Correspondence

Nonallergic childhood asthma: A common diagnosis for transient and nonatopic wheezers?

To the Editor:

The Tucson Children's Respiratory Study has provided the scientific community with invaluable information about wheezing disorders in childhood, from birth to adulthood.[1] Their authors have described 3 different asthma phenotypes: transient, nonatopic, and atopic wheezers. We suggest that the first and second groups could have been segregated from a common illness as a consequence of the study design that enhances the differences depending on the time of inception and the course of the disease instead of the pathogenetic mechanisms involved. From our point of view, transient and nonatopic wheezers share enough similarities to be classified together as having a single syndrome or disease, namely nonallergic childhood asthma.

Nonallergic childhood asthma could be seen as the lung response to an early injury in a sensitive period of the development of this organ[2] as a result of perinatal or early infant insults, leading to dysplasia and inflammation (and resulting in reduced lung function and hyperresponsiveness). This could be the common pathway in the recovery from bronchopulmonary dysplasia or respiratory syncytial virus–induced bronchiolitis as the most representative examples of harmed infant lungs. Clinical differences in this group of children would depend mainly on the lung development stage (age of the patient: preterm or term newborn or infant), the nature of the injury (eg, oxygen, tobacco, or infection), and the genetic background of the subject, which could play a secondary but relevant role. Spontaneous recovery caused by growth and maturation is the rule sooner or later in childhood, whereas the long-term prognosis is unknown.[3]

Nonallergic asthma should be differentiated from allergic or atopic asthma, in which genetic susceptibility prevails, producing a systemic immune imbalance with lung involvement. The disease is modulated by environment and lifestyle and evolves in an early stage of life (usually in infancy or childhood), and the natural history tends toward persistence.[4]

Nonallergic and atopic asthma share some similarities that have favored the confusion between them, such us the age of appearance, the recurrence of wheezing triggered by viral diseases, and a good response to the same pharmacologic agents. Furthermore, neither disease is exclusive, and because they are prevalent, some infants and children can be affected by both of them. The symbolic relative prevalence of this disorder in childhood is represented in Fig 1. The right diagnosis and prognosis is not so easy in the wheezing child only a few years of age.[5]

Many studies have found no correspondence between impaired lung function at birth or an early respiratory syncytial virus infection and later atopic asthma,[6-8] but we do not know of any work looking for a link between bronchopulmonary dysplasia, lowered pulmonary function at birth, and viral (respiratory syncytial virus) infections as a common source of recurrent, self-limited, nonallergic wheezing in childhood. Future studies could elucidate whether nonatopic wheezers (transient or persistent) share enough genetic, pathologic, and immunobiologic similarities to be grouped under the diagnosis of nonallergic childhood asthma.

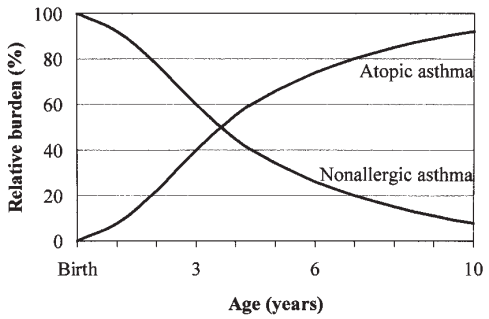

FIG 1. Estimated relative burden of recurrent wheezing (or asthma as a syndrome) in childhood attributable to nonallergic and atopic asthma related to age. The shape of this symmetric curve might depend on local and temporal circumstances affecting the risk factors for both diseases.

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Reply

To the Editor:

We appreciate the kind words about the Tucson Children's Respiratory Study from Dr Moral Gil and colleagues.[1] We certainly agree with them that childhood wheezing remains a complex subject and that we have not yet finished sorting out the various wheezing phenotypes. It is also quite possible that the various wheezing groups we and others have described are heterogeneous and that further studies are necessary to define more precisely the characteristics of these wheezing groups of infants and children. Future genetic studies should also be helpful in this regard.

We do believe that the transient wheezers are different as a group from the nonatopic wheezers, as we summarized in our review article.[2] The transient wheezers have lower lung function early in life before any respiratory insult, and although their lung function improves with growth, it remains lower than that in infants or children who never wheezed. This is in contrast to the nonatopic group, who start out with normal lung function but end up with slightly lower lung function and enhanced airway reactivity later in childhood. As we noted in the review article, it is likely that these children have increased airway reactivity from birth, which they progressively lose in the first 10 to 15 years of life.[3] We would agree with Moral Gil et al[1] that it is possible to have more than one pathophysiologic process ongoing in any individual infant, but we have yet to understand all of this. We would not necessarily conclude, at this point in time, that the nonatopic wheezers will end up with persistent abnormalities, as they suggest.

It should be noted that the infants enrolled in the Tucson Children's Respiratory Study had no evidence of neonatal lung problems or bronchopulmonary dysplasia and therefore had no apparent lung insult before their first lower respiratory tract illnesses.

We look forward to studies by Dr Moral Gil and coworkers and others to help clarify these illnesses in childhood and, more importantly, to help develop preventative strategies and better therapies for these children.

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