

Prevalence of *Chlamydia trachomatis* and *Mycoplasma pneumoniae* in Children With and Without Pharyngitis

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The prevalence of Chlamydia trachomatis, Mycoplasma pneumoniae, group A β-hemolytic streptococcus, and other treatable organisms was studied in children with and without pharyngitis. Children aged 2 to 12 years were evaluated between November 1985 and April 1986 in three family practice offices in the Salt Lake City area. Chlamydia trachomatis was not detected in the pharynx of any of the children studied. Mycoplasma pneumoniae was cultured from 5 percent of the 242 children studied, group A β-hemolytic streptococcus from 30 percent, non-group A β-hemolytic streptococcus from 5 percent, Hemophilus influenzae from 4 percent, and Staphylococcus aureus from 14 percent. The symptoms reported were not statistically associated with any organism isolated, and clinical signs of pharyngitis were associated only with the presence of group A β-hemolytic streptococcus. Based on these results, management of pharyngitis in children should continue to be based on the detection and treatment of group A β-hemolytic streptococcus.

Pharyngitis is one of the most common illnesses seen in children. Traditionally, the primary concern of physicians has been to detect and treat group A β-hemolytic streptococcal (GABHS) infections to prevent the potential sequelae of rheumatic fever and post-streptococcal glomerulonephritis. Alternatively, pharyngitis that was not culture-positive for GABHS was considered to be primarily of viral origin, and the use of antibiotics in these cases was discouraged.

In the past few years, interest has grown in nonstreptococcal, but potentially treatable nonviral causes of pharyngitis. Komaroff et al¹ evaluated 763 adult patients with sore throats and found serologic evidence of *Chlamydia trachomatis* infection in 20.5 percent and of *Mycoplasma pneumoniae* in 10.6 percent, whereas only 9.1 percent of the patients were culture positive for GABHS.

Since their publication in 1983, several articles have quoted these results when discussing the causes and treatment of pharyngitis.^{2,3}

These suggestive results deserve reevaluation because of their potential effect on the workup and treatment of pharyngitis. If Komaroff's findings—which suggest that *C trachomatis* and *M pneumoniae* may be frequent causes of pharyngitis—were confirmed, a higher rate of empirical treatment of pharyngitis, despite or without culturing for GABHS, might result. The drug of choice for the treatment of pharyngitis could then change from penicillin to erythromycin, which, theoretically, is effective against all three agents. On the other hand, if treatable causes of pharyngitis other than GABHS are not prevalent, empirical treatment with antibiotics could result in a substantial overuse of antibiotic therapy for patients with pharyngitis.

Although children comprise a large percentage of patients seeking medical evaluation for sore throats, the prevalence of *C trachomatis* and *M pneumoniae* in children with pharyngitis as the primary symptom has not been studied. Children with pharyngitis are frequently treated with antibiotics for a presumed bacterial diagnosis prior to, or in lieu of, culture results.⁴ Data are needed to clarify whether these potentially treatable agents cause

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pharyngitis in children so that appropriate antibiotic therapy is used.

The prevalence in children of potentially treatable causes of pharyngitis (ie, *C trachomatis* and *M pneumoniae*, as well as several bacterial organisms) was studied. In addition, whether the presence of each organism was associated with either the complaint of sore throat or with clinical evidence of pharyngitis was assessed.

METHODS

Study Population and Design

The study was performed between November 1, 1985, and April 1, 1986, at three family practice offices in the Salt Lake City community: (1) a two-physician family practice office in a rural suburb, (2) an office in the downtown area staffed by four full-time family practice faculty and a physician's assistant, and (3) an urban family practice teaching office staffed by two family physicians and 12 family practice residents.

Children were eligible for the study if they were between the ages of 2 and 12 years and presented at one of the three participating family practice offices for either a sore throat or an unrelated reason (ie, a noninfectious complaint or were accompanying a family member who had a noninfectious complaint). Children with symptoms of an upper or lower respiratory tract infection without complaints of sore throat were ineligible, as were siblings of these patients. Only one child per family could enter the study.

The purpose and the protocol of the study were explained to the eligible child and parent, and informed consent was obtained if both agreed to participate. The parent was then asked to complete a questionnaire covering the child's current symptoms, past medical history, epidemiologic factors, and environmental exposures.

A physical examination was performed by the physician, with emphasis placed on the upper and lower respiratory tract, lymph nodes, and skin. These findings, along with the physician's diagnosis and treatment plan, were entered on a form designed to standardize the physical finding data.

Microbiology

The child's posterior pharynx and tonsillar pillars were swabbed with two Dacron swabs followed by a second swabbing in an area not covered with exudate using a Dacron swab from the Syva Microtrak Chlamydia Specimen Collection kit.

