

*Clinical pearls***Among young children who wheeze, which children will have persistent asthma?**Gail G. Shapiro, MD *Seattle, Wash***Key words:** Airway hyperresponsiveness, allergic rhinitis, atopy, childhood asthma, childhood eczema

We are frequently faced with answering questions regarding the persistence of asthma and which children will outgrow the disease. Consider 2 similar children you might see during the same clinic session. Patient 1 is a 2-year-old boy who presents with a history of wheezing episodes with each upper respiratory tract infection during the previous fall and winter. He has needed aggressive use of bronchodilators and prednisone courses 3 times over the last 6 months. It is not clear whether he wheezes between colds, but his parents notice some coughing when he is upset and crying. He has had mild eczema since infancy, severe skin test reactivity to peanut (which he has never ingested), and parental history of asthma and seasonal rhinitis. Patient 2 is somewhat similar with a normal first year of life and the same sort of difficulty, with apparent viral syndromes precipitating worrisome wheezing exacerbations several times in the past fall and winter. This child has no history of atopic rash or food sensitization, and his parents have never had allergic problems or asthma. What risk factors do these children have in terms of future asthma persistence and severity, likelihood of remission of bronchial reactivity, and residual lung function deficits? What treatment approaches would lead to the best outcome for these 2 children?

While we form our own impressions from our clinical practices, several longitudinal studies give us more scientifically genuine information that we can use in counseling our patients about the persistence and remission of asthma. Table 1¹⁻⁵ summarizes some observations gleaned from a small group of observational clinical trials. Because entry criteria and outcome variables were different for each study, one can only compare patterns.

Regarding the persistence of asthma, the level of bronchial reactivity correlated with the persistence of disease in the Dunedin¹ trial of children aged 9 to 26 years and the Perth² trial of children aged 0 to 11 years. Other trials either did not measure this variable or did not follow it with a consistent protocol. A consistent risk factor in all of these trials is allergen sensitization.¹⁻⁵ Features of atopic disease, including rhinitis, eczema, and eosinophilia, were notable risk factors in all of these trials.¹⁻⁵ Decrease in lung function by age 3 years (not associated with an acute exacerbation) was noted in several cohorts.²⁻⁴ Other features suggesting persistence included female sex and tobacco smoke exposure^{1,4} and parental history of asthma.^{3,4}

The consistency of findings between trials is impressive and underscores several recurring factors. The early expression of bronchial reactivity in the form of wheezing and coughing during viral insults is a risk factor for persistence of disease through childhood: the earlier the onset, the worse the severity. Personal signs of atopy in the form of both allergen sensitization and diseases such as allergic rhinitis and atopic eczema are strongly predictive risk factors. Decrease in lung function in the first years of life is another consistent predictor of persistent disease among clinical trials, although infrequently subject to measurement in clinical practice.

Those trials that have followed children into adulthood^{1,3,5} note little progressive change in lung function after the decreases in early childhood. The Melbourne experience documents the longest period of longitudinal follow-up, with subjects being in their 40s. They note that those with few episodes of wheezing in childhood, mainly associated with respiratory infection, tended to outgrow their disease, whereas those with a consistent wheezing pattern in childhood tended to continue to wheeze into adulthood, with those with more severe trouble in childhood being most likely to have significant troubles as adults. There was no progressive loss in lung function, however, after age 14 years.⁵

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TABLE I. Longitudinal trials of childhood asthma persistence

Location	Sample type	Age at entry and conclusion* (y)	Summary of factors correlating with persistence
Dunedin ¹	Birth cohort	9-26	• Early age at onset of wheezing • Airway hyperresponsiveness • Persistently low lung function • Sensitization to house dust mites • Female sex • Smoking
Manchester ⁴	Birth cohort	0-5	• Poor lung function at age 3 y • Allergen sensitization • Maternal asthma, maternal smoking during pregnancy
Perth ²	Birth cohort	0-11	• Increased airway responsiveness • Reduced airway function in early infancy • Atopy • Parental asthma
Tucson ³	Birth cohort	0-22	• Transient early and persistent wheezers have lower flows at multiple time points than never wheezers • Level of lung function stabilized in all groups by age 6 y • Atopy more prevalent in persistent and late-onset wheezers than never or transient wheezers, along with more eczema, rhinitis eosinophils, parental asthma
Melbourne ⁵	Children with wheezing and control subjects	7-42	• Episodic childhood asthma tends to resolve in adolescence and adulthood with no lung impairment • Persistent asthma in childhood more likely to show modest lung function impairment, seen by age 14 y and not progressive • Atopy increases risk for more severe disease

*Related to citation in reference list.

Investigators from the Tucson longitudinal observational trial have created a valuable predictive index for asthma persistence based on major and minor criteria applied to their trial participants.⁶ Children with at least one of the major criteria of parental history of asthma or eczema and 2 of 3 minor criteria (ie, eosinophilia, allergic rhinitis, and wheezing without colds) had at least a several-fold increase in risk of active asthma during the school years.

Returning to the 2 youngsters who seem so similar in presentation but with important differences, we see certain limitations in clinical practice regarding our ability to look at all of these risk factors. Chances are that we do not have the ability to measure lung function or to do bronchial provocation testing to define bronchial reactivity in young children. We do have clinical evidence of exacerbations with airway reversibility to confirm airway reactivity. In addition, we have history and physical examinations and allergy skin test results that elucidate allergen sensitization. This information suggests that patient 2 shows airways reactivity as his sole risk factor, whereas patient 1 also has a positive family history of asthma, allergen sensitization, eczema, and allergic rhinitis.

Several important questions are obvious: Do these differences influence treatment? Can we do something to alter the natural history of asthma in these children? Do they influence the counseling we give to the families?

Both of these children have shown repetitive bouts of significant airway obstruction with at least partial reversibility with bronchodilator and oral steroid. This pattern suggests there will be more acute exacerbations. National asthma guidelines and randomized clinical trials recommend regular therapy with inhaled corticosteroids to decrease the number and severity of symptomatic episodes and to improve quality of life for these families.^{7,8} We have learned that early and aggressive anti-inflammatory therapy has no beneficial effect on the natural history of asthma.^{8,9}

The answer to the question of how to counsel the families of these 2 children is more subjective and more dependent on the physician's relationship with these families and on the art of medicine. Clearly, the parents of the child with low risk of persistent disease can be comforted and reassured that if they follow an action plan for daily maintenance and acute exacerbations of asthma, they are likely to avoid major disruption and will see their child experience less morbidity over time. They are likely to have a child who is free of symptoms around the time he enters elementary school. The parents of the child with high risk of persistent disease can also be comforted and reassured that there is a plan of action that will allow them to have a life that is not dominated by asthma crises. In addition to symptom monitoring and education regarding medication, this family needs to know more about their child's allergic sensitization so that they can attend to

environmental control measures. These parents need direction regarding the overall management of atopic disease, for example, allergic rhinitis as it relates to airway reactivity. Although remission of asthma remains a possibility for their child, putting energy into establishing a contented lifestyle with asthma that is usually under control and a protocol to minimize the stress of exacerbations is the most realistic approach for accomplishing a comfortable existence for both the short term and long term.

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