

Editorial

Childhood wheezing

Sibilância na infância

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Cough and wheezing are respiratory symptoms that are quite common in children. These symptoms can be the clinical expression of a wide variety of problems occurring in the respiratory tract. Regardless of the cause, wheezing is a reason to seek emergency medical attention, especially when it occurs in children less than one year of age. Children less than two years of age who experience at least three episodes of wheezing within the space of a six-month period are designated "early wheezers". There are various potential causes of wheezing in this age bracket, and, although asthma is the most common cause, the differential diagnosis should always be made in order to rule out other causes.⁽¹⁾

It is difficult to establish the true incidence of the "early wheezer" syndrome and of recurrent wheezing. It is known that at least 20% of all children below two years of age present transitory wheezing, in part related to the airway diameter, which is genetically predetermined, as well as to the coexistence of viral infections of the upper airways, passive exposure to maternal smoking and genetic factors. It is believed that one third of all children who begin wheezing before the age of three years will continue to do so, and that 60% of those will become atopic by the age of six. Viral infections, those caused by the respiratory syncytial virus in particular, have been cited as the principal infectious factors related to the onset of wheezing in children, especially in non-atopic children.⁽²⁾

The factors that determine the establishment, evolution and prognosis of the "early wheezer" syndrome have not been well defined. However, immunocompetence of the host is certainly involved, as are factors of risk/predisposition, the pathogenicity of the aggressor agents and immediate, specific diagnosis, as well as the treatment administered. Various studies have implicated passive smoking, age, male gender, poor socioeconomic conditions, atopy and pollution as predisposing factors for the development of recurrent wheezing. Nevertheless, it remains unknown which of the principal markers or phenotypes of wheezing are capable of identifying those children that will develop asthma and of predicting asthma prevalence. Nor is it clear whether early treatment can impede the progression to asthma. In addition, these markers and phenotypes can vary depending on the population under study.

It has been reported that the incidence of wheezing is high during the first years of life. Prospective populational

studies with long-term follow-up periods have demonstrated that at least 50% of all children experience at least one episode of wheezing during the three first years of life.⁽²⁾ In the Tucson cohort study, 40% of the children monitored presented one episode of wheezing during the first years of the follow-up period.^(2,3) Another cohort study involved term neonates born into families of low socioeconomic status.⁽⁴⁾ The authors found that 80.3% had experienced episodes of wheezing in the first year of life, as well as that, before the age of three months, 43.1% had presented three or more crises, and 44.1% had experienced episodes of wheezing. In a study conducted in the city of São Paulo, Brazil, the prevalence of recent wheezing (one or more episodes in the preceding 12 months) was found to be 11% among children 6-11 months of age and 14.3% among those 12-23 months of age.⁽⁵⁾ Our research group studied a cohort of children residing in the city of São Paulo and at high risk for developing asthma.⁽⁶⁾ We found that 52% of the children evaluated presented recurrent wheezing by the end of the 30-month follow-up period.

Although wheezing is a common reason for scheduling medical visits, the true extent of wheezing, recurrent or otherwise, remains unknown, especially among children in developing countries. This situation gave rise to the *Estudio Internacional de Sibilancias en Lactantes* (EISL, International Study of Wheezing in Suckling Infants), whose objectives are to determine the prevalence of wheezing in children from 12 to 15 months of age and to identify the potential risk factors associated with such wheezing.⁽⁷⁾ Employing the instrument standardized in the EISL study, Chong et al. determined that the incidence of "ever wheezing" among children treated at basic health care clinics during routine visits or immunizations was 45.4%,⁽⁸⁾ which is slightly lower than the 58% reported by Muiño et al. (58%) in a 1993 birth cohort study conducted in the city of Pelotas, Brazil, in which the children were evaluated at ten to twelve years of age.⁽⁹⁾

The importance of investigating pediatric patients with recurrent wheezing lies in the fact that such children, upon reaching adolescence, are at high risk for developing persistent asthma, the probability of which is greater among those who are atopic.^(10,11) In addition, the intensity of asthma symptoms during the first two years of life is strongly associated with its later prognosis.⁽¹²⁾ Therefore, the identification

of the different phenotypes of wheezing and their future expression of asthma has been the object of study for numerous researchers.^(2,10-15)

The PRACTALL Consensus,⁽¹⁶⁾ a recently published document created jointly by specialists at the European and American Academies of Asthma, Allergy and Immunology, describes four distinct patterns of wheezing during infancy and thereafter:

- a) transitory wheezing (wheezing only during the first two or three years of life)
- b) non-atopic wheezing (wheezing principally caused by a virus and tending to disappear with age)
- c) persistent asthma, characterized by wheezing associated with one of the following:
 - clinical manifestations of atopy: eczema; rhinitis/conjunctivitis; food allergy; and eosinophilia or elevated serum levels of total immunoglobulin E (IgE)
 - sensitization confirmed on the basis of food-specific IgE levels in early infancy and aeroallergen-specific IgE levels later in life⁽¹⁷⁻²¹⁾
 - sensitization to aeroallergens before three years of age, especially if exposed to elevated levels of perennial allergens in the home⁽¹⁰⁾
 - maternal or paternal asthma⁽¹⁸⁾
- d) severe intermittent wheezing (rare episodes of acute wheezing accompanied by few symptoms unrelated to the acute profiles and presenting characteristics of atopy: eczema; allergic sensitization and eosinophilia in the peripheral blood)⁽²²⁾

In addition to simply providing a clinical characterization of wheezing phenotypes, this system of classification allows a prognosis value to be assigned to each phenotype.⁽¹⁴⁾ Phenotypes a and b are typically benign in their evolution and are usually confirmed retrospectively.

In this issue of the Brazilian Journal of Pulmonology, Muiño et al., for the first time in a study conducted in Brazil, analyze the clinical patterns of expression of wheezing, evaluating 87.5% of the original members of the Pelotas cohort.⁽⁹⁾ The criteria to define those patterns were the same as those employed by other investigators: transitory wheezing (wheezing only until four years of age); late-onset wheezing (wheezing onset at ten

to twelve years of age); and persistent wheezing (in all evaluations) with an irregular pattern. The authors identified associations between each of these patterns and a number of variables.

The prevalence of transitory wheezing was 43.7%, compared with 6.4% for persistent wheezing and 3.3% for late-onset wheezing. These values are different from those reported by other authors. The transitory pattern was found to be significantly associated with low family income, shorter duration of breastfeeding, respiratory infections in the first year and a family history of asthma at four years of age. The persistent pattern was more prevalent among male children, children born to mothers that had asthma during pregnancy and children having respiratory infections in the first year of life, as well as among children with a family history of asthma at four years of age or at ten to twelve years of age. Late-onset wheezing was found to be associated with a family history of asthma at ten to twelve years of age, physician-diagnosed rhinitis at ten to twelve years of age, lower frequency of respiratory infections in the first year of life and physician-diagnosed eczema at ten to twelve years of age.

Different from other studies, this study shows that a family history of asthma, which is usually associated with persistent asthma, was not a factor that distinguished the various phenotypes observed. In addition, the fact that the authors did not perform skin tests for immediate sensitivity precludes the drawing of distinctions among the phenotypes evaluated in terms of which would be associated with atopy. These data convince us of the need for local studies aimed at identifying the different wheezing patterns, principally those that carry a risk of progression to persistent asthma. The EISL study protocol certainly provides data that are more specific and that allow us to identify which patterns progress to asthma, as well as promoting the more timely initiation of treatment regimens.

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