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# *Chlamydia trachomatis* respiratory infection in Dutch infants

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## ABSTRACT

*Chlamydia trachomatis* is the most common bacterial pathogen causing sexually transmitted infections in Dutch adults. As prenatal screening for *C trachomatis* and treatment of pregnant women is not routine practice in The Netherlands, perinatal transmission of *C trachomatis* may therefore occur. The presence of *C trachomatis* in infants less than 6 months of age who presented with respiratory complaints to the Erasmus MC-Sophia hospital was evaluated. Respiratory specimens, primarily nasopharyngeal swabs, were tested for *C trachomatis*, respiratory viruses and *Mycoplasma pneumoniae* using PCR, viral isolation in cell cultures and direct immunofluorescence. *C trachomatis* respiratory tract infection was confirmed to be relatively common with detection in 10 of 148 (7%) infants tested. *C trachomatis* had not been tested for by the attending physicians, but was the second most frequently detected respiratory pathogen after human Respiratory Syncytial Virus, which was found in 41 (28%) infants.

Although *Chlamydia trachomatis* is currently the most prevalent sexually transmitted bacterial infection in The Netherlands, pregnant women are not screened for *C trachomatis* infection in The Netherlands, and it is not a notifiable disease. The prevalence of *C trachomatis* infection among pregnant women in Rotterdam, however, is approximately 6%.<sup>1</sup> Recently, we reported that *C trachomatis* was a major cause of neonatal conjunctivitis in infants less than 3 months of age in our population in Rotterdam.<sup>2</sup>

In the present study, we evaluated the presence of *C trachomatis* respiratory-tract infection in infants presenting with respiratory complaints in the same region in Rotterdam, The Netherlands.

## METHODS

The study was conducted at the Erasmus MC-Sophia Hospital, Rotterdam, The Netherlands. *C trachomatis* screening is not standard practice in pregnant women in the study area; testing is done on clinical suspicion only. Respiratory specimens (nasopharyngeal aspirates or broncho-alveolar lavages) were collected from infants less than 6 months of age who presented with symptoms and signs compatible with respiratory-tract infection to the hospital between January 2002 and January 2003. All specimens were prospectively tested for viral pathogens and *Mycoplasma pneumoniae*, and retrospectively tested for *C trachomatis*. Clinical data, eosinophil count and chest x ray results were collected through a systematic review of medical records.

Initially, the samples were sent to the virology laboratory specifically requesting a test for respiratory viruses. Routine virological testing for respiratory pathogens was performed using direct immunofluorescence on cells in respiratory specimens, virus isolation in cell cultures and immunofluorescence, and included human Respiratory Syncytial Virus (hRSV), influenza A, B and C viruses, human p-influenza virus types 1–4, adenovirus and rhinovirus. Following a diagnosis of picornavirus, nucleic acid amplification techniques were performed with specific primers. Thereafter, samples were stored at  $-70^{\circ}\text{C}$  until processing for *C trachomatis* detection in the present study. Detection of human Metapneumovirus (hMPV), *M pneumoniae* and *C trachomatis* was done by PCR.

Data were analysed using SPSS 10.0.0 (SPSS, Chicago). A p value of  $<0.05$  was considered significant.

## RESULTS

A total of 157 infants were eligible for the study. From nine infants, the specimens were consumed while testing for viral pathogens during admission. From 148 (94%) infants, 187 respiratory specimens (184 nasopharyngeal aspirates and three broncho-alveolar lavage fluids) were available for *C trachomatis* testing. The mean age of the infants was 67 (SD 49) days (range 1 to 172 days); 68 of 148 (46%) were female and 80 of 148 (54%) male.

Potential respiratory pathogens were identified in 67 of 148 (45%) infants. *C trachomatis* was detected in 10 [7%] infants. Among the viral pathogens, hRSV was detected in 41 [28%] infants, followed by rhinovirus (six of 148 (4%)), influenza A virus (three of 147 (2%)), adenovirus (two of 147 (1%)), p-influenza 3 virus (two of 147 (1%)) and p-influenza 1 virus (1 of 147 (1%)). Influenza B and C virus, p-influenza 2 and 4 virus, hMPV and *M pneumoniae* were not detected. One (10%) *C trachomatis* positive infant was also infected with hRSV.

