

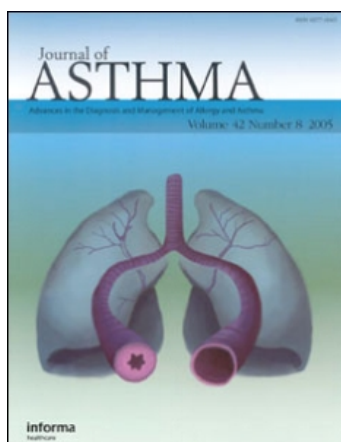
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A SHORT ORIGINAL REPORT

Does *Chlamydia pneumoniae* Infection Trigger to Development of Asthma in Wheezy Infants?

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The role of *Chlamydia pneumoniae* (CP) infection in infantile asthma remains obscure. CP infection was serologically determined (Immunoglobulin M antibody titer of index (ID) ≥ 2.00) in wheezing infants who were then re-examined at 3 years of age to determine whether asthma is associated with CP infection. Wheezing infants with CP infection progressed to asthma more frequently than those who were not infected. These findings may suggest that CP infection triggers the development of asthma in wheezy infants.

Keywords asthma; *Chlamydia pneumoniae*; *Chlamydia pneumoniae* specific IgM antibody; infant; wheezing

Chlamydia pneumoniae (CP) is a frequent and important cause of respiratory tract infections. Recent reports have suggested that CP infection of the respiratory tract might exacerbate and/or initiate asthma. We have already reported the findings (1) of CP infection serologically diagnosed in wheezy infants as a single immunoglobulin (Ig) M antibody titer of index (ID) ≥ 1.00 according to the Guidelines for the Management of Respiratory Infectious Diseases in Children in Japan 2004 (2). That study demonstrated that CP infection in infants with wheezing is associated with the development of asthma (1). However, the Guidelines were revised in 2007 and ID ≥ 2.00 was recommended as the single IgM antibody titer for a diagnosis of CP infection. We re-evaluated whether CP infection in infants with wheezing is associated with the development of asthma using the diagnosis by the Guidelines for the Management of Respiratory Infectious Diseases in Children in Japan 2007 (3).

We enrolled 202 infants between 3 and 23 months of age in our study. All of them attended our hospital with a first episode of wheezing. The control subjects comprised 120 healthy children who were randomly selected and matched for gender and age. Written informed consent was obtained from the parents of all participants of the study. At the first examination, we confirmed the age, gender, and family history of allergic diseases in addition to laboratory findings including eosinophil counts IgE, and the CP-specific serum titers of IgG, IgA, and IgM. Infection with CP was defined as a single IgM antibody titer of ID ≥ 2.00 according to the Guidelines for the Management of Respiratory Infectious Diseases in Children in Japan 2007 (3). We also confirmed whether infants with wheezing at the age of 3 years had been diagnosed with bronchial asthma. Asthma was diagnosed based on (1) the effectiveness of inhaled beta-agonists, (2) recurrent wheezing and dyspnea attacks that started after the first examination, and (3) a high level of serum IgE or a fam-

ily history of allergic diseases. The results were statistically analyzed using the chi-square and Mann-Whitney U tests for categorical and continuous variables, respectively. A *p* value below 0.05 was considered statistically significant.

A family history of allergic diseases was significantly more frequent among infants with wheezing than among control subjects. The number of eosinophils and serum IgE levels in infants with wheezing were significantly higher than those from control subjects (177.9 ± 206.2 vs. $113.2 \pm 147.5/\mu\text{L}$ and 235.1 ± 51.8 vs. 96.5 ± 250.0 IU/mL, respectively). The levels of serum IgG and IgA against CP-specific antibody did not significantly differ between the two groups. We also found that levels of CP-specific IgM antibody were elevated in 13.9% (28 of 202) of infants with wheezing and in 2.5% (3 of 120) of controls with ID ≥ 2.00 (odds ratio, 6.3; 95% CI, 1.9–21.1) and confirmed that CP is an important cause of wheezing in early childhood.

