

## ORIGINAL ARTICLE

# An Outbreak of Conjunctivitis Due to Atypical *Streptococcus pneumoniae*

Michael Martin, M.D., M.P.H., John H. Turco, M.D., Michael E. Zegans, M.D., Richard R. Facklam, Ph.D., Samir Sodha, M.D., M.P.H., John A. Elliott, Ph.D., John H. Pryor, M.A., Bernard Beall, Ph.D., Dean D. Erdman, Dr.P.H., Yolanda Y. Baumgartner, M.B.A., Paul A. Sanchez, M.D., Joseph D. Schwartzman, M.D., José Montero, M.D., Anne Schuchat, M.D., and Cynthia G. Whitney, M.D., M.P.H.

## ABSTRACT

**BACKGROUND**

In February 2002, clinicians at the Dartmouth College Health Service recognized an outbreak of conjunctivitis; cultures of conjunctival swabs implicated *Streptococcus pneumoniae*. An investigation was begun to determine the extent of the outbreak, confirm the cause, identify modes of transmission, and implement control measures.

**METHODS**

Investigators reviewed the health service's data base for diagnoses of conjunctivitis. Viral and bacterial cultures were obtained from ill students. Bile-soluble isolates that were susceptible to ethylhydrocupreine (optochin) and therefore were presumed to be pneumococci underwent serotyping, capsular staining, pulsed-field gel electrophoresis, a DNA probe, and multilocus sequence typing. A cohort study of risk factors was conducted with the use of the Internet. Control measures included distribution of alcohol-based hand gel and messages about prevention.

**RESULTS**

Among 5060 students, 698 (13.8 percent) received a diagnosis of conjunctivitis from January 1, 2002, through April 12, 2002, including 22 percent of first-year students. Presumed pneumococci were isolated from 43.3 percent of conjunctival swabs (110 of 254); viral cultures performed on 85 specimens were negative. DNA probes and multilocus sequence typing confirmed that the organisms were pneumococci, although the bacteria did not have the characteristic capsule. On pulsed-field gel electrophoresis, strains were found to be identical to pneumococci that caused outbreaks of conjunctivitis in other parts of the country in 1980. Analysis of survey data from 1832 students indicated that close contact with a student with conjunctivitis, wearing contact lenses, membership on a sports team, and attending parties at or living in a fraternity or sorority house were associated with conjunctivitis. The rate of diagnosis of conjunctivitis declined after the implementation of control measures and after spring break.

**CONCLUSIONS**

This large outbreak of conjunctivitis on a college campus was caused by an atypical, unencapsulated strain of *S. pneumoniae* that was identical to strains that had caused outbreaks two decades earlier.

From the Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases (M.M., R.R.F., J.A.E., B.B., A.S., C.G.W.), and the Division of Viral and Rickettsial Diseases (D.D.E.), National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta; the Dartmouth College Health Service (J.H.T., Y.Y.B.), Dartmouth-Hitchcock Medical Center (M.E.Z., J.D.S.), and Dartmouth Medical School (J.H.P., P.A.S.) — all in Hanover, N.H.; the UCLA School of Medicine, Los Angeles (S.S.); and the Office of Community and Public Health, New Hampshire Department of Health and Human Services, Concord (J.M.). Address reprint requests to Dr. Whitney at the Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd. N.E., MS C23, Atlanta, GA 30333, or at cwhitney@cdc.gov.

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**S** *TREPTOCOCCUS PNEUMONIAE* IS A primary cause of meningitis and pneumonia.<sup>1,2</sup> The bacterium is also responsible for a substantial proportion of milder infections, including otitis media and sinusitis.<sup>3,4</sup> Pneumococci are cited as a common cause of sporadic conjunctivitis.<sup>5-7</sup> Although outbreaks of conjunctivitis are not unusual, few outbreaks of pneumococcal conjunctivitis have been reported, and little is known about transmission, risk factors, and control of the infection.<sup>8-10</sup>

From January 1, 2002, through February 15, 2002, 197 students received diagnoses of conjunctivitis at Dartmouth College in New Hampshire (Fig. 1). A viral cause was initially suspected, but cultures of conjunctival swabs collected from 12 students grew bacteria identified as *S. pneumoniae*. Because of the number of cases and the unusual cause, an investigation began. Objectives of the investigation were to determine the extent of the outbreak, confirm the cause, identify risk factors for infection, and implement control strategies.