Comparison of *C trachomatis* and viral pathogens by age group (less than 3 months vs 3–6 months) showed that both *C trachomatis* and hRSV infections were more often observed in the younger group (fig 1). Eight of 10 (80%) *C trachomatis* infections occurred before 3 months of age. hRSV was the most common pathogen detected in both age groups.

The underlying pathology and clinical characteristics of the 10 *C trachomatis* positive infants and their mothers are shown in table 1. Most infants had significant underlying disease except for patients 4 and 5. Five infants had a history of

## Short report

**Table 1** Characteristics of *Chlamydia trachomatis* positive infants and their mothers

Infant no	1	2	3	4	5	6	7	8	9	10
Underlying pathology	Meconium stained liquor, pulmonary haemorrhage eci	Hypoplastic left heart syndrome	IUGR, dysmorphism, microcephaly, unilateral choanal atresia stenosis	–	–	Antenatal asphyxia, generalised hypotonia, epilepsy	Hypoplastic left heart syndrome	Acute myeloid leukemia	Very long-chain acetyl coenzyme A dehydrogenase deficiency, hypertrophic cardiomyopathy	Chronic eczema, feeding intolerance
Characteristics										
Mother										
Maternal age	32	31	26	24	28	31	27	23	35	21
Gravidity	1	1	2	1	4	2	1	1	5	1
Term delivery	+	+	+	+	+	+	+	+	+	+
Vaginal delivery	+	+	+	+	+	Caesarean section	+	+	+	+
Infant										
Appropriate for gestational age	+	+	Small for gestational age	+	+	+	+	+	+	+
Age at testing (days)	11	17	26	32	33	45	48	65	147	168
Rhinorrhoea/congestion	+	–	–	+	+	+	+	+	+	–
Fever	–	–	+	–	–	–	–	+	+	–
Cough	–	+	–	–	+	–	+	–	–	–
Apnoea	–	–	–	–	+	–	–	–	–	–
Cyanosis	+	+	–	–	+	+	+	–	–	–
Retractions	–	–	+	–	+	+	–	–	–	+
Wheezing	–	+	–	–	+	–	–	–	–	+
Creptitations	+	–	–	–	–	–	–	–	–	–
Dyspnoea	+	+	+	–	+	+	+	+	–	+
Tachypnoea	+	+	–	+	–	+	+	+	–	+
Oxygen requirement	+	+	+	–	+	+	+	–	–	–
Feeding difficulties	+	+	+	+	+	+	+	+	+	+
Chest x ray										
Hyperinflation	–	–	–	–	+	–	+	–	ND	+
Atelectasis	+	+	–	–	+	+	–	–	ND	–
Interstitial infiltrates	–	–	–	–	–	–	–	–	ND	+
Consolidation	+	–	–	–	–	–	–	–	ND	–
Laboratory										
Leucocytes ( $\times 10^9/l$ )	12.7	9.0	9.0	14.1	4.6	10.8	9.4	1.3	23.0	26.0
Eosinophils ( $mm^3$ )	889	720	90	1128	ND	ND	752	0	ND	780
Viral pathogens										
Human Respiratory Syncytial Virus	–	–	–	–	+	–	–	–	–	–

IUGR, intra-uterine growth retardation; ND, not done.

