Role of *Chlamydia trachomatis* in Acute Pharyngitis in Young Adults

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It has recently been suggested that *Chlamydia trachomatis* may be a common cause of acute pharyngitis in adults. In a prospective investigation of 95 college students with acute pharyngitis, *C. trachomatis* was not isolated from any pharyngeal cultures. Further investigations are needed to better define the role of *C. trachomatis* in upper respiratory tract infections.

Pharyngitis is the third leading reason given by patients for office visits to physicians in the United States, accounting for over 30 million visits annually (3). A recent survey in Rhode Island revealed that ca. 150,000 throat cultures were performed in that state in 1980 (4). Extrapolating from this figure would indicate that over 30 million throat cultures are performed annually in this country. For most patients, pharyngitis is attributed to a group A streptococcal infection if the throat culture is positive for that organism or to a viral infection if the throat culture is negative. A recent serological study, however, suggested that as much as 20% of the pharyngitis seen in adult patients may be caused by *Chlamydia trachomatis* (6). We conducted a prospective investigation to determine how often *C. trachomatis* could be isolated from the upper respiratory tracts of college students with acute pharyngitis.

From 30 January 1983 until 17 February 1984, ca. 2,100 students were seen at the University of Connecticut Student Health Service, Storrs, Conn., 270 with a chief complaint of a sore throat. Throat cultures were done for a group of 95 of these 270 students, randomly selected for inclusion in this study, by the simultaneous swabbing of the posterior pharynx with two rayon-tipped, plastic swabs (Culturette; Marion Laboratories, Kansas City, Mo.). One of the swabs was streaked onto a 5% sheep blood agar plate, which was then processed in the usual manner for the isolation of group A streptococci. The other swab was immediately placed in 0.2 M sucrose-phosphate transport medium containing amphotericin B (5 μg/ml), gentamicin (50 μg/ml), and 2% fetal calf serum. Each specimen was then stored at 4°C until it was transported to the diagnostic microbiology laboratory at the University of Connecticut Health Center, Farmington, Conn., usually within 6 h and always within 24 h of collection. Upon arrival at the laboratory, the specimens were immediately stored at −70°C until they were inoculated into tissue cultures, usually within 24 h and always within 72 h of arrival. Frozen specimens were quickly thawed in a 37°C water bath. Monolayers of McCoy cells were prepared in sterile, flat-bottomed tubes containing a round, 13-mm cover slip. The growth medium was removed from the McCoy cells, and 0.5 ml of each specimen was then added. The tubes were centrifuged at 3,000 × *g* for 60 min at room temperature and then incubated for 1 to 2 h at 35°C. The

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inoculum was then removed and replaced with Eagle minimal essential medium with Earle balanced salt solution containing cycloheximide (1 μg/ml). The tubes were incubated for 48 h at 35°C in 5% CO_2. The cover slips were then removed and stained with *C. trachomatis* fluorescein-labeled monoclonal antibody (Syva Co., Palo Alto, Calif.). No additional cultures for other agents associated with acute pharyngitis (e.g., viruses, mycoplasmas) were performed.

Of the 95 students in the study group, 41% were male, and the mean age was 20.6 years (range, 18 to 32 years). All complained of a sore throat and, in addition, 64% had a headache, 17% had nausea, 11% had abdominal pain, and 5% had vomited. Although 43% reported having been febrile, at the time of presentation only 17% had documented oral temperatures greater than 37.8°C. Patients reported having been ill for an average of 5 days. Of the 95 students, 9 (9%) had throat cultures positive for group A streptococci. Pharyngeal culture for *C. trachomatis* were negative for all 95 students.

C. trachomatis is recognized as one of the most important causes of male and female genitourinary tract infections (9). *C. trachomatis* has also been established as an important pathogen in certain respiratory tract infections. It is one of the most common causes of afebrile pneumonia in infants (1) and may also produce pneumonia in adults (12). In addition, *C. trachomatis* has been cultured from the pharynx in isolated cases of symptomatic pharyngitis (13) and from the pharynges of asymptomatic people who have engaged in orogenital sex (7). Komaroff et al. (6) have recently demonstrated, by examining serological responses, that *C. trachomatis* may be a common cause of pharyngitis in adults, accounting for as much as 20% of these cases. However, in a prospective investigation of chlamydial cultures of the pharynx, we were unable to isolate *C. trachomatis* from any of the 95 college students presenting with a chief complaint of a sore throat. This discrepancy could be attributed to the fact that the serological responses noted by Komaroff et al. may represent nonspecific polyclonal stimulation, cross-reactivity to another microorganism, or an asymptomatic chlamydial infection somewhere else in the body (6).

This discrepancy could also be attributed to the inactivation of *C. trachomatis* during the transport and storage of the pharyngeal specimens. It has been demonstrated, however, that storage in 0.2 M sucrose-phosphate transport medium at 4°C produces only a 16% reduction in inclusion-

forming units after 4 h and only a 53% reduction after 24 h. In addition, storage of a specimen at −70°C for 24 h with a single freeze-thaw cycle results in only a 30% reduction in inclusion-forming units (10). Others have shown that storage for up to 48 h at 4°C followed by storage at −70°C will produce only about a 20% loss in demonstrable infectivity (8). During the course of this study, the diagnostic microbiology laboratory continued to receive clinical specimens for *C. trachomatis* culturing. These clinical specimens were processed in the same manner as the study specimens, and no change in the rate of isolation of *C. trachomatis* from these clinical specimens was noted. We therefore believe it unlikely that *C. trachomatis* was present in the pharynges of a large number of our patients but could not be isolated because of inactivation during transport and storage.

