Respiratory Tract Infections and Asthma

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Introduction

For many patients with asthma, especially children, respiratory infections provoke wheezing. Initial attention focused on bacteria as the etiological agents; however, prospective studies conclusively indicated that viral, not bacterial, respiratory infections triggered asthma. Less well established is the possibility that respiratory infections are a pivotal event in the pathogenesis of asthma. This chapter will focus on the role of respiratory tract infections, particularly viral illnesses, and asthma. Three major areas will be covered:

1. The epidemiology of respiratory infections and asthma;
2. Respiratory syncytial virus bronchiolitis as a model for respiratory infections and asthma; and

Epidemiology of Respiratory Infection and Asthma

Viral Respiratory Infections Exacerbate Asthma

For decades, clinicians “knew” that respiratory infections provoked asthma in many of their patients. However, proof of this association came only after prospective studies proved by culture that respiratory viruses were the causative infectious organism. A number of respiratory viruses have been associated with exacerbations of asthma (Table 1). As will be noted in the discussion that follows, the particular respiratory virus that provokes asthma is often dependent on the age of the subject. Consequently, the worsening of asthma with a respiratory infection may be related to the illness and not specifically one particular virus. Clearly there will be unique features with many of the respiratory viruses but it is our belief that the general effects of such illnesses on asthma will have many similarities.

A prospective outpatient study from the University of Wisconsin evaluated 16 children, ages 3–11 yr, with histories of four or more asthma attacks associated with respiratory illnesses during the previous year (1). Detailed clinical
Table 1
Respiratory Viruses Associated with Asthma Exacerbations

<table>
<thead>
<tr>
<th>Virus</th>
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<tbody>
<tr>
<td>Respiratory syncytial virus</td>
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<tr>
<td>Rhinovirus</td>
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<tr>
<td>Parainfluenza</td>
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<tr>
<td>Adenovirus</td>
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<td>Influenza</td>
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records profiled each child’s asthma severity, which was further substantiated with biweekly examinations. During an asthma exacerbation, or apparent URI, additional bacterial and viral cultures were collected and asthma symptoms carefully quantitated. The 16 children experienced 61 episodes of asthma; 42 of which occurred in conjunction with a symptomatic respiratory infection, and 24 were confirmed to be of a viral etiology by culture and/or serum hemagglutination titers. In this study, rhinovirus was the most frequently isolated virus in association with wheezing. Some patients had episodes of asymptomatic viral infection, but asthma was not worsened. Only one episode of wheezing coincided with a bacterial infection.

In a large study of pediatric outpatients at the University of North Carolina, 6165 subjects were evaluated with lower respiratory illnesses during which 1851 (30%) had wheezing (2). Wheezing with a respiratory illness was more common in children under the age of two. Yet, 19% of patients over age nine still wheezed with respiratory infections. RSV, parainfluenza, adenovirus, and *Mycoplasma pneumoniae* accounted for over 80% of the isolates in children with wheezing.

McIntosh and coworkers (3) selected 32 young children, ages 1–5 yr, and prospectively evaluated exacerbations of wheezing with respiratory tract infections. Of the 139 asthma attacks experienced by these children, 58 episodes (42%) occurred during a viral respiratory infection, of which RSV was the most frequent. Although bacteria, such as *Haemophilus influenzae*, *Streptococcus pneumoniae*, β-hemolytic streptococcus, and *Staphylococcus aureus* were also cultured from these patients, their recovery did not correlate with an asthma attack.

Horn et al. (4) also found that RSV was an important pathogen for children who wheezed with respiratory infections. Further, they noted that the development of constitutional symptoms was important for a flare of asthma to occur, and wheezing was more likely to occur with the cold if the child was symptomatic with malaise, mucous production, or cough. Some asymptomatic patients had respiratory viruses recovered on routine culture, but experienced no increase in wheezing. Taken together, these observations indicate that wheez-