For routine bacteriologic culture, the specimens collected were immediately plated on 5 percent Columbia

sheep blood agar (BBL) and peptic digest agar (MicroBio), and were incubated in candle extinction jars (5 to 10 percent carbon dioxide) at 35.5 °C. The organisms were isolated and confirmed according to routine methods as follows.

Group A β -hemolytic streptococci were isolated on Columbia sheep blood agar, identified by their morphology, and confirmed by both bacitracin-disk susceptibility and Streptex (Wellcome Diagnostics) type-specific latex agglutination tests.⁵

Hemophilus influenzae were isolated on peptic digest agar (MicroBio), and colonies were confirmed according to their XV requirements. The encapsulated strains were tested with type-specific latex antisera for type B *H influenzae* (Bacto-Haemophilus *influenzae* antisera, Difco Laboratories).⁶

The presence of *Chlamydia trachomatis* was confirmed by the MicroTrak direct immunofluorescent test (Syva) for elementary bodies, using the techniques described by Uyeda et al.⁷ Slides were evaluated by the microbiologist (with experience of over 10,000 evaluations). Diagnosis of *C trachomatis* was made under 500 \times and 1000 \times oil objectives using a Zeiss epifluorescence microscope. Any questionable slides were referred to Syva technical services for a second opinion.

Mycoplasma pneumoniae were detected by swabbing the posterior pharynx with a Dacron swab, placing the swab in a tube of modified selective pleuropneumonia-like organisms (PPLO) glucose transport and enrichment medium, and subsequently inoculating in modified New York medium. Both media were incubated for 10 days and were checked daily. The broth was observed for a pH change, indicated by a color change that occurs in the presence of *Mycoplasma*. Colonies growing on the modified New York medium were stained with Diene's stain.

Microbiological results were reported to the physicians at day 1 (*C trachomatis*), at days 2 to 3 (GABHS, non-GABHS, *H influenzae*, *Staphylococcus aureus*), and at days 10 to 14 (*M pneumoniae*). Treatment was instituted at the discretion of the physician.

Statistical Analysis

Frequency distributions of the microbiological results were constructed and prevalence-risk ratios along with chi-square analysis and Fisher's exact test were used to compare associations between the results and the historical and clinical data. The Miettinen test-based method was used to calculate 95 percent confidence intervals.

RESULTS

Between November 1, 1985, and April 1, 1986, 242 patients entered the study. Of these, 140 (58 percent) had a

TABLE 1. CHARACTERISTICS OF CHILDREN STUDIED

Demographics*	Had Sore Throat (n = 140) No. (%)	Denied Sore Throat (n = 96) No. (%)	P value
Mean age (years \pm SD)	6.5 \pm 2.9	5.9 \pm 3.0	.95
Range (years)	2-12	2-12	
Household income**			
<\$10,000	38 (29)	23 (25)	.74
\$10,000-\$40,000	79 (60)	57 (62)	
>\$40,000	14 (11)	12 (13)	
Ethnic group			
White	108 (77)	70 (73)	.61
Mexican-American	20 (14)	14 (14)	
Other	12 (9)	12 (13)	
Average number of siblings	2.1	1.7	.14
Attended daycare or school	40 (29)	34 (35)	.27
Exposed to smoke at home	49 (35)	42 (44)	.17

* Demographic data were available from 236 patients

** Income data were missing on 13 additional patients

current sore throat by history. Estimated participation by eligible patients with sore throats was greater than 90 percent. Fifty percent were seen at the private suburban family practice office, 32 percent at the community family practice teaching office, and 18 percent at the faculty family practice office. Patients without sore throats were enrolled within a week of patients with sore throats to minimize any temporal effects. Demographic characteristics of the children studied are shown in Table 1.

The most prevalent organism found was group A β -hemolytic streptococcus (30 percent); *Chlamydia trachomatis*, on the other hand, appeared in none of the subjects. Overall, 5 percent of the children had non-group A β -hemolytic streptococcus, 5 percent had *Mycoplasma pneumoniae*, 4 percent had *Hemophilus influenzae* (1.7 percent type B, 2.5 percent non-type B), and 14 percent had *Staphylococcus aureus* cultured from the pharynx specimens. Of the 242 subjects, 109 (45 percent) had none of these organisms detected, while six patients (2 percent) had more than one of these organisms.

Each organism detected (GABHS, non-GABHS, *M pneumoniae*, *H influenzae* species, and *S aureus*) was compared with the historical and epidemiologic factors, using chi-square and Fisher's exact tests. The presence or absence of a complaint of a sore throat was not associated statistically with the presence in the pharynx of any of the organisms studied (Table 2). No association was found

between the microorganism detected and the historical factors of fever, anorexia, rhinorrhea, skin rash, diarrhea, or waking up at night. Similarly, no correlation was found between the organism detected and age (grouped 2 to 5 years, 6 to 9 years, and 10 to 12 years), ethnic group, household income, exposure to household tobacco smoke, number of siblings, use of antibiotics in the previous year, or attendance at a day-care center or school.