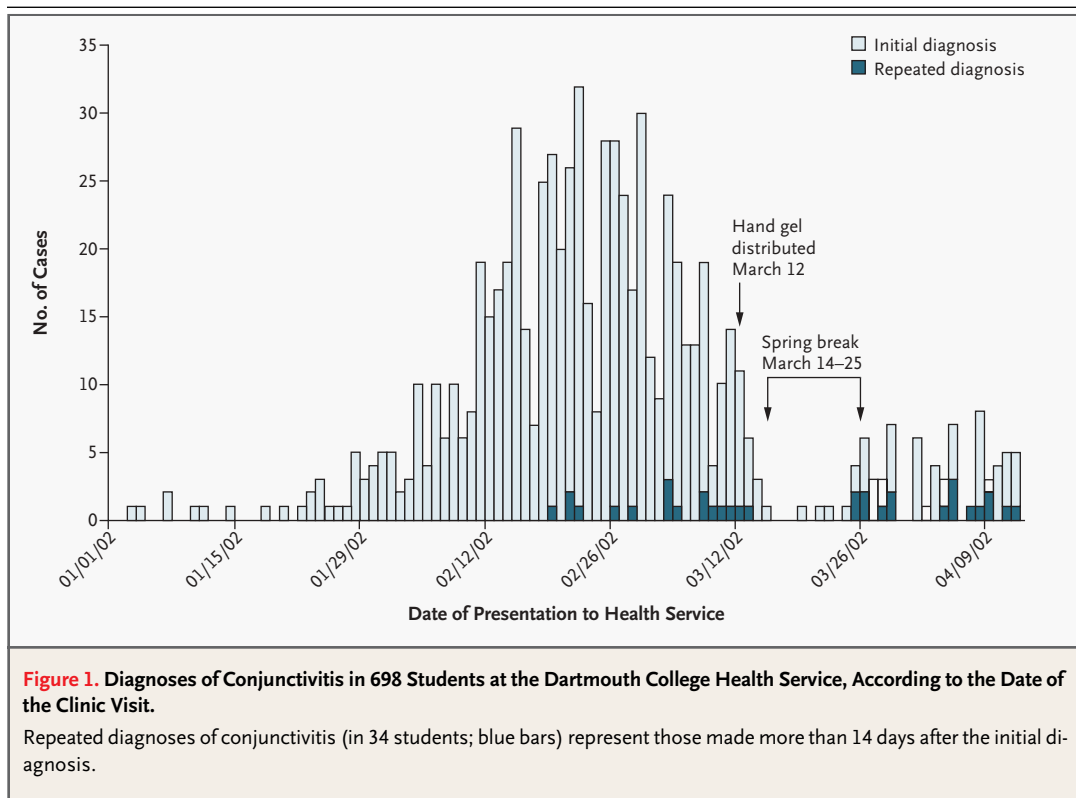
METHODS

EPISODES OF CONJUNCTIVITIS

Discharge data from the Dartmouth College Health Service were reviewed for diagnoses of conjunctivitis occurring from January 1, 2002, through April 12, 2002. Visits to the health clinic for conjunctivitis by the same student occurring more than 14 days apart were considered to represent separate episodes. Members of the health staff of the clinic were monitored for conjunctivitis.

LABORATORY TESTS

Clinicians obtained conjunctival swabs from students with symptoms of conjunctivitis. Specimens were sent to the Dartmouth-Hitchcock Medical Center for culture and identification. Subcultures of presumed *S. pneumoniae* isolates were sent to the Centers for Disease Control and Prevention (CDC) for testing of solubility in bile and susceptibility to ethylhydrocupreine (optochin), serotyping (quellung reaction), antimicrobial-susceptibility testing by broth microdilution,<sup>11</sup> capsular staining,<sup>12</sup> pulsed-field gel electrophoresis (PFGE),<sup>13</sup> multilocus sequence typing,<sup>14</sup> analysis with a DNA probe (Accu-



**Figure 1. Diagnoses of Conjunctivitis in 698 Students at the Dartmouth College Health Service, According to the Date of the Clinic Visit.**

Repeated diagnoses of conjunctivitis (in 34 students; blue bars) represent those made more than 14 days after the initial diagnosis.

Probe *Streptococcus pneumoniae*, Gen-Probe),<sup>15</sup> and sequencing of the 16S ribosomal RNA (rRNA). Results of multilocus sequence typing were compared with data from a large data base of pneumococcal sequences<sup>16</sup>; 16S rRNA was amplified with the use of primers fD1 and rD1 and sequenced with the use of 16 primers, including those described previously.<sup>17</sup> The Basic Local Alignment Search Tool (National Center for Biotechnology Information) was used to find the closest 16S rRNA match in GenBank. For comparison, we performed capsular staining and PFGE testing on isolates from outbreaks of pneumococcal conjunctivitis in New York and California in 1980 and in Illinois in 1981.

Viral cultures were performed on the first 15 conjunctival swabs that were obtained; cultures were performed at the laboratory of the New Hampshire Department of Health and Human Services with the use of rhesus-monkey kidney cells and human foreskin diploid cells, with screening for adenovirus by direct immunofluorescence staining (Chemicon International). Seventy subsequent specimens were tested at the CDC by viral culture (i.e., A549 cells) and indirect immunofluorescence staining (Chemicon International); 15 of these specimens were tested for adenovirus by polymerase-chain-reaction (PCR) assay.

#### ASSESSMENT OF RISK FACTORS

A cohort study was conducted to assess risk factors for conjunctivitis; survey questions addressed symptoms of conjunctivitis, demographic variables, and exposure to persons with conjunctivitis.<sup>18</sup> The 56-item questionnaire was placed on a college-protected Web site. An e-mail message was sent out, encouraging students, faculty members, and staff members to complete the questionnaire. Responses were forwarded electronically to a data base.<sup>18</sup> A response to the survey was considered to indicate informed consent.

Our criteria for an episode of conjunctivitis among survey respondents were their reports of the following eye symptoms: redness; gray or yellow discharge; itching, burning, pain, or dryness; and crusting in the morning. We used university data bases to compare the demographic characteristics of those who responded to the survey with the characteristics of those who did not respond.

#### STUDY OF CARRIAGE

Two of every five students who responded to the questionnaire were invited to participate in an investigation of pharyngeal carriage.<sup>18</sup> After obtaining

written informed consent, investigators used calcium alginate-treated swabs to obtain conjunctival, nasopharyngeal, and oropharyngeal specimens. Swabs were placed in skim milk, tryptone, glucose, and glycerol medium,<sup>19</sup> frozen, and sent to the CDC for culture, identification, serotyping, and PFGE. Laboratory results were linked to responses to the questionnaire.