Table 1 shows the risk factors of development to asthma at 3 years of age in 202 infants with wheezing. Progression to asthma was significantly related to a family history of allergic diseases, the number of eosinophils, and the serum IgE level at the first examination. Furthermore, asthma developed significantly more frequently in wheezing infants with than without elevated (ID ≥ 2.00) levels of CP-specific IgM antibody (53.6%, 15/28 vs. 31.6%, 55/174; relative risk; 1.7, 95% CI; 1.1–2.5). We confirmed that wheezing infants tended to develop asthma more frequently after CP infection.

In a previous study (1), we reported that 44.7% (46/103) of infants with wheezing and 17.2% (11/64) of healthy infants had an elevated CP-specific IgM antibody (ID ≥ 1.00). The positive rate was unexpectedly high in both groups, and we speculated that the data might not include only the acute CP infection but also the past infection with CP. In this study, we reconfirmed that levels of CP-specific IgM antibody were elevated in 13.9% (28 of 202) of infants with wheezing with ID ≥ 2.00 . This positive rate was almost similar to the rate of CP infection diagnosed using polymerase chain reaction (PCR) methods. This result demonstrated that CP is an important cause of wheezing in early childhood. Both of our

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TABLE 1.—Risk factors of progress to asthma at 3 years age among 202 wheezing infants.

	Asthma –	Asthma +
Infants (n)	132	70
Gender (M/F)	79/53	40/30
Age (months)	12.9 ± 6.6	14.7 ± 6.5 $p=0.06$
Family history of atopic diseases (n)	73	53* RR 1.8 (95%CI 1.2–3.0)
Number of eosinophils (/μL)	153.6 ± 177.8	223.9 ± 246.0* $p=0.02$
Serum IgE (U/mL)	109.2 ± 138.6	472.5 ± 805.0* $p=0.001$
CP infection (n)	13	15* RR 1.7 (95%CI 1.1–2.5)

CP = *Chlamydia pneumoniae*; RR = relative risk; 95%CI = 95% confidence interval; IgE = immunoglobulin E. Data are values at first examination and are shown as numbers or means ± SD. * $p < 0.05$ vs. no asthma.

studies confirmed that the development of asthma in infants with wheezing was significantly related to a family history of allergic diseases, the number of eosinophils, and the serum IgE level. In addition, asthma developed significantly more frequently in wheezing infants with than without CP infection in a previous report (76.1%, 35/46 vs. 26.3%, 15/57; relative risk; 2.9, 95% CI; 1.8–4.6) and also in this present study.

Infection with CP might trigger wheezing and progression to airway inflammation in infants. Th1 type immunoreactions are believed to remove CP, but CP infection might elicit Th2

type-inflammation associated with the onset and/or exacerbation of asthma, which is insufficient time for deviation to Th1, such as during infancy (4). Modulation of the CP infection-immune response in early childhood might represent a therapeutic target for the prevention of asthma. Further large-scale studies are required to confirm the relationship between CP infection and asthma in early childhood.

DECLARATION OF INTEREST

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REFERENCES

1. Zaitzu M. The development of asthma in wheezing infants with *Chlamydia pneumoniae* infection. *J Asthma* 2007; 44:565–568.
2. Uehara S, Sunagawa K. *Chlamydia* infection. In Uehara S, Sunagawa K, eds. Guidelines for the management of respiratory infection diseases in children in Japan 2004. Tokyo, Japan: Kyowakikaku Co. Ltd. 2004: 16–17.
3. Uehara S, Sunagawa K. *Chlamydia* infection. In Uehara S, Sunagawa K, eds. Guidelines for the management of respiratory infection diseases in children in Japan 2007. Tokyo, Japan: Kyowakikaku Co. Ltd. 2007: 17–18.
4. Hansbro PM, Beagley KW, Horvat JC, Gibson PG. Role of atypical bacterial infection of the lung in predisposition/protection of asthma. *Pharmacol Ther* 2004; 101:193–210.