The data were also stratified by whether the children exhibited clinical signs of pharyngitis (erythema of the pharynx, enlarged tonsils, pharyngeal exudate, anterior cervical adenopathy, fever, or an accompanying rash). There was a statistically significant association between the presence of GABHS in the pharynx and physical examination findings in several of these categories (Table 3). In contrast, no association was found between physical examination findings and non-GABHS, *M pneumoniae*, *H influenzae*, or *S aureus*.

DISCUSSION

The primary objective of this study was to document the prevalence of several potentially pathogenic organisms in the throats of children. The role of these organisms in children with and without pharyngitis by history or by examination was of interest because of preliminary but inconclusive data suggesting treatable causes of pharyngitis other than GABHS.

Chlamydia trachomatis

Data on the prevalence of *C trachomatis* in the pharynx of groups of children have not been previously available. Despite results of a study by Komaroff et al¹ suggesting that *C trachomatis* may be a common cause of pharyngitis in adults, other reports have cast doubt on the role of this organism as a common cause of adult pharyngitis.⁸⁻¹⁰

Chlamydia trachomatis is a known pathogen during the first four to six months of life as a consequence of exposure of infants during passage through an infected cervix,¹¹ but is rare in children older than one year. Studies that report isolating this organism from the pharynx of either adults or children suggest that it is more likely to be found in sexually active populations.¹²⁻¹⁶

The variation in the methods used to establish the presence of *C trachomatis* may partially explain the differences in prevalence reported by Komaroff et al compared with this study and others.^{8,9,17} Komaroff et al used rising levels of anti-*Chlamydia* immunoglobulin G and immunoglobulin M in patients with pharyngitis to define an infection with *C trachomatis*. Elevated antibody levels to *C trachomatis* are common in adults and have been shown to be

TABLE 2. RISKS OF HAVING SELECTED MICROORGANISMS IN THE PHARYNX OF CHILDREN WITH SORE THROATS VS THOSE WITHOUT SORE THROATS*

Microorganisms	Had Sore Throat (n = 136) No. (%)	Denied Sore Throat (n = 96) No. (%)	Risk Ratios (95% confidence intervals)
Group A β -hemolytic streptococcus (GABHS)	44 (32)	25 (26)	1.23 (.83-1.82)
Non-GABHS	6 (4)	5 (5)	0.85 (.26-2.73)
Staphylococcus aureus	17 (12)	16 (17)	0.70 (.40-1.41)
Mycoplasma pneumoniae	6 (4)	5 (5)	0.85 (.26-2.73)
Hemophilus influenzae	4 (3)	6 (6)	0.47 (.14-1.58)
Chlamydia trachomatis	0 (0)	0 (0)	—
None of the above	61 (45)	43 (45)	1.00 (.81-1.24)

* n = 232 patients with complete data available

TABLE 3. RELATIONSHIP BETWEEN PHYSICAL FINDINGS AND POSITIVE AND NEGATIVE CULTURES FOR GROUP A β -HEMOLYTIC STREPTOCOCCUS (GABHS)

Physical Findings	GABHS Positive No. (%)	GABHS Negative No. (%)	Risk Ratios (95% confidence intervals)
Pharyngeal erythema	50 (73)	86 (51)	2.1 (1.3-3.2)*
Tonsillar enlargement	58 (85)	99 (61)	2.7 (1.6-4.7)**
Pharyngeal exudate	27 (39)	34 (20)	1.9 (1.3-2.8)*
Rash	12 (18)	9 (5)	3.2 (1.4-4.0)*
Anterior cervical adenopathy	22 (32)	42 (25)	1.3 (.8-1.9)***
Fever > 37.5 °C	18 (31)	27 (21)	1.4 (.9-2.3)***

* P < .01
** P < .001
*** P > .10

persistently elevated in as many as 87 percent of patients in a sexually active high-risk population despite negative chlamydial cultures.¹⁸⁻²⁰ Furthermore, cross-reactivity of antibodies with chlamydial organisms other than *C trachomatis* may occur.²¹ Serological evidence of current infection for the diagnosis of acute chlamydial infections, therefore, may include a high false-positive rate.

The direct immunofluorescent antibody test (Syva) has been shown to correlate closely to cell cultures in detecting *C trachomatis* in the endocervix, the conjunctiva, the nasopharynx, and the oropharynx^{7,22-27} and may be more sensitive than routine *Chlamydia* culture in some anatomical sites.^{25,28} Thus, if *C trachomatis* were present in the throats of the children in this study, the direct immunofluorescent antibody test would be expected to detect it.