#### CONTROL OF TRANSMISSION

To limit transmission of infection, we disseminated messages about prevention through e-mail, posters, and the daily college newspaper. Messages about prevention encouraged students, staff members, and faculty members to wash their hands frequently, to avoid sharing eating utensils, and to seek care for symptoms of conjunctivitis. Once the bacterial cause was known, a topical antibiotic (sulfacetamide or bacitracin) was recommended for students with symptoms of conjunctivitis. Two days before spring break, we distributed 4-oz bottles of alcohol-based hand gel (Endure 300, Ecolab) to undergraduate students through the college mailroom.

To evaluate control measures, we continued to track visits to the health service for conjunctivitis after spring break. All students visiting the health service the week after spring break were asked to complete a seven-item questionnaire. Information requested included the reason for the visit, whether the hand gel had been retrieved from the student's mailbox, and how much they had used.

Local primary care clinicians, ophthalmologists, and optometrists were alerted to the outbreak by telephone. Health departments and college health officials were notified of the outbreak through the *Morbidity and Mortality Weekly Report*,<sup>20</sup> and an e-mail list for college health services.

#### STATISTICAL ANALYSIS

Statistical analyses for the cohort study of risk factors were conducted with the use of Epi Info 2000 software (CDC) and SAS software, version 8 (SAS Institute). Logistic regression was used to construct multivariable models of factors independently associated with conjunctivitis. P values of 0.05 or less were considered to indicate statistical significance. In the study of carriage, we conducted a univariate analysis of risk factors for carriage of the outbreak strain as defined by PFGE. Associations of risk factors with carriage for which the P value was 0.05 or less by the chi-square test were considered to be significant.

## RESULTS

**MAGNITUDE OF THE OUTBREAK**

Among 5060 students enrolled at Dartmouth College for the winter term of 2002, 698 (13.8 percent) were given a diagnosis of conjunctivitis between January 1, 2002, and April 12, 2002 (Fig. 1). During similar periods in 2000 and 2001, 66 and 92 students, respectively, were given a diagnosis of conjunctivitis. In 2002, attack rates among 3682 undergraduate and 1378 graduate students were 18.7 percent and 2.5 percent, respectively. Among undergraduate students, attack rates were highest among first-year students (22.3 percent), followed by sophomores (19.9 percent), juniors (18.0 percent), and seniors (16.1 percent). No clinicians at the student health service received a diagnosis of conjunctivitis. Of 698 students evaluated for conjunctivitis, 34 (4.9 percent) had repeated infections.

**LABORATORY RESULTS**

Conjunctival swabs were obtained from 254 students for bacterial culture. Bacteria isolated from 110 of these swabs (43.3 percent) were identified as *S. pneumoniae* by optochin-sensitivity and bile-solubility testing. Nineteen (7.5 percent) grew *Haemophilus influenzae*; one specimen grew both *S. pneumoniae* and *H. influenzae*. A DNA probe identified all presumed pneumococcal isolates tested (30 of 30) as *S. pneumoniae*. Of 12 presumed *S. pneumoniae* isolates evaluated at the CDC, all were susceptible to optochin and soluble in bile. None of the isolates, however, could be serotyped, and capsular staining indicated that the bacteria did not have a polysaccharide capsule. The pneumococci were susceptible to penicillin (minimal inhibitory concentration, <0.03 µg per milliliter), amoxicillin, ciprofloxacin, tetracycline, and trimethoprim-sulfamethoxazole; all 12 isolates were resistant to erythromycin (minimal inhibitory concentration, 64 µg per milliliter).

PFGE testing showed two distinct but closely related patterns of banding (Fig. 2). Multilocus sequence typing of isolates representing the two PFGE patterns revealed allelic profile ST448 (*aroE8*, *gdh5*, *gki2*, *recP27*, *spi2*, *xpt11*, *ddl71*). Although each of these alleles except *ddl71* has been previously noted in pneumococcal clones that could be serotyped, ST448 was dissimilar to pneumococcal profiles previously reported on multilocus sequence typing (≤3 matches) and had been reported only once before in this large data base. The 16S rRNA was 99.4 percent similar to the corresponding sequence of

TIGR4, the reference strain of *S. pneumoniae* whose sequence is included in GenBank.<sup>21</sup>

