 1.8–7.8) asthma groups compared with those with mild intermittent asthma and healthy controls. ROC curve analysis showed that sBT levels are both sensitive (75.4%) and specific (88.2%) in discriminating asthmatic children from healthy controls at a cut-off value of 3.2 μg. ROC curve analysis showed that sBT levels are considerably sensitive (85.9%) and specific (88.9%) in distinguishing patients with persistent asthma from intermittent asthma at a cut-off value of 3.6 μg. Correlation analysis revealed that sBT levels strongly correlated with C-ACT scores, serum IgE levels, eosinophil counts, pulmonary function parameters, and IL-13 levels in all asthma subgroups.

CONCLUSIONS. Serum blood tryptase levels may help support the diagnosis of asthma in children and predict disease severity.

REVIEWER COMMENTS. Tryptase is a marker of human mast cell activation, and elevated levels have been associated with increased risk of insect venom hypersensitivity and anaphylaxis in children with food allergies. This is one of the first studies to suggest a role for serum blood tryptase levels in the diagnosis of asthma. This marker could support the diagnosis of asthma in pediatric patients who are too young for or are unable to complete pulmonary function tests.

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Use of Management Pathways or Algorithms in Children With Chronic Cough: CHEST Guideline and Expert Panel Report

Chang AB, Oppenheimer JJ, Weinberger MM, et al. *Chest*. 2017;151(4):875–883

PURPOSE OF THE STUDY. Use of cough algorithms or pathways can potentially lead to earlier diagnosis and reduce morbidity, unnecessary costs, and medication use associated with chronic cough. The 2006 CHEST guidelines on chronic cough in children advocated use of a cough pathway based on limited data, and research in chronic cough has progressed in the past decade. This study looked at 10 years of systematic reviews to present the summary of evidence behind these CHEST recommendations.

STUDY POPULATION. The age cutoff for the CHEST cough guidelines is $\leq$14 years. Chronic cough is defined as the presence of daily cough for at least 4 weeks in duration.

METHODS. Data were collected from systemic reviews, existing guidelines, and primary studies published in English until August 2015. The study then examined various aspects in the approach to chronic cough management in children based on key questions (KQs) by using the Population, Intervention, Comparison, Outcome format. CHEST methodical guidelines and Grading of Recommendations Assessment, Development, and Evaluation framework were used to support the evidence-based graded recommendations. A consensus-based Delphi method was employed for the final grading.

RESULTS. There is high-quality evidence that the use of a systemic approach to pediatric-specific cough management improves clinical outcomes and that management should be based on cough characteristics and associated clinical history. Although there was evidence from several pathways, the highest evidence was from the use of the CHEST approach.

CONCLUSIONS. CHEST pediatric chronic cough guidelines have been around for over a decade but were initially based on limited evidence. There are now more studies showing high-quality evidence for standardizing the management of cough >4 weeks in children $\leq$14 years of age to improve our diagnosis of these children, manage them more appropriately, and improve quality

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