The data in this study support the conclusion that *C trachomatis* in the pharynx is unusual in children and that it should not be accepted as a likely cause of pharyngitis in children without previous sexual exposure.

Mycoplasma pneumoniae

Mycoplasma pneumoniae was isolated from 4 to 5 percent of the children studied regardless of whether they complained of a sore throat. These results are in contrast to those reported by Komaroff et al,¹ which suggest *M pneumoniae* may be causal in 10.6 percent of pharyngitis in adults.

Isolated pharyngitis is infrequently caused by *M pneumoniae* in children,^{29,30} and previous studies have isolated this organism only in a small percentage of asymptomatic controls.^{29,31} No recommendations have been made to treat pharyngitis associated with *M pneumoniae* unless lower respiratory tract symptoms coexist.³⁰

Clinically the presence of *M pneumoniae* is assessed by culture or serologic testing. Elevated serologic titers do occur, however, secondary to cross-reactivity between the antigen used in the complement fixation tests and a variety of microorganisms, plants, and body tissues,³²⁻³⁵ and also occur in patients without symptoms of disease.³¹⁻³³ For these reasons, one might question a causal relationship between a serologic response to *M pneumoniae* and pharyngitis without other supporting evidence, such as isolation of the organism.

The data revealing equivalent numbers of positive cultures in children with and without sore throats suggest that an asymptomatic carrier state in the pharynx does occur. There is no evidence that treatment of this organism in the throat alters the natural course of the disease or eradicates the organism. Further studies are needed to define any long-term sequelae of *M pneumoniae* carriers and the risks and benefits of treatment.

Other Bacterial Organisms

Although group A β -hemolytic streptococcus was not statistically associated with the complaint of a sore throat, this organism was more likely to be found in children with signs of pharyngitis or rash as opposed to those without such signs. Group A β -hemolytic streptococcus is known to have a variable but high asymptomatic carrier rate,^{36,37} and a minority of patients with a sore throat and a positive culture for GABHS displayed an immunologic response suggestive of infection.³⁸ The development of an antibody response to GABHS is thought to be a prerequisite to the development of rheumatic fever or post-streptococcal nephritis.³⁹ Because active infection with GABHS is associated with the development of rheumatic fever, recommendations are to treat children with fever and signs of pharyngitis who have a culture positive for GABHS.⁴⁰

Non-GABHS is not commonly considered pathogenic in the pharynx and has been found in equivalent percentages of children with and without pharyngitis.⁴¹ Group G and group C β -hemolytic streptococcus, however, have been shown to be associated with outbreaks of pharyngitis.^{42,43} This study reconfirms the data that in nonepidemic periods, non-group A β -hemolytic streptococcus is not associated with clinical pharyngitis.

Similarly, H influenzae and S aureus have not been described as common causal agents in pharyngitis, although both are reported to be commensal organisms in the pharynx.⁴¹ The possibility that H influenzae could be an opportunistic organism in an inflamed pharynx has been suggested,^{44,45} but not yet confirmed. In this study, the presence of these organisms did not correlate significantly with either a complaint of sore throat or signs of pharyngitis. Further research is needed to clarify the role of these organisms in patients with pharyngitis.

In this study no associations between the complaint of sore throats and organisms isolated were found. The power of the study to detect various differences in detection rates was calculated for the primary organisms studied. A two-tailed z reflecting an alpha of .05 and the percentage of positive cultures found in the children without sore throats were used in the power calculations. The study had greater than 80 percent power to detect risk ratios of 1.75 for group A β -hemolytic streptococcus, 3.5 for Mycoplasma pneumoniae, 3.0 for Hemophilus influenzae, and 2.0 for Staphylococcus aureus. Because no Chlamydia trachomatis was detected in any of the children studied, the power could not be calculated. Detection of smaller differences would take larger numbers of patients.

In summary, this study evaluated the prevalence of certain organisms in the throat that may cause pharyngitis in children (group A β -hemolytic streptococcus, non-group A β -hemolytic streptococcus, Chlamydia trachomatis,

Mycoplasma pneumoniae, Hemophilus influenzae, and Staphylococcus aureus). In the current study, only group A β -hemolytic streptococcus was associated with signs of pharyngitis; no Chlamydia trachomatis was identified from the pharynx. Although 5 percent of the children had non-group A β -hemolytic streptococcus, 5 percent had Mycoplasma pneumoniae, 4 percent had Hemophilus influenzae, and 14 percent had Staphylococcus aureus isolated from their pharynges, these organisms were not associated with either the complaint of sore throat or clinical signs of pharyngitis in the children.

Current management of pharyngitis should continue to be based on the detection and treatment of group A β -hemolytic streptococcus as the major treatable causal organism in children.

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