

Predicting the future for recurrent respiratory symptoms in young children: Applying a dash of science to the art of medicine

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At the medical school entry interview, students in the United Kingdom are highly likely to be asked the following question: “Why do you want to be a doctor?” Many will respond, “because I am good at science and want to help people, and medicine seems to be the right way to do this.” Those who are awarded a place at medical school experience an epiphany during their first year when they discover that there is little science behind much clinical decision making. Asthma is one of a number of conditions that might awaken a student’s consciousness to the art of medicine because the diagnosis is commonly made despite there being no unifying definition or diagnostic test.

The diagnosis of asthma in children aged less than 5 years can present a particular challenge. The problems are that young children (1) are more likely to have respiratory tract infections that cause cough, shortness of breath, and respiratory noises that might be reported as “wheeze”; (2) make genuine wheezing sounds with lower respiratory tract infections; and (3) are more likely to have alternative causes of recurrent wheeze, including acute episodic (viral) wheeze, undiagnosed cystic fibrosis, ciliary dyskinesia, and congenital airway abnormalities, when compared with older children.^{1,2}

There have been 3 phases in the evolution of the diagnosis of asthma in young children. Initially, there was the “denial” phase, in which there was debate as to the lower age limit at which an asthma diagnosis could be made, with the consensus being somewhere between 7 and 10 years of age. In an entirely non-Darwinian process, the second phase occurred in the early 1980s, in which, after a “meteorite” of an article³ that described improved asthma symptoms in young children treated with inhaled corticosteroids, asthma became a diagnosis of exclusion. The liberation of diagnostic criteria from “none” to “all” perhaps not unsurprisingly coincided with a worldwide increase in asthma prevalence and brought us to the present third (and hopefully final) phase, in which asthma is a diagnosis that has to be made.

Although the majority of health care professionals now agree that asthma does occur in young children and is not a diagnosis of exclusion, how do you objectively diagnose asthma in a young child? Examination findings are invariably within normal limits, and a test for asthma remains elusive; therefore the patient’s history has to hold the answer. A number of groups have used details collected as part of cohort studies to introduce some evidence into the extremely subjective process of diagnosing asthma in young children. These studies are able to do what the clinician cannot and look forward in time to see what factors predicted asthma outcome at age 5 years or older. The assumption is that if they have asthma in the future, then their present symptoms are also asthmatic in nature. Ideally, the predictive algorithms would be sensitive and specific for asthma across a number of populations and languages and also be easily applied in primary and secondary care. Inevitably, these aspirations have not yet been met, and in part, this is explained by the challenge in relating subjective outcomes in very young children to a subjective outcome in slightly older children. Additionally, differences between studies for ages at assessment and outcomes initially captured will contribute to heterogeneity between studies for the best predictors of asthma risk.

In the present issue of the *Journal*, Pescatore et al⁴ use data collected in a cohort of children in Leicester to create a 10-item questionnaire that can be used to assist clinicians in predicting asthma outcome in 1- to 3-year-old children with respiratory symptoms. The strengths of this study include the large number of children included, recruitment from the community, and the novel statistical approach taken. Of the 5878 children surveyed at 1 to 3 years of age, 2444 had some respiratory symptoms, of whom 1226 were assessed at 5 years of age, including 345 (28%) who had asthma. This study design allowed the team to ask the following question: “What did we know at 1 to 3 years of age that predicted the outcome at age 5 years?” The team used their LASSO-penalized logistic regression to work out which of the 24 questions asked at 1 to 3 years of age helped to predict asthma in this population. The distillation yielded 10 predictors, and the 5 most relevant were shortness of breath, frequency of wheeze, wheeze without colds, exertional wheeze, and cough. The addition of male sex, age greater than 1 year, eczema, parental asthma, and cough on exposure to aeroallergen further increased the model’s precision. The authors found that their model had superior precision for more severe asthma compared with asthma *per se*.

Where does this leave the clinician who tomorrow meets a young child with recurrent respiratory symptoms and concerned parents? Unfortunately, at present, this study does not yet provide a scientifically rigorous solution; as the authors acknowledge, their algorithm needs validation in other populations, and there is

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a track record of such algorithms not performing as well as hoped in external validation. However, there are 2 important points made by the authors. First, the diagnosis of asthma in all ages, but particularly in young children, requires a good history, and this article details the possible focus of these questions. Second, Table III usefully compares and contrasts the precision of similar questions used in other studies, and there is consistency emerging from the different populations that wheeze that is frequent, present without a cold, and induced by exercise has good precision for later asthma; this supports current international guidelines.²

Although this and similar articles help address the question of whether this child will have asthma, what remains uncertain is the answer to the following question: “Does this child have asthma now?” Fortunately, the young child with asthma symptoms does not worry about the science if he or she is treated with inhaled steroids with substantial symptom improvement. National guidelines,^{1,2} which have an evidence base,⁵ advocate a trial (eg, 3 months) of low-dose inhaled corticosteroids as safe and

effective in asthmatic children. The take-home point is that, regardless of the child’s age, if the wheeze is frequent (eg, 3 times a year) and present without a cold (eg, on exercise), the response to a 3-month trial of inhaled corticosteroids will answer one more question: “Do you think it is asthma?”

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