Brief Report

Whooping Cough Caused by Bordetella pertussis and Bordetella parapertussis in an Immunized Population

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Context.—The prevalence of Bordetella pertussis and Bordetella parapertussis infections among outpatients in an immunized population is not known.

Objective.—To study the prevalence of these infections in outpatients with paroxysmal cough in Finland, where the pertussis vaccine coverage of 4 doses is 98%.

Design.—Prospective cohort study.

Setting.—Thirty-two health centers in southwestern Finland.

Patients.—A total of 584 patients with paroxysmal cough seen at local health centers from October 1994 through March 1997 from whom nasopharyngeal swabs were collected.

Main Outcome Measures.—Prevalence of positive cultures for B pertussis or B parapertussis and/or positive polymerase chain reaction (PCR) results and frequency of symptoms in those with pertussis and parapertussis.

Results.—A total of 153 subjects (26.2%) had Bordetella infection by culture or PCR: 93 (60.8%) had B pertussis infection, 49 (32.0%) had B parapertussis infection, and 11 (7.2%) had both. Of these cases, 39 (25.5%) had positive cultures and 55 (35.9%) had positive PCR results for B parapertussis. At the time of diagnosis, no difference was found in the frequency of symptoms between patients with B parapertussis infection and those with B pertussis infection. Bordetella parapertussis infection was as common as B pertussis infection in children before school entry, whereas in schoolchildren and adults, B pertussis infection was more common than B parapertussis infection (P<.001).

Conclusion.—Bordetella infections are common in an immunized population, and B parapertussis infections apparently are more prevalent than previously documented.

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BORDETELLA pertussis and Bordetella parapertussis cause whooping cough in humans. They are almost identical at the DNA level and produce many similar virulence factors. The pathogenetically important difference between the two is that B parapertussis does not secrete pertussis toxin.1

In the prevaccination era, the relative frequency rates of B parapertussis isolates varied from 1% to 35% of Bordetella isolates,4 and similar frequency rates, from 2% to 25%, were also found during recent acellular vaccine efficacy trials.5,6 Although cases of infection with B parapertussis, even outbreaks, have been reported in immunized populations,5,7,11 community-based data on the occurrence of B parapertussis infection are limited. This study investigated the epidemiology of both infections in a highly immunized population.

METHODS

Immunization and Surveillance of Pertussis in Finland

Bordetella pertussis vaccination was introduced in Finland (population, 5.1 million) in 1952. Since 1958 the vaccine has contained strain 18530. Because serotype 1.2 strains emerged in the 1970s, strain 1772 was introduced to the vaccine (v/v) in 1976. The vaccine is manufactured by the National Public Health Institute, Helsinki, Finland, and contains 5 x 10^7 formalin-killed B pertussis organisms per dose combined with diphtheria and tetanus toxoids. The vaccine is used at 3, 4, 5, and 24 months, and the coverage is 98%.12

In the last 10 years, based on the report of the official reporting system, the annual number of laboratory-confirmed B pertussis infection cases have ranged from 498 to 2574. Most patients are schoolchildren. In the last decade, 648 patients with B pertussis infection and 13 patients with B parapertussis infection were hospitalized and 76% of them were younger than 1 year.

To collect more reliable data, we started an enhanced surveillance in southwestern Finland (population, 702 000) in October 1994 that lasted 30 months and ended in March 1997. Swabs (calcium alginate), culture transport tubes, and questionnaires were provided for all 32 health centers free of charge. Culture results were reported to the health centers 7 days after the sample arrived at our laboratory.

In Finland, the health centers are major sources for primary health care of children and adults. There is at least 1 health center in each community. The services offered by these centers are usually free.

Inclusion Criteria and Clinical Information

In the health centers, nasopharyngeal specimens were taken by physicians from all patients with paroxysmal cough, characterized as bouts of uncontrollable coughing of any duration. During the 30 months of the study, swabs were obtained from 584 eligible patients (number of male patients, 257; age range, 7 days to 74 years; median age, 9 years). No hospitalization was needed. At the time of sampling, 135 (23.1%) were experiencing whooping and 208 (35.6%) were experiencing vomiting. Twenty-nine health centers (90.6%) sent samples to the laboratory. The average number

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Bordetella parapertussis was detected from samples sent by 17 health centers (53%), and B pertussis was detected from samples sent by 23 health centers (72%).

Detailed clinical information on each subject was obtained by a structured questionnaire asking about the date of onset and the nature of symptoms. The questionnaires were completed by physicians at the health centers and mailed to the laboratory. The symptoms of subjects were not followed up after this first contact with the health center.

Laboratory Methods

The swabs were inoculated onto the slant of the transport medium (of the same composition as the charcoal agar plate) supplemented with cephalexin, placed in sterile empty tubes with caps, transported to the laboratory, and stored at −40°C for polymerase chain reaction (PCR). Twenty swabs were not sent to the laboratory after inoculation. Thus, 564 swabs were tested by PCR.

Details of bacterial culture and identification, DNA extraction, and PCR have been described earlier. Two sets of primers derived from insertion sequence elements IS481 and IS1001 that are specific for B pertussis and B parapertussis. The positivity rates of laboratory-confirmed Bordetella parapertussis and Bordetella pertussis infections in various age groups (number of subjects = 2 years, 53; 2-6 years, 163; 7-15 years, 220; and ≥16 years, 147).