Our inability to isolate *C. trachomatis* from the pharynges of these college students could also be attributed to the fact that cultures were obtained during a relatively limited period of time. However, seasonal variation in the incidence of chlamydial pneumonia in infants has not been observed (11), and seasonal variation in the incidence of chlamydial pharyngitis in young adults would not be anticipated. In addition, a review of the patients' records, as well as the fact that approximately the same number of students with acute pharyngitis had been seen during this period in each of the past 3 years, suggested that the study patients were not part of an outbreak in the student population of some other organism that could have interfered with the isolation of *C. trachomatis*.

Despite a very high chlamydial isolation rate from the genital tracts of homosexual men, pharyngeal chlamydial infections in this population are uncommon (7). Bowie et al. (2) reported their inability to isolate *C. trachomatis* from the pharynges of any of a group of 11 women who practiced fellatio on sex partners with culture-proven *C. trachomatis* urethritis. In a recent study, investigators were able to produce clinical chlamydial urethritis in three adult male chimpanzees after urethral inoculation of 80 inclusion-forming units of *C. trachomatis* (5). However, they were unable to produce an infection in one of the chimpanzees after pharyngeal inoculation of *C. trachomatis* and, in the other two chimpanzees, produced a pharyngeal infection only after inoculation of 10^5 and 7×10^2 inclusion-forming units. In addition, neither of the chimpanzees with positive pharyngeal cultures for *C. trachomatis* had clinical evidence of pharyngitis. The investigators were unable to explain this relative resistance of the chimpanzees to pharyngeal chlamy-

dial infections; however, this finding appears to parallel clinical observations made in humans.

Further investigations are needed to better define the role of *C. trachomatis* in upper respiratory tract infections.

LITERATURE CITED

1. **Beem, M. O., and E. M. Saxon.** 1977. Respiratory-tract colonization and a distinctive pneumonia syndrome in infants infected with *Chlamydia trachomatis*. N. Engl. J. Med. **296:**306–310.
2. **Bowie, W. R., E. R. Alexander, and K. K. Holmes.** 1977. Chlamydial pharyngitis? Sex. Transm. Dis. **4:**140–141.
3. **Cypress, B. K.** 1981. Patients' reasons for visiting physicians: national ambulatory care survey, United States, 1977–78, p. 26. *In* Vital and health statistics, ser. 13, no. 56. Department of Health and Human Services publication (PHS)82-1717. National Center for Health Statistics, Hyattsville, Md.
4. **Holmberg, S. D., and G. A. Faich.** 1983. Streptococcal pharyngitis and acute rheumatic fever in Rhode Island. J. Am. Med. Assoc. **250:**2307–2312.
5. **Jacobs, N. F., E. S. Arum, and S. J. Kraus.** 1978. Experimental infection of the chimpanzee urethra and pharynx with *Chlamydia trachomatis*. Sex. Transm. Dis. **5:**132–136.
6. **Komaroff, A. L., M. D. Aronson, T. M. Pass, C. T. Ervin, and W. T. Branch, Jr.** 1983. Serologic evidence of chlamydial and mycoplasmal pharyngitis in adults. Science **222:**927–929.
7. **McMillan, A., R. G. Sommerville, and P. M. K. McKie.** 1981. Chlamydial infection in homosexual men: frequency of isolation of *Chlamydia trachomatis* from the urethra, ano-rectum, and pharynx. Br. J. Vener. Dis. **57:**47–49.
8. **Reeve, P., J. Owen, and J. D. Oriel.** 1975. Laboratory procedures for the isolation of *Chlamydia trachomatis* from the human genital tract. J. Clin. Pathol. **28:**910–914.
9. **Schachter, J., L. Hanna, E. C. Hill, and S. Massad.** 1975. Are chlamydial infections the most prevalent venereal disease? J. Am. Med. Assoc. **231:**1252–1255.
10. **Smith, T. F., L. A. Weed, G. R. Pettersen, and J. W. Segura.** 1977. Recovery of chlamydia and genital mycoplasma transported in sucrose phosphate buffer and urease color test medium. Health Lab. Sci. **14:**30–34.
11. **Stagno, S., D. M. Brasfield, M. B. Brown, G. H. Cassell, L. L. Pifer, R. J. Whitley, and R. E. Tiller.** 1981. Infant pneumonitis associated with cytomegalovirus, chlamydia, pneumocystis, and ureaplasma: a prospective study. Pediatrics **68:**322–329.
12. **Tack, K. F., P. K. Peterson, F. L. Rasp, M. O'Leary, D. Hanto, R. L. Simmons, and L. D. Sabath.** 1980. Isolation of *Chlamydia trachomatis* from the lower respiratory tract of adults. Lancet **i:**116–120.
13. **Watanakunakorn, C., and D. H. Levy.** 1983. Pharyngitis and urethritis due to *Chlamydia trachomatis*. J. Infect. Dis. **147:**364.