

Influence of Viral and Bacterial Respiratory Infections on Exacerbations and Symptom Severity in Childhood Asthma

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INTRODUCTION

The role of viral and bacterial infections in asthma severity is an enormous subject. In this paper I will concentrate on recent work examining the importance of viral infections in acute exacerbations of asthma, and *Chlamydia pneumoniae* infection in asthma symptom severity.

VIRAL INFECTIONS IN ASTHMA EXACERBATIONS

Previous studies on viral infections in exacerbations of asthma have proven inconclusive, chiefly due to low viral detection rates resulting from difficulties in obtaining an early adequate specimen for testing, and deficiencies in the viral diagnostic methods available¹. The common respiratory viruses are rhinoviruses (around 60% of upper respiratory infections) and coronaviruses (15%) - the remainder of infections are caused by the better known influenza, parainfluenza, respiratory syncytial virus (RSV) and adenoviruses.

We have developed polymerase chain reaction (PCR) assays for rhinoviruses and human coronaviruses that detect 2-3 times more infections than the best available standard techniques^{2,3}. Using these new methods in a community based epidemiological study of exacerbations of asthma in 9-11 year old children, we were able to detect respiratory viral infections in 80-85% of exacerbations⁴. A further study also demonstrated a powerful association of viral infections with more severe exacerbations of asthma leading to hospital admissions, in both adults and children. There was also a strong relationship between the hospital admission rates in children and school attendance, with a peak in admissions in the first few weeks of each school term⁵.

We have recently studied infants and children admitted to hospital with severe wheezing illness and

bronchiolitis, using PCR for rhinoviruses, enteroviruses and RS virus. Of 1-15yr olds with wheezing illness, rhinovirus alone was found in 65% and RS virus 3%, while in cases of bronchiolitis, RS virus alone was found in 50%, rhinovirus and enterovirus each in 10%, and dual infection with RSV and rhinovirus in 30%⁶.

Other studies have used similar methodologies to examine the importance of viruses in asthma exacerbations in adults and infants with wheezing illness. Virus infections have been found to be important in all age groups^{4,5,7-9}. Studies of children presenting to the Emergency Room with wheeze found that viruses were the major factor in children under the age of 2 years, while an interaction between allergic sensitization and viral infection seemed important after the age of 2 yrs^{7,8}. In all these studies, the most frequently identified viruses in association with wheezing illness under 2 years of age were RSV (50-60%) followed by rhinoviruses (30%), while rhinoviruses account for over 60% of viruses detected in children over 2 years of age.

ASSOCIATION BETWEEN LOCAL ANTIBODY TO CHRONIC *Chlamydia pneumoniae* AND ASTHMA SYMPTOM SEVERITY

During the same longitudinal study⁴, we examined the importance of atypical bacterial infection in exacerbations of asthma using sensitive nested PCR for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. Detection rates for *C. pneumoniae* in reported and

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asymptomatic samples were similar (24% vs 28% respectively) and 47% of children were PCR positive for *C. pneumoniae* at some stage during the study¹⁰. Children positive on any one occasion were likely to be positive again if tested subsequently, suggesting chronic infection. *C. pneumoniae*-specific sIgA antibodies in nasal aspirates were measured by amplified EIA and were seven times greater in subjects who reported 4 or more exacerbations in the study compared to those who reported just one ($p < 0.02$). There was no evidence for a role for *M. pneumoniae* in acute exacerbations of asthma. This study found an unexpectedly high rate of chronic *C. pneumoniae* infection, and immune responses to *C. pneumoniae* were positively associated with frequency of asthma exacerbations. The high prevalence of *C. pneumoniae* was confirmed in children admitted to hospital with bronchiolitis and wheezing illness. We found prevalences of *C. pneumoniae* infection varying from 18% in those aged less than 3 months, to 58% in those aged over 5 years (Johnston SL, Xie P, Johnson W, unpublished data). The very high prevalence in these children with severe disease also supports a possible pathogenic role for *C. pneumoniae* infection in asthma symptom severity. Further larger and carefully controlled studies are now required to investigate this possibility.

SUMMARY

The recent development of PCR for the diagnosis of respiratory viral infection has highlighted the importance of these infections in acute exacerbations of asthma. Rhinoviruses are important in all age groups, but particularly over 1 yr, while the role of RSV in bronchiolitis and wheezing in infants has been reaffirmed.

Recent studies using the same technique for the detection of *C. pneumoniae* suggest a high prevalence of chronic infection in asthmatic children, and that the immune response to this organism may play a

pathological role. These studies now require confirmation with larger carefully controlled studies.

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