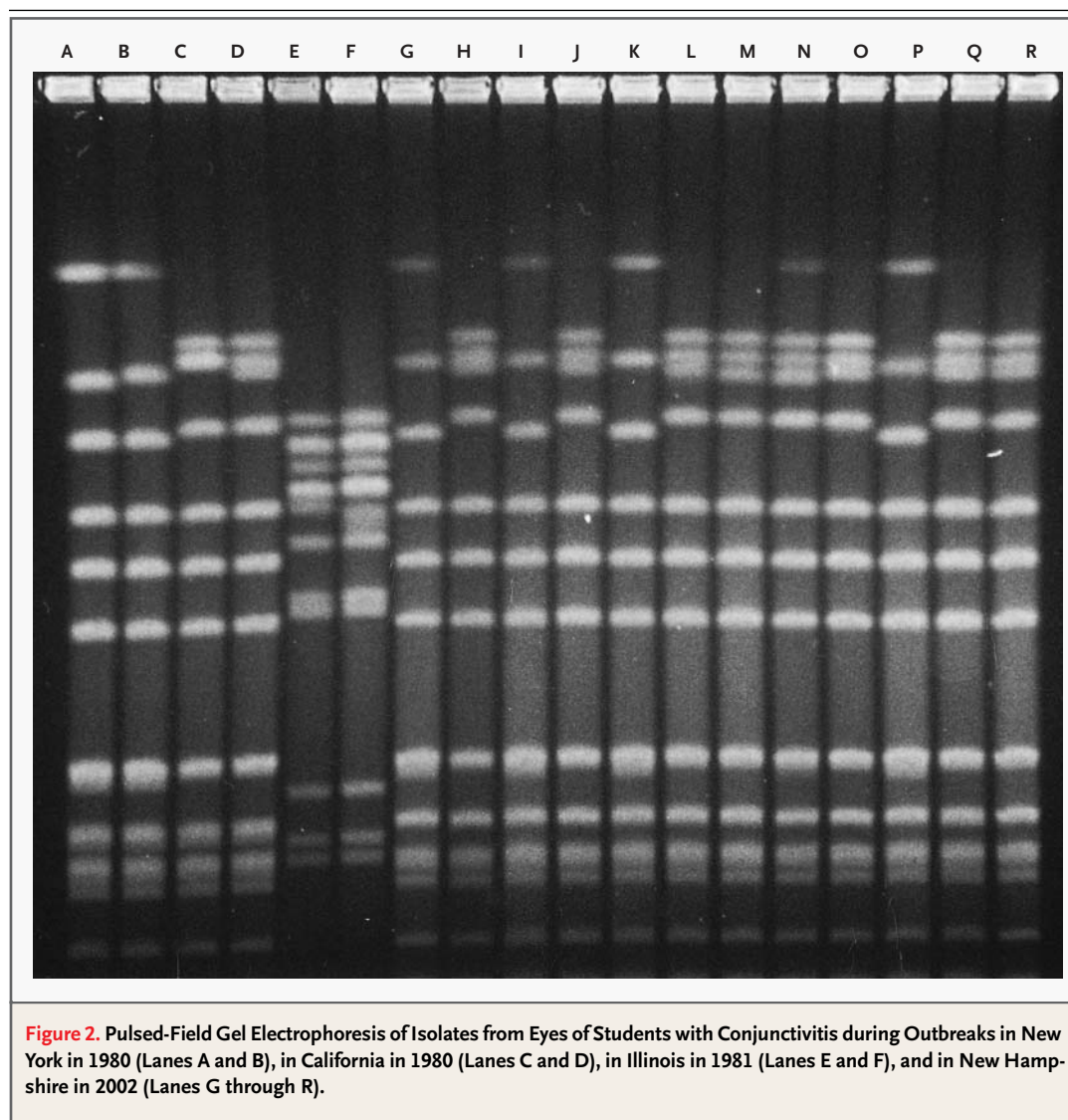
Capsular staining of isolates from outbreaks of conjunctivitis in New York and California in 1980 and in Illinois in 1981 showed that these bacteria also did not have a capsule. PFGE patterns of the strains from New York and California were identical to that of the New Hampshire strain (Fig. 2).

A total of 85 specimens were cultured and were negative for viral growth; adenoviral immunofluorescence staining of these specimens was also negative, as were PCR assays for adenovirus in 15 specimens.

**RISK-FACTOR SURVEY**

Of 3682 undergraduate students, 1832 (49.8 percent) responded to the Internet-based survey. Demographic characteristics of respondents differed somewhat from those of nonrespondents (Table 1). Among 1832 respondents, 288 (15.7 percent) met the criteria for conjunctivitis; 456 (24.9 percent) reported eye redness, 386 (21.1 percent) reported discharge, 493 (26.9 percent) reported pain, and 481 (26.3 percent) reported crusting. The mean duration of symptoms was 5.9 days (range, 1 to 43). Smaller proportions of students reported swelling of the eyelid (12.7 percent), photophobia (13.6 percent), and vision problems (11.9 percent). Of the respondents, 146 (8 percent) missed classes because of eye symptoms and 191 (10.4 percent) reported more than one episode of conjunctivitis. Of the 288 students reporting symptoms that met the criteria for conjunctivitis, 209 (72.6 percent) saw a health care provider. Among those who saw a health care provider, we found no significant difference in the duration of symptoms between students who reported using antibiotic eyedrops (189 students; median duration, 5.0 days) and students who did not (22 students; median duration, 4.5 days; *P*=0.93).

Several factors were associated with conjunctivitis in the univariate analysis, including having a roommate with conjunctivitis (relative risk, 2.14; *P*<0.001), having another close contact with conjunctivitis (relative risk, 1.98; *P*<0.001), membership on a varsity sports team (relative risk, 1.60; *P*<0.001), going to a gym (relative risk, 1.40; *P*=0.005), attending a fraternity or sorority party (relative risk, 2.51; *P*<0.001), living in a fraternity house (relative risk, 1.55; *P*=0.05), wearing contact lenses (relative risk, 1.27; *P*=0.03), sleeping while wearing contact lenses (relative risk, 1.51; *P*=0.003), smoking (relative risk, 1.52; *P*<0.001), and sharing drinking



glasses (relative risk, 1.36;  $P=0.01$ ). Students with conjunctivitis had more roommates (t-test statistic, 2.40;  $P=0.02$ ) and reported going to a gym more often (t-test statistic, 3.80;  $P<0.001$ ). The self-reported frequency of hand washing and sharing of towels was not significantly associated with conjunctivitis.

On multivariable analysis, having close contact with someone with conjunctivitis, attending a party at or living in a fraternity or sorority house, wearing contact lenses, and being a first-year student were significantly associated with conjunctivitis (Table 2). We found a significant interaction between membership on a varsity sports team and having a roommate with conjunctivitis.