RESULTS

Of 584 samples tested by culture, 19 (3.4%) were positive for B parapertussis and 39 (6.7%) for B pertussis. Of 564 samples tested by both culture and PCR, 15 had positive cultures and 35 (9.4%) had positive PCR results for B parapertussis, and 95 (16.3%) had positive PCR results for B pertussis. Forty-four (86.3%) of 51 samples with positive cultures for Bordetella also had positive PCR results. In 11 specimens, B parapertussis and B pertussis DNA were simultaneously detected. Men and women had similar culture and PCR positivity rates. Altogether, 153 subjects (26.2%) were confirmed as having B pertussis (60.8%), B parapertussis (32.0%), or both (7.2%).

Of 564 subjects whose samples were tested by both culture and PCR, 198 (35.1%) had had paroxysmal cough for 7 days or less, and 366 (64.9%) had had paroxysmal cough for more than 7 days at the time of sampling.

Of the 198 patients who had experienced paroxysmal cough for 7 days or less, 24 (12.1%) had positive cultures or PCR results for B parapertussis and 35 (17.7%) had positive cultures or PCR results for B pertussis. Of the 366 patients who had experienced paroxysmal cough for more than 7 days, 32 (8.7%) had positive cultures or PCR results for B parapertussis and 96 (26.0%) had positive cultures or PCR results for B pertussis. No statistically significant difference was found in positivity rates of culture or PCR results for B pertussis (relative risk [RR], 0.98; 95% confidence interval [CI], 0.68-1.42; P = .99) and for B parapertussis (RR, 1.39; 95% CI, 0.82-2.34; P = .26) between specimens taken from patients during the first 7 days after the onset of paroxysmal cough and specimens taken during the later course of illness.

Bordetella parapertussis and B pertussis were detected during 13 and 22 months of the surveillance period and from samples sent by 17 and 23 health centers, respectively. Both B parapertussis and B pertussis were detected during 11 months of the surveillance period and from samples sent by 11 health centers (Figure 1).

At the time of sampling, no difference was found in the frequency of whooping (11 [25%] of 44 vs 23 [36%] of 88; RR, 0.96; 95% CI, 0.52-1.79; P = .94), vomiting (19 [43%] of 44 vs 26 [30%] of 88; RR, 1.46; 95% CI, 0.91-2.33; P = .17), or mean duration (in days) of paroxysmal cough at the time of sampling (15.2 [95% CI, 11.8-18.6] vs 15.3 [95% CI, 12.7-17.6]; P = .95) between patients with positive cultures or PCR results for B parapertussis and B pertussis. No difference was found in the frequency of whooping (6 [19%] of 26 vs 27% of 22; RR, 0.71; 95% CI, 0.25-2.0; P = .73) and vomiting (13 [50%] of 26 vs 12 [55%] of 22; RR, 0.92; 95% CI, 0.54-1.58; P = .98) between patients younger than 7 years with positive cultures or PCR results for B pertussis and B parapertussis, or in the frequency of whooping (6 [27%] of 22 vs 5 [23%] of 22; RR, 1.20; 95% CI, 0.43-3.36; P > .99) and vomiting (12 [55%] of 22 vs 7 [32%] of 22; RR, 1.70; 95% CI, 0.83-3.50; P = .22) between patients younger than 7 years and those aged 7 years or older with positive cultures or PCR results for B parapertussis.

The positivity rate of laboratory-confirmed B parapertussis infection was highest in 2- to 6-year-olds, whereas the positivity rate of B pertussis infection was highest in 7- to 15-year-olds (Figure 2). Bordetella pertussis infection was signifi-
cantly more common than B parapertussis infection in schoolchildren and adults (P<.001). The annual incidences of B pertussis and B parapertussis infections were 5.9 and 3.4 cases per 100 000, respectively. The annual incidences of B pertussis and B parapertussis infections were 16.6 and 9.5 in children younger than 2 years, 19.6 and 20.5 in children aged 2 to 6 years, 27.2 and 15.1 in children aged 7 to 15 years, and 1.5 and 0.2 in persons aged 16 years or older, respectively.

Based on the culture-proven cases reported by the official system, the annual incidences of B pertussis infection in 1995 and 1996 were 1.3 and 0.6 per 100 000 in southwestern Finland and 1.2 and 1.9 per 100 000 in the whole country, respectively. In southwestern Finland, only 1 case of B parapertussis infection was reported during the surveillance period, and 3 cases were reported during the last 6 years.

**COMMENT**

This study confirms that in an immunized population B pertussis and B parapertussis infections remain common. Furthermore, B parapertussis infections were more prevalent than usually documented, with one third of laboratory-confirmed Bordetella infections caused by B parapertussis. Bordetella parapertussis infection was as common as B pertussis infection in children before school entry, whereas in schoolchildren and adults B pertussis infection was markedly more prevalent. High rates of B pertussis infection in schoolchildren and adults B pertussis infection was markedly more prevalent. High rates of B pertussis infection in schoolchildren and adults B pertussis vaccination decreases with time. The sensitivity of B pertussis PCR was about 3 times higher than that of culture. The assay has been shown to be specific by testing panels of bacterial species. Its specificity was also confirmed clinically in this study by the low positivity rates obtained between infection peaks and in subjects 16 years and older. The incidences of B pertussis and B parapertussis infections reported by the official reporting system, based on patients with laboratory-confirmed infection, were lower than those obtained from the enhanced surveillance. The enhanced surveillance clearly supplemented the existing reporting system. Underdiagnosis of Bordetella infections is a more likely reason for the low incidences reported by the official system than failure to report diagnosed cases.

The disease caused by B parapertussis is usually milder than that caused by B pertussis.

**References**