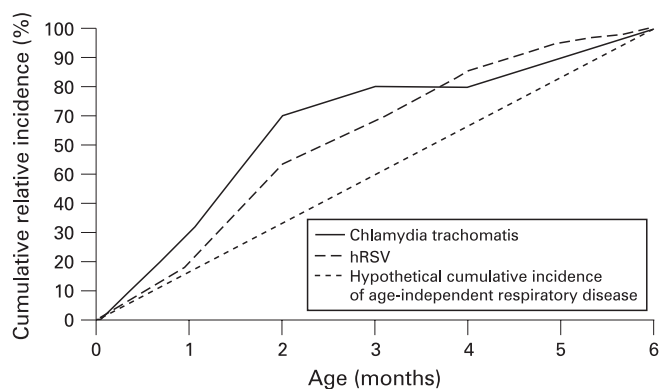
conjunctivitis: patient 1 had *Klebsiella pneumoniae* cultured from a conjunctival specimen 4 days after birth, and patient 3 had *Haemophilus influenzae* at 22 days of age; eye cultures from the other infants showed no growth. None of the eye samples were tested for *C trachomatis*. Seven infants had signs compatible with upper-respiratory-tract infection, and most infants had signs compatible with lower-respiratory-tract infection. However, only one patient (#10) had a characteristic chest x ray with hyperinflation and interstitial infiltrates compatible with chlamydial pneumonia. Bacterial cultures of the nasopharynx, sputum and/or blood were negative for all infants except patients 3 and 5, who had *H influenzae* and *Moraxella catarrhalis* with *Klebsiella oxytoca* in the sputum.

Two *C trachomatis* positive nasopharyngeal specimens were obtained from patient 8: at the age of 65 days and 174 days. On both occasions, she had rhinorrhoea and congestion.

## DISCUSSION

In this study, *C trachomatis* was detected in 7% of infants less than 6 months of age presenting to hospital with respiratory-tract infection. The role of *C trachomatis* as a causative pathogen for respiratory disease in young infants is well described in the literature.<sup>3 4</sup> All respiratory specimens in our study were sent for viral tests, but none were sent for *C trachomatis*. This suggests that the attending physicians have a low index of suspicion for *C trachomatis* infection in these infants.

The main limitations of the study are the retrospective design, lack of controls and the fact that we only included infants who presented to hospital. Therefore, this study cannot be regarded as a population-based study of the frequency of chlamydial infections. Neither can we be sure that *C trachomatis* is the causative pathogen of the respiratory complaints in these infants instead of being coincidental finding. It does, however,



**Figure 1** Cumulative relative incidence of *Chlamydia trachomatis* and human Respiratory Syncytial Virus (hRSV) infection in infants presenting with respiratory tract infection.

demonstrate the relative importance of perinatally acquired *C trachomatis* infection among infants with respiratory complaints in this population.

The nasopharynx is the most frequent site for perinatally acquired *C trachomatis* infection, but only about 20% of infants with nasopharyngeal infection go on to develop pneumonia. Nasopharyngeal infection is usually asymptomatic and self-limiting but may persist for periods of up to 1 year. *C trachomatis* pneumonia has a characteristic presentation. Infants usually present between 3 and 12 weeks of age with tachypnoea, with a distinctive (staccato paroxysmal) cough and are usually afebrile. Chest auscultation reveals crepitations, with no or minimal wheezing. Chest x rays show hyperexpansion with bilateral, diffuse interstitial and patchy alveolar infiltrates. Peripheral eosinophilia and elevated anti-*C trachomatis* IgM antibodies may be present.<sup>3 4</sup> In our study, we found 10 infants with *C trachomatis* nasopharyngeal infection, and only

one infant had the characteristic presentation of chlamydial pneumonia with infiltrates present on chest x ray. Interestingly, more than half the infants were dyspnoeic or cyanotic, or required oxygen support. Respiratory failure has been described with chlamydial infection, but is relatively uncommon and mainly described in preterm infants with an early-onset respiratory distress syndrome.<sup>5</sup> Therefore, the more severe, atypical course of chlamydial infection in our infants may rather be due to underlying pathology, which included significant cardiopulmonary disease, antenatal hypoxia, acute myeloid leukaemia and intrauterine growth retardation with microcephaly and dysmorphic features.

In conclusion, this study demonstrated that perinatal respiratory infection with *C trachomatis* is common in The Netherlands. We recommend that in countries such as The Netherlands, where screening for *C trachomatis* is not part of routine antenatal care, testing for *C trachomatis* should be included in diagnostic and treatment protocols for respiratory disease in infants during the first 6 months of life.

**Competing interests:** None.

**Ethics approval:** Ethics approval was provided by Erasmus MC.

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