



ORIGINAL ARTICLE

The 1993 Epidemic of Pertussis in Cincinnati -- Resurgence of Disease in a Highly Immunized Population of Children

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Abstract

BACKGROUND

In 1993 there was a resurgence of pertussis in the United States. Altogether, 6335 cases were reported, the most in 26 years.

METHODS

Using active microbiologic surveillance, we investigated the epidemic of pertussis in Greater Cincinnati in 1993. The population of 1.7 million in this area is served by a single children's hospital and pertussis laboratory. We prospectively followed patients given a new diagnosis of

pertussis in July through September 1993 to determine the characteristics of the epidemic.

RESULTS

From 1979 to 1992, there was a cumulative total of 542 cases of pertussis. In 1993, 352 cases were diagnosed, an increase of 259 percent over the 1992 total. Sixty-three percent of the cases had positive cultures for *Bordetella pertussis*, 18 percent were positive on direct fluorescent-antibody testing only, and 19 percent were diagnosed clinically. The outbreak began in the suburbs during the summer and spread through Greater Cincinnati. Of 255 total cases diagnosed in July through September (195 excess cases over the maximal base-line level of 20 per month in the previous 14 years), 75 percent were in white patients and 67 percent of the patients had private insurance or paid for care out of pocket. In 1993, as compared with 1979 through 1992, there was a shift in incidence from younger infants to older children; the percentages of cases according to age group were as follows: 0 to 6 months, 53 percent from 1979 through 1992 and 35 percent in 1993 ($P < 0.001$); 7 months to 5 years, 33 percent and 43 percent ($P < 0.002$); 6 to 12 years, 5 percent and 11 percent ($P < 0.001$); and more than 12 years, 5 percent and 11 percent ($P < 0.003$). Immunization records revealed that 74 percent (75 of 101) of the children with pertussis who were 19 months to 12 years old had received four or five doses of the combined diphtheria-pertussis-tetanus (DPT) vaccine, and that 82 percent (103 of 126) of those 7 to 71 months old had received at least three doses of DPT vaccine. The whole-cell vaccines used came from both of the major manufacturers (Connaught Laboratories and Lederle Laboratories). Disease was not severe, but 80 of the 255 children (31 percent) given diagnoses during the three epidemic months were hospitalized. There were no deaths.

CONCLUSIONS

Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease.

Introduction

THROUGHOUT THE WORLD, PERTUSSIS REMAINS A MAJOR CAUSE OF MORBIDITY AND MORTALITY AMONG INFANTS; IT IS estimated to account for more than 600,000 deaths annually¹. Whole-cell pertussis vaccines have been effective in controlling the disease but have not eliminated circulation of *Bordetella pertussis*^{2,3}. Although estimates of the efficacy of the pertussis vaccine vary widely according to the methods used,⁴ the efficacy of whole-cell vaccines used in the United States has been substantiated in recent studies of household exposure^{3,5,6}. Traditionally, pertussis has affected primarily infants and children who are not immunized and children who are incompletely immunized^{7,8}. Adolescents and adults with waning immunity and mild, atypical disease also have an important role in transmitting *B. pertussis* to susceptible infants and children⁹⁻¹⁶. During 1993, there was a dramatic resurgence of pertussis in the United

States, with 6335 cases reported¹⁷ -- the highest number since 1967¹⁸. Although there has been increased recognition of pertussis in adults^{18,19} and new clinical case definitions have been adopted,¹⁸⁻²⁰ the reason for this resurgence is largely unknown¹⁸.

After two decades during which the incidence of pertussis was stable in Greater Cincinnati (0.4 to 5.8 cases per 100,000 population), an epidemic occurred in 1993 (incidence, 20.7 per 100,000), involving all age groups. Nearly all (93 percent) of the first 285 cases reported to the Centers for Disease Control and Prevention (CDC) were identified at the Children's Hospital Medical Center (CHMC)¹⁸. Most disturbing was the number of cases in older children who had been appropriately immunized. In this report we describe the clinical epidemiologic features, immunization status, and microbiologic characteristics of pertussis cases that occurred in Cincinnati during 1993.

Methods



MICROBIOLOGIC SURVEILLANCE

The CHMC is a 361-bed university hospital providing regional pediatric services to Greater Cincinnati, defined as an area in southwest Ohio, northern Kentucky, and southeast Indiana with a referral population base of 1.7 million. For 15 years, the CHMC has been the only regional microbiology laboratory performing cultures for *B. pertussis* and *B. parapertussis* and direct fluorescent-antibody (DFA) staining of nasopharyngeal secretions for these pathogens. Patients with suspected clinical cases of pertussis in the community are referred directly to our test referral center or to the emergency room. Laboratory studies include the examination of specimens by DFA assay and culture for *B. pertussis*^{21,22}. Hospitalized patients with suspected pertussis are routinely placed in respiratory isolation and treated with erythromycin or trimethoprim-sulfamethoxazole.

MICROBIOLOGIC TESTS

After collection of nasopharyngeal secretions, one swab is immediately placed in 5 ml of Regan-Lowe medium²³. Another is placed in a fatty acid-free solution of 1 percent casamino acids²⁴. Swabs are inoculated onto freshly prepared Bordet-Gengou medium and Regan-Lowe medium^{21,22,25}. Plates are incubated at 35 °C in a non-carbon dioxide incubator for five days. Smears for testing by DFA staining are prepared from nasopharyngeal secretions with polyclonal antibodies to *B. pertussis*^{21,22}.