#### RATES OF CARRIAGE

Of 787 students invited, 244 (31.0 percent) agreed to participate in the study of carriage. *S. pneumoniae* was isolated from the pharyngeal specimens of 30 of these students (12.3 percent) (Table 3); 20 of the isolates (66.7 percent) could not be serotyped. PFGE patterns for 13 of the pharyngeal isolates that could not be serotyped matched isolates from eyes of students with conjunctivitis. *S. pneumoniae* was isolated from the conjunctival specimens of six of the participating students (2.5 percent); all six isolates matched the outbreak strain on PFGE.

Among participants in the study of carriage, 47 (19.3 percent) reported recent eye symptoms that

**Table 1. Characteristics of Undergraduates Who Responded to the Questionnaire and Those Who Did Not Respond.**

| Characteristic   | Respondents<br>(N=1832) | Nonrespondents<br>(N=1850) | P<br>Value |
|------------------|-------------------------|----------------------------|------------|
|                  | no. (%)                 |                            |            |
| <b>Sex</b>       |                         |                            |            |
| Female           | 1011 (55.2)             | 769 (41.6)                 | <0.01      |
| <b>Class*</b>    |                         |                            |            |
| First year       | 566 (30.9)              | 553 (32.0)                 | 0.49       |
| Sophomore        | 421 (23.0)              | 454 (26.2)                 | 0.02       |
| Junior           | 312 (17.0)              | 244 (14.1)                 | 0.02       |
| Senior           | 533 (29.1)              | 479 (27.7)                 | 0.35       |
| <b>Residence</b> |                         |                            |            |
| Fraternity       | 84 (4.6)                | 122 (6.6)                  | 0.01       |
| Sorority         | 57 (3.1)                | 36 (1.9)                   | 0.02       |
| Residence hall   | 1323 (72.2)             | 1351 (73.0)                | 0.58       |
| Off campus       | 254 (13.9)              | 280 (15.1)                 | 0.27       |
| Other            | 114 (6.2)               | 61 (3.3)                   | <0.01      |

\* The class was unknown for 120 nonrespondents, who were excluded from this analysis.

met the criteria for conjunctivitis. Of these 47, 11 (23.4 percent) had the outbreak strain isolated from their pharynx or conjunctiva. Eleven of 16 students carrying the outbreak strain (68.8 percent) had symptoms meeting criteria for conjunctivitis during the previous three weeks; 9 of 16 (56.2 percent) were asymptomatic at the time of the carriage study.

Of 6 students with the outbreak strain isolated from conjunctival cultures, 5 (83.3 percent) had symptoms consistent with conjunctivitis, as compared with 8 of 13 students with the strain in their pharynx (61.5 percent). Overall, students who carried the outbreak strain in either site were more likely to meet the criteria for conjunctivitis than students who did not carry the outbreak strain (68.8 percent [11 of 16] vs. 15.8 percent [36 of 228]; relative risk, 4.35;  $P < 0.001$ ). Having a roommate with conjunctivitis (relative risk, 3.65;  $P = 0.02$ ) was the only exposure-related factor that was significantly associated with carriage of the outbreak strain.

**EFFICACY OF CONTROL EFFORTS**

Visits to the student health center for conjunctivitis declined after distribution of hand gel (Fig. 1). Of

181 students who visited the health center during the week after spring break, 167 (92.3 percent) reported retrieving the hand gel from their mailboxes; 106 of those who retrieved it (63.5 percent) used it at least once, 49 (29.3 percent) used at least half the bottle, and 6 (3.6 percent) finished the bottle. Twenty-two of the students who visited the health center during the week after spring break (12.2 percent) visited because of symptoms of conjunctivitis; no association was found between the use of hand gel and conjunctivitis.

In late February, the director of the Princeton University Health Service noted an increase in the number of students visiting the clinic with symptoms of conjunctivitis. Because of the notice posted on the e-mail list for college health services, the Princeton outbreak was reported to the New Jersey Department of Health and Senior Services. Cultures of conjunctival swabs obtained from symptomatic students at Princeton grew *S. pneumoniae* that could not be serotyped, and on PFGE, 11 isolates were identical to the strain identified at Dartmouth. From February 15, 2002, through March 20, 2002, a total of 274 Princeton students were given a diagnosis of conjunctivitis.

**DISCUSSION**

This report describes a large outbreak of conjunctivitis caused by an unencapsulated strain of *S. pneumoniae*. During the outbreak, 698 students received diagnoses of conjunctivitis, including 22 percent of first-year students. More than 1 in 20 students carried the outbreak strain at the time of our investigation. Students carried the outbreak strain after conjunctivitis symptoms had resolved; some students carried the strain without having symptoms. Analysis of risk factors suggested that the outbreak strain was highly transmissible from person to person; students who reported having had close contact with a student with conjunctivitis and those who participated in activities that involved physical contact were more likely to become infected. The organism was probably spread through respiratory secretions from students carrying the bacteria, as is the case with typical pneumococci, and through contact with eye secretions of students with conjunctivitis.

