

# Wheezing Exacerbations in Early Childhood: Evaluation, Treatment, and Recent Advances Relevant to the Genesis of Asthma

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Children who begin wheezing during early childhood are frequently seen by health care providers in primary care, in hospitals, and in emergency departments, and by allergists and pulmonologists. When a young child, such as the 2-year-old patient presented here, is evaluated for wheezing, a frequent challenge for clinicians is to determine whether the symptoms represent transient, viral-induced wheezing or whether sufficient risk factors are present to suspect that the child may experience recurrent wheezing and develop asthma. Most factors that influence prognosis are not mutually exclusive, are interrelated (ie, cofactors), and often represent gene-environment interactions. Many of these risk factors have been, and continue to be, investigated in prospective studies to decipher their relative importance with the goal of developing new therapies and interventions in the future. The etiologies of wheezing in young children, diagnostic methods, treatment, prognostic factors, and potential targets for prevention of the development of asthma are discussed. © 2014 American Academy of Allergy, Asthma & Immunology (*J Allergy Clin Immunol Pract* 2014;2:537-43)

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## CASE

A 2-year-old white boy presented to the emergency department (ED) in December 2013 with increased work of breathing. His mother reported that he had a 3-day history of cough and congestion, with intermittent fever. Tonight, she noticed that he was “breathing harder than usual.” Results of a physical examination showed that he was afebrile and tachypneic, at 40 breaths per minute, with oxygen saturation of 98% on room air. He had significant nasal congestion and diffuse wheezing throughout all lung fields, with subcostal retractions. His medical history is significant for premature birth (32 weeks estimated gestational age), atopic dermatitis, and bronchiolitis that required hospitalization but not intubation during the spring of his first year of life. In the neonatal period, he did not require oxygen supplementation beyond 2 weeks of age. He was not breastfed. The family history was significant for maternal atopic asthma and for a 4-year-old sibling in preschool with an acute respiratory illness at home. The patient was not in day care, and there was no household exposure to domestic pets or tobacco smoke.

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**Abbreviations used**

API- Asthma Predictive Index  
 EGA- Estimated gestational age  
 RV- Human rhinovirus  
 ICS- Inhaled corticosteroids  
 mAPI- Modified Asthma Predictive Index  
 RSV- Respiratory syncytial virus

## ETIOLOGIES, EVALUATION, AND TREATMENT OF EARLY CHILDHOOD WHEEZING

Wheezing during the infant and toddler years is a common problem, estimated to affect 1 of 3 children at least once during the first 3 years of life.<sup>1</sup> The differential diagnosis of acute wheezing is protean, and information available to the clinician about the evaluation, treatment, and prognosis of infants and toddlers with wheezing exacerbations is somewhat controversial. Not enough is known about the distinction between asthma and episodic viral wheezing in young infants because many infants and toddlers who wheeze do not develop chronic and/or recurrent symptoms. However, 4- to 6-year-old children with wheezing during acute viral infections are often atopic and can have airway inflammation and reversible airflow limitation in addition to asthma-type signs and symptoms, including cough, difficulty breathing, wheezing, and tachypnea.<sup>2</sup>

### Etiologies

Respiratory viral infections are the most common etiologies of acute wheeze in children and are identified in up to 90% of children younger than age 3 years who are hospitalized with wheezing.<sup>3,4</sup> During mid winter months in the Northern hemisphere, common pathogens associated with preschool wheezing include respiratory syncytial virus (RSV), human metapneumovirus, and influenza virus, especially in infants younger than 6 months of age who are wheezing<sup>4,5</sup>; whereas, atypical bacteria *Mycobacteria pneumoniae* and *Chlamydia pneumoniae* occur more often in school-age children and adolescents.<sup>6,7</sup> During the first 6 months, however, up to 24% of infants with lower respiratory tract illness can test positive for *Chlamydia trachomatis*.<sup>8</sup> During other months of the year, notably spring and fall, human rhinovirus (RV) is the most prevalent virus detected and continues to be the most common viral pathogen linked to asthma among older children and adults. A newly described group of RVs called RV-C may be prevalent during mid winter months as well.<sup>9</sup>

Evaluation of a child with wheezing illness relies on a careful history and physical examination. The clinician should consider the differential diagnoses and differentiate wheezing from rhonchi generated from the upper and large lower airways. Acute wheezing in the young child may be infectious (often with associated fever or upper respiratory symptoms) or may be related to foreign body aspiration (sometimes with abrupt onset, choking episode, unilateral wheezing, unequal breath sounds, or typical radiographic findings). Noninfectious etiologies of chronic or recurrent wheezing in the infant and toddler age groups may include structural abnormalities (which usually do not respond to bronchodilator therapy and may include cardiovascular disease, anomalies of the tracheo-bronchial tree, mediastinal masses) or functional causes (including aspiration syndromes, eg, gastroesophageal reflux, which may present with vomiting; hoarseness; symptoms while supine or after feedings; or "recurrent croup"). Other conditions that may present

**TABLE I.** Host and environmental factors that may influence the genesis of asthma during childhood

Host factors that increase asthma risk	Reference no.
Male sex	23, 26
Premature birth (<28 wk EGA)	27, 28
Low lung function	26, 30
Delayed maturation of Th1 antiviral immunity	31
Decreased antiviral innate immunity	32, 33
Familial or personal atopy	See Table II (26, 34-36, 75, 76)
Environmental factors	
Increase risk of asthma	
Wheezing caused by viruses (especially RSV and rhinovirus)	40-43
Exposure to dust mite allergen at home during infancy	55
Neonatal pharyngeal colonization with respiratory bacterial pathogens* and virus and/or bacteria interactions	44
Courses of antibiotics	45, 46
Environmental tobacco smoke exposure	58
Urban air pollution (eg, diesel fuel particles)	59
Acetaminophen in early childhood	53
Decrease risk of asthma	
Day care attendance and exposure to older siblings	38, 39
Bacterial colonization of the gut, airway, and skin	44, 47, 49, 52
Exposure to dogs in early life	56, 57

EGA, Estimated gestational age.

\*For example, *S pneumoniae*, *H influenzae*, *M catarrhalis* (from Ref 44).

with recurrent wheeze include immune deficiency, cystic fibrosis, and other host-related diagnoses. In general, localized wheezing, recurrent pneumonia, feeding difficulties, and a lack of response to bronchodilator therapy suggest a nonviral etiology of wheezing.

Important information to guide therapy for acute infectious wheeze and to assess the risk of developing asthma includes a history of prior wheeze, frequency of recurrent wheezing, recurrent or chronic cough, cough with exercise, severe wheeze that requires hospitalization and/or an emergency department visit, nocturnal symptoms (marker of diffuse airway inflammation and/or obstruction), wheezing caused by documented viral respiratory infections, and response of previous episodes to short-acting  $\beta$ -2-agonist treatments and oral corticosteroids. Also important are the birth history (gestational age, delivery mode), feeding history (breastfed), family history of atopy and asthma, personal history of atopic dermatitis or food allergies, and environmental exposures known to increase or decrease the risk for symptom severity and persistence of wheezing (Table I).

### Diagnostic evaluation

A chest radiography may be helpful in the acute setting for a young child with fever or persistent wheezing, or with concerns about anatomic etiologies or foreign body. Elevated blood eosinophils (obtained before starting systemic steroids in the acute care setting) in a young child may indicate atopy and be a risk

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