

Natural History: Wheeze from childhood to adulthood

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The recent well designed longitudinal studies which followed children from early in life to adulthood produced a remarkable change in our understanding of the natural history of asthma. It seems established that, in the majority of cases of persistent asthma, the symptoms begin during the preschool years and track significantly thereafter. Moreover, the two longest longitudinal studies of asthma conducted in Australia¹ and New Zealand² have shown that deficits in lung function are already present by 9 years of age among asthmatic children, and that these deficits persist up to adulthood³.

The cohort from New Zealand has followed children from 9 to 26 years of age with questionnaires, pulmonary function tests and allergy testing. At 26 years of age, about 27% of the study participants were still wheezing; in 14.5%, wheezing had persisted from onset, whereas 12.4% presented a remission followed by a relapse by the age of 26 years. These data are consistent with data from Australian studies which found that approximately two thirds of subjects with asthma in the first years of life did not persist with their symptoms during adulthood^{4,5}. Wheezing was considered to be transient in 21.2% of the participants¹s.

From childhood to adulthood, study participants who were persistent wheezers had consistently lower lung function measurements, when compared with other study participants who never reported any wheezing. No significant differences in FEV₁/FVC ratios were observed among children with remission, intermittent wheezing or transient wheezing. Moreover, the slopes of change in FEV₁/FVC were similar in each group, indicating that impairment of lung function occurred in early childhood¹.

Similar results were observed in an Australian longitudinal study. The children that represented a large population were enrolled at 7 years of age. The results were based on a questionnaire concerning the children's history of asthma and wheezing episodes. Children were classified into four categories: those who never wheezed; those with fewer than five episodes associated with apparent respiratory infection (mild wheezy bronchitis); those with five or more episodes associated with appar-

ent respiratory infections (wheezy bronchitis) and those with wheezing not associated with respiratory infection (asthma). A fifth group of children with severe asthma was added to the same cohort at 10 years of age and evaluations were conducted every 7 years².

Of the subjects who had mild wheezy bronchitis at 7 years of age, 77% were free of symptoms at 35 years of age, whereas only 23% had frequent or persistent asthma. Of the participants with asthma at 7 years of age, 50% had no recent asthma or infrequent asthma as adults, whereas 50% had frequent or persistent asthma. Importantly, 75% of those who had severe asthma at 10 years of age had frequent or persistent asthma at 35 years of age. The more severe their asthma is, the less likely they are to remit².

Subjects with asthma and severe asthma at 7 years of age who were followed up to 28 years of age experienced abnormal pulmonary function as adults, although in the participants with mild asthma, the abnormalities were relatively minor. Children with mild wheezy bronchitis and wheezy bronchitis at 7 years of age had no evidence of airway obstruction at 35 years of age. These patterns suggest once again that no significant loss of pulmonary function occurs after the age of 7-10 years up to 35 years of age, even in individuals with severe disease².

Data from the Tucson Children's Respiratory Study suggest that the main loss of lung function occurs very early in life. At 6 years of age, children were classified into four wheezing categories based on the current and previous history of their wheezing symptoms: non-wheezers (children who never wheezed), transient wheezers (at least one lower respiratory tract illness with wheezing during the first 3 years of life but who had no wheezing at 6 years of age), late-onset wheezers (no lower respiratory tract illness with wheezing during the first 3 years of life and wheezing at 6 years of age) and persistent wheezers (at least one lower respiratory tract illness with wheezing during the first 3 years of life and wheezing at 6 years of age)⁶.

Based on pulmonary function measurements made before 1 year of age, non-wheezers and persistent wheezers showed no significant difference in pulmonary function

parameters. At 6 years of age, however, persistent wheezers had significantly lower pulmonary function compared with non-wheezers⁶. This difference was still detected at 11 years of age and recently, the follow-up for these children was completed and report up to the age of 16 years, both in terms of lung function and respiratory symptoms during the school years³.

Recently, Lowe et al showed that children with a strong family history of asthma who had become sensitized to local allergens had significantly lower specific airway conductance at age three compared to non-sensitized children⁷. One could speculate that the early development of allergic responses in the airways may facilitate a process of remodelling occurring at a time of very fast lung growth, before 3 years of age³.

Morgan et al have shown that the transient early wheezers, the largest group of children who wheezed early in life, were unlikely to wheeze thereafter³. However, these children continue to have lower levels of lung function. Individuals who enter adult life with lower levels of lung function are probably more likely to develop chronic obstructive pulmonary disease during adult years, especially if they had lower respiratory illnesses in early life⁸. Whether transient early wheezers are also predisposed to chronic obstructive pulmonary disease is not yet known³.

In summary, many children do not remit from their asthma and the more severe their asthma is, the less likely they are to remit. These data support the concept that children with mild disease usually remit during adolescence, whereas children with severe asthma during the first decade of life are more likely to present persistent asthma when they reached adulthood².

Furthermore, the deficits in lung function in asthmatic children are not present shortly after birth, but seem to be acquired before 3 years of age⁹. Identifying the factors that influence these deficits will be decisive for the prevention and treatment of asthma.

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