Initially, we were unsure whether the outbreak strain was a pneumococcus. Typical pneumococci have a polysaccharide capsule, which is considered a key virulence factor. Among 14,643 isolates of pneumococci causing invasive disease from 1998

**Table 2. Types of Exposure Significantly Associated with Conjunctivitis According to Multivariable Logistic-Regression Analysis.\***

| Type of Exposure                              | No. with Conjunctivitis/<br>No. Responding (%) | Adjusted Odds Ratio<br>for Conjunctivitis (95% CI) | Adjusted<br>P Value |
|---|--|--|---------------------|
| <b>Wearing contact lenses</b>                 |  |  |                     |
| Yes   | 137/764 (17.9)                                 | 1.47 (1.12–1.93)                                   | 0.005               |
| No  | 149/1054 (14.1)                                | 1.00   |                     |
| <b>Close contact with ill student†</b>        |  |  |                     |
| Yes   | 126/516 (24.4)                                 | 1.74 (1.31–0.32)                                   | <0.001              |
| No  | 162/1311 (12.4)                                | 1.00   |                     |
| <b>Attending fraternity or sorority party</b> |  |  |                     |
| Yes   | 253/1357 (18.6)                                | 2.11 (1.41–3.15)                                   | <0.001              |
| No  | 34/457 (7.4)                                   | 1.00   |                     |
| <b>Living in a fraternity house</b>           |  |  |                     |
| Yes   | 20/84 (23.8)                                   | 2.12 (1.18–3.83)                                   | 0.01                |
| No  | 268/1743 (15.4)                                | 1.00   |                     |
| <b>Living in a sorority house</b>             |  |  |                     |
| Yes   | 14/57 (24.6)                                   | 2.10 (1.01–4.35)                                   | 0.05                |
| No  | 274/1770 (15.5)                                | 1.00   |                     |
| <b>Sports-team membership and roommates</b>   |  |  |                     |
| Team member and roommate ill                  | 11/50 (22.0)                                   | 1.54 (0.75–3.14)                                   | 0.24                |
| Team member and roommate well                 | 52/227 (22.9)                                  | 1.84 (1.27–2.66)                                   | 0.001               |
| Not a team member and roommate ill            | 58/191 (30.4)                                  | 2.43 (1.67–3.52)                                   | <0.001              |
| Not a team member and roommate well           | 152/1280 (11.9)                                | 1.00   |                     |
| <b>Class</b>                                  |  |  |                     |
| First year                                    | 119/566 (21.0)                                 | 2.14 (1.46–3.12)                                   | <0.001              |
| Sophomore                                     | 65/421 (15.4)                                  | 1.47 (0.97–2.23)                                   | 0.07                |
| Junior  | 40/312 (12.8)                                  | 0.96 (0.59–1.56)                                   | 0.87                |
| Senior  | 64/533 (12.0)                                  | 1.00   |                     |

\* Data are the results of the Web-based cohort study involving 1832 students. Only students who responded are shown for each variable. Conjunctivitis was defined by self-report of eye redness; gray or yellow discharge; itching, burning, pain, or dryness; and crusting in the morning. Odds ratios and P values were determined by stepwise logistic-regression analysis. The final model contained all types of exposure listed. CI denotes confidence interval.

† Data are the numbers of students with conjunctivitis among those with and those without prolonged close contact with a person other than a roommate (e.g., member of a study group, girlfriend, or boyfriend) who had conjunctivitis.

through 2001, 99.6 percent had an identifiable capsular serotype (unpublished data). DNA–DNA reassociation is considered the definitive test for the evaluation of a species.<sup>22</sup> Preliminary results of such testing indicate that this unencapsulated strain is *S. pneumoniae* (unpublished data). Other evidence collected to date, including susceptibility of the iso-

late to optochin, solubility in bile, reaction to a DNA probe, results of multilocus sequence typing, and sequencing of 16S rRNA, also suggests that this strain is a pneumococcus. Further studies are needed to explain how, in contrast to typical pneumococci, certain unencapsulated strains are capable of causing large outbreaks and why they cause conjunctivi-

**Table 3. Carriage of *Streptococcus pneumoniae* and of the Outbreak Strain among 244 Students According to Site of Isolation.\***

| Site of Culture               | <i>S. pneumoniae</i> Isolated |   | Outbreak Strain Isolated |                                 |
|-------------------------------|-------------------------------|---|--------------------------|---------------------------------|
|                               | Total                         | Criteria for Conjunctivitis Met<br>number (percent) | Total                    | Criteria for Conjunctivitis Met |
| Conjunctiva                   | 6 (2.5)                       | 5 (83.3)  | 6 (2.5)                  | 5 (83.3)                        |
| Pharynx                       | 30 (12.3)                     | 9 (30.0)  | 13 (5.3)                 | 8 (61.5)                        |
| Either conjunctiva or pharynx | 33 (13.5)                     | 12 (36.4)   | 16 (6.6)                 | 11 (68.8)                       |
| Both conjunctiva and pharynx  | 3 (1.2)                       | 2 (66.7)  | 3 (1.2)                  | 2 (66.7)                        |

\* The outbreak strain was identified by comparison of results of pulsed-field gel electrophoresis for carriage strains with results for clinical isolates. Conjunctivitis was defined by self-report of eye redness; gray or yellow discharge; itching, burning, pain, or dryness; and crusting within 21 days before swabbing of the eye. Nasopharyngeal and oropharyngeal specimens were collected separately but cultured together.

tis rather than other pneumococcal syndromes. The high attack rate suggests that few students had pre-existing immunity to this strain. The absence of a capsule may limit this strain’s ability to cause more serious infections.

Outbreaks of conjunctivitis are not unusual. Large outbreaks of adenoviral conjunctivitis have occurred on military bases,<sup>23</sup> in eye clinics,<sup>24,25</sup> and in child care centers.<sup>26</sup> Outbreaks of bacterial conjunctivitis also have been described, including haemophilus conjunctivitis in schools,<sup>27</sup> child care centers,<sup>28</sup> and communities,<sup>29</sup> and moraxella conjunctivitis at a boarding school.<sup>30</sup> Previous outbreaks have been attributed to transmission from a common source or prolonged close contact with affected persons. Although few large outbreaks of pneumococcal conjunctivitis have been reported, this strain of pneumococcus appears to be well suited to a residential college environment. The outbreak strain was identical on PFGE to strains that had caused outbreaks of conjunctivitis among college students in New York and California in 1980; evidence recorded on the Multi Locus Sequence Typing Web site<sup>16</sup> indicates that this nonencapsulated strain is also present in Europe. No outbreaks caused by this strain have been reported for 20 years, although outbreaks due to other unencapsulated pneumococci have been reported. An unencapsulated pneumococcus that differed from our outbreak strain on PFGE caused an outbreak among college students in Illinois in 1981.<sup>10</sup> In 1996, a strain that differed from the 1980 and 1981 outbreak strains according to PCR analysis with BOXA1R oligonu-

cleotide primers caused an outbreak of conjunctivitis among attendees of a military training school in Illinois.<sup>9</sup>

None of the members of the health center staff developed conjunctivitis during the outbreak, despite a regular flow of patients through the clinic. This experience differs markedly from those in other reported outbreaks of adenoviral conjunctivitis, in which health care settings have served as amplifiers and strict infection-control practices have been required in order to end the outbreaks.<sup>25</sup> The absence of conjunctivitis among exposed health care workers suggests that contact with infected patients in a health care setting is not an efficient route of transmission for pneumococcal conjunctivitis.

We used electronic data sources to speed up data acquisition, analysis, and public health action.<sup>18</sup> In 2000, Dartmouth ranked as the fifth “most wired” college in the country.<sup>31</sup> The college administration routinely uses electronic means to contact students and conduct surveys. We used the college e-mail system and college-protected Web sites to alert students to the outbreak quickly, to provide messages about prevention, to administer and analyze a survey, and to recruit subjects for a study of carriage. The highly wired Dartmouth campus enabled students to participate in the investigation at the time when interest was high and data could be used effectively.

Whether our interventions to stop the outbreak were helpful remains unclear. Messages about prevention encouraged students to wash their hands, seek treatment for symptoms of conjunctivitis, and

reduce contact that would foster transmission. In addition, alcohol-based hand gel was distributed to undergraduate students. Although the use of hand gel improves hand hygiene in the hospital setting,<sup>32,33</sup> its benefit in the setting of a community outbreak is unknown. Our evaluation of the effectiveness of hand gel may not have been conclusive because of the timing of its distribution, just before the spring break. The number of students given a diagnosis of conjunctivitis declined markedly after the break, but whether this decline resulted from our interventions, decreased contact among students during the break, or the fact that there were no more susceptible students in the college population is unknown.

The arrival of spring break was cause for concern as well as celebration. Many students left campus with active conjunctivitis or as carriers of the outbreak strain, and some students traveled to places that are popular vacation spots for college students. The outbreak of conjunctivitis at Princeton, caused by the same strain identified at Dartmouth, suggests that transmission occurred between the two campuses. Students from these two Ivy League schools compete in sporting matches and participate in a variety of joint social events. Outbreaks at other college campuses may still occur.

Since the available pneumococcal vaccines work by inducing type-specific antibodies targeting the polysaccharide capsule, infection-control measures are the only available means of controlling outbreaks

and preventing sporadic disease caused by unencapsulated pneumococci. New vaccines that are now being developed target highly conserved pneumococcal surface proteins and could prove to be useful as control measures.<sup>34,35</sup> Enzymes with the potential to eradicate carriage may be useful in future outbreaks.<sup>36</sup> When such outbreaks occur, investigators should evaluate whether the use of antibiotic eyedrops helps to limit symptoms and transmission and should determine which infection-control measures are useful for preventing the spread of the infection.

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#### REFERENCES

- Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995. *N Engl J Med* 1997;337:970-6.
- Marston BJ, Plouffe JF, File TM Jr, et al. Incidence of community-acquired pneumonia requiring hospitalization: results of a population-based active surveillance study in Ohio. *Arch Intern Med* 1997;157:1709-18.
- Bluestone CD, Stephenson JS, Martin LM. Ten-year review of otitis media pathogens. *Pediatr Infect Dis J* 1992;11:Suppl:S7-S11.
- Gwaltney JM Jr. Acute community-acquired sinusitis. *Clin Infect Dis* 1996;23:1209-23.
- O'Brien TP. Conjunctivitis. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 5th ed. Vol. 1. Philadelphia: Churchill Livingstone, 2000:1251-6.
- Austrian R. Pneumococcal infections. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's principles of internal medicine*. 13th ed. Vol. 1. New York: McGraw-Hill, 1994: 607-11.
- Seal DV, Barrett SP, McGill JI. Aetiology and treatment of acute bacterial infection of the external eye. *Br J Ophthalmol* 1982;66: 357-60.
- Leibowitz HM. The red eye. *N Engl J Med* 2000;343:345-51.
- Ertugrul N, Rodriguez-Barradas MC, Musher DM, et al. BOX-polymerase chain reaction-based DNA analysis of nonserotypeable *Streptococcus pneumoniae* implicated in outbreaks of conjunctivitis. *J Infect Dis* 1997; 176:1401-5.
- Shayegani M, Parsons LM, Gibbons WE Jr, Campbell D. Characterization of nontypable *Streptococcus pneumoniae*-like organisms isolated from outbreaks of conjunctivitis. *J Clin Microbiol* 1982;16:8-14.
- Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically: approved standard. 5th ed. Wayne, Pa.: National Committee for Clinical Laboratory Standards, 2000. (NCCLS document M7-A5.)
- Chapin K. Clinical microscopy. In: Murray PR, ed. *Manual of clinical microbiology*. 6th ed. Washington, D.C.: ASM Press, 1995: 33-51.
- Elliott JA, Farmer KD, Facklam RR. Sudden increase in isolation of group B streptococci, serotype V, is not due to emergence of a new pulsed-field gel electrophoresis type. *J Clin Microbiol* 1998;36:2115-6.
- Enright MC, Spratt BG. A multilocus sequence typing scheme for *Streptococcus pneumoniae*: identification of clones associated with serious invasive disease. *Microbiology* 1998;144:3049-60.
- Geslin P, Fremaux A, Picq C, Sissia G, Georges S. Use of a DNA probe test for identification of *Streptococcus pneumoniae* nontypable strains. *Adv Exp Med Biol* 1997;418:383-5.
- Multi Locus Sequence Typing home page. London: Imperial College, 2002. (Accessed January 23, 2003, at <http://www.mlst.net/new/index.htm>.)
- Schinsky MF, McNeil MM, Whitney AM, et al. *Mycobacterium septicum* sp. nov., a new rapidly growing species associated with catheter-related bacteraemia. *Int J Syst Evol Microbiol* 2000;50:575-81.

18. Pryor JH, Martin MT, Whitney CG, Turco JH, Baumgartner YY, Zegans ME. Rapid response to a conjunctivitis outbreak: the use of technology to leverage information. *J Am Coll Health* 2002;50:267-71.
19. O'Brien KL, Bronsdon MA, Dagan R, et al. Evaluation of a medium (STGG) for transport and optimal recovery of *Streptococcus pneumoniae* from nasopharyngeal secretions collected during field studies. *J Clin Microbiol* 2001;39:1021-4.
20. Outbreak of bacterial conjunctivitis at a college — New Hampshire, January–March 2002. *MMWR Morb Mortal Wkly Rep* 2002; 51:205-7.
21. Tettelin H, Nelson KE, Paulsen IT, et al. Complete genome sequence of a virulent isolate of *Streptococcus pneumoniae*. *Science* 2001; 293:498-506.
22. Stackebrandt E, Frederiksen W, Garrity GM, et al. Report of the ad hoc committee for the re-evaluation of the species definition in bacteriology. *Int J Syst Evol Microbiol* 2002; 52:1043-7.
23. Paparello SF, Rickman LS, Mesbahi HN, Ward JB, Siojo LG, Hayes CG. Epidemic keratoconjunctivitis at a U.S. military base: Republic of the Philippines. *Mil Med* 1991;156: 256-9.
24. Jernigan JA, Lowry BS, Hayden FG, et al. Adenovirus type 8 epidemic keratoconjunctivitis in an eye clinic: risk factors and control. *J Infect Dis* 1993;167:1307-13.
25. Epidemic keratoconjunctivitis in an ophthalmology clinic — California. *MMWR Morb Mortal Wkly Rep* 1990;39:598-601.
26. McMinn PC, Stewart J, Burrell CJ. A community outbreak of epidemic keratoconjunctivitis in central Australia due to adenovirus type 8. *J Infect Dis* 1991;164:1113-8.
27. Buehler JW, Holloway JT, Goodman RA, Sikes RK. Gnat sore eyes: seasonal, acute conjunctivitis in a southern state. *South Med J* 1983;76:587-9.
28. Trottier S, Stenberg K, Von Rosen IA, Svanborg C. *Haemophilus influenzae* causing conjunctivitis in day-care children. *Pediatr Infect Dis J* 1991;10:578-84.
29. Brazilian purpuric fever: *Haemophilus aegyptius* bacteremia complicating purulent conjunctivitis. *MMWR Morb Mortal Wkly Rep* 1986;35:553-4.
30. Schwartz B, Harrison LH, Motter JS, Motter RN, Hightower AW, Broome CV. Investigation of an outbreak of *Moraxella conjunctivitis* at a Navajo boarding school. *Am J Ophthalmol* 1989;107:341-7.
31. 50 Most wired universities 2000. (Accessed February 27, 2003, at [http://www.zdnet.com/zdsubs/yahoo/content/100mostwired/table\\_uni.html](http://www.zdnet.com/zdsubs/yahoo/content/100mostwired/table_uni.html).)
32. Bischoff WE, Reynolds TM, Sessler CN, Edmond MB, Wenzel RP. Handwashing compliance by health care workers: the impact of introducing an accessible, alcohol-based hand antiseptic. *Arch Intern Med* 2000;160: 1017-21.
33. Parienti JJ, Thibon P, Heller R, et al. Hand-rubbing with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates: a randomized equivalence study. *JAMA* 2002;288:722-7. [Erratum, *JAMA* 2002;288:2689.]
34. McDaniel LS, Sheffield JS, Delucchi P, Briles DE. PspA, a surface protein of *Streptococcus pneumoniae*, is capable of eliciting protection against pneumococci of more than one capsular type. *Infect Immun* 1991;59:222-8.
35. Sampson JS, Furlow Z, Whitney AM, Williams D, Facklam R, Carlone GM. Limited diversity of *Streptococcus pneumoniae* PsaA among pneumococcal vaccine serotypes. *Infect Immun* 1997;65:1967-71.
36. Loeffler JM, Nelson D, Fischetti VA. Rapid killing of *Streptococcus pneumoniae* with a bacteriophage cell wall hydrolase. *Science* 2001; 294:2170-2.

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