SURVEILLANCE FOR PERTUSSIS

The hospital epidemiology program has tracked pertussis cases for 15 years. Culture-positive cases and cases positive on DFA testing are reported daily by the microbiology laboratory. Hospitalized patients with pertussis syndrome diagnosed by a physician who have negative

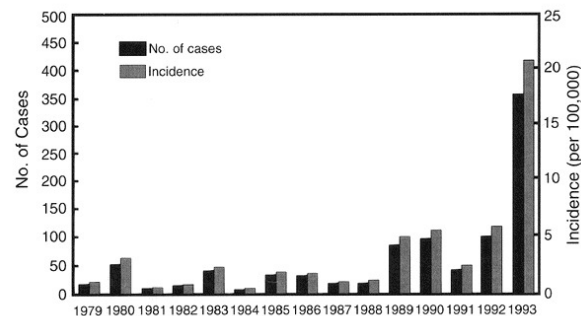
cultures and DFA tests are defined as having “clinical pertussis”; these children are prescribed 14 days of erythromycin. Cases are identified by daily reviews of the charts of discharged patients. Cases are plotted monthly on an epidemic curve to monitor disease trends in the community.

The cases diagnosed during July, August, and September 1993 were analyzed prospectively to determine the characteristics of the pertussis epidemic. Addresses were mapped according to ZIP Codes in order to characterize geographic spread (Atlas Geographic Information Systems, Strategic Mapping, San Jose, Calif.). Hospital computer records were reviewed to determine each patient's ethnic group, insurance status, health care provider, and age. Charts of patients admitted to the CHMC were reviewed in order to assess the severity of illness. Histories of DPT vaccination were obtained by telephone calls to physicians' offices. Microbiologic surveillance records for 1993 were also reviewed. The age groups of patients with endemic pertussis diagnosed from 1979 through 1992 were compared with those for 1993, the epidemic year. Data were entered in the statistical program Epi Info (version 5.1)²⁶ with univariate analysis with the two-tailed Fisher's exact test. The results of microbiologic testing were evaluated for concordance²⁷.

Results

PERTUSSIS IN CINCINNATI, 1979 TO 1993

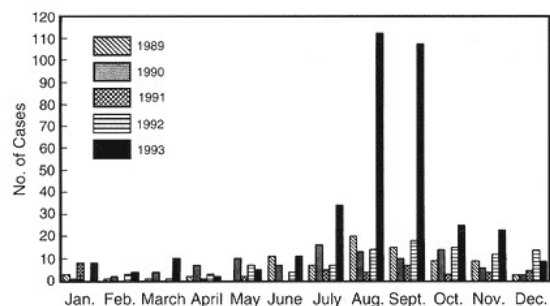
Figure 1.



Incidence of Pertussis in Greater Cincinnati, 1979 through 1993.

Fewer than 50 cases of pertussis were identified annually during 1979 through 1988 and fewer than 100 cases per year from 1989 through 1992 (Figure 1). From 1979 through 1992, the cumulative total was 542 cases. The 352 cases diagnosed in 1993 represented a 259 percent increase from the 98 cases in 1992 (Figure 1). Thirteen cases were diagnosed in the first five months of 1994, of which nine were diagnosed in January.

Figure 2.



Number of Cases of Pertussis in Greater Cincinnati According to Month, 1989 through 1993.

Table 1.

MONTH	NO. OF SAMPLES	CULTURE- POSITIVE	DFA- POSITIVE ONLY	CLINICAL DIAGNOSIS*
			<i>number (percent)</i>	
January–May	668	25 (4)	0	4 (1)
June	81	9 (11)	1 (1)	1 (1)
July	148	31 (21)	3 (2)	0
August	628	59 (9)	42 (7)	12 (2)
September	2097	66 (3)	12 (1)	30 (1)
October	728	17 (2)	2 (<1)	6 (1)
November	181	10 (6)	3 (2)	10 (6)
December	110	6 (5)	1 (1)	2 (2)
Total	4641	223 (5)	64 (1)	65 (1)

*Culture-negative and DFA-negative.

Microbiologic Surveillance for *B. pertussis* and *B. parapertussis* in 1993.

In July 1993, 34 cases were identified ([Figure 2](#)). Because this exceeded the 10-year monthly maximum of 20 cases in August 1989, a “pertussis alert” was announced to the Cincinnati Health Department, the public, and physicians in the community. Information about the outbreak was promulgated through the media, by facsimile communication between the CHMC and community physicians, and by bulletins and educational conferences on pertussis. Age-appropriate DPT immunizations were encouraged. Community surveillance for pertussis cases increased ([Table 1](#)). Our laboratory received 148 respiratory swabs for evaluation by culture for pertussis in July 1993. This number increased to 628 samples in August, when 113 cases of pertussis were diagnosed.

DECLARATION OF PERTUSSIS EPIDEMIC

On September 3, 1993, the CHMC and the Cincinnati Health Department issued a joint declaration that a pertussis epidemic existed in Greater Cincinnati. To decrease morbidity among young infants, the age of DPT immunization was lowered to one month, with doses recommended as frequently as one month apart^{28,29}. For children exposed to pertussis, it was recommended that those who had received their third DPT vaccination six months or more before exposure should receive a fourth dose immediately. For others who had received at least four doses of pertussis vaccine, a booster was recommended, unless a dose had been given within the past three years or the child was more than six years of age. Medical evaluation was strongly encouraged for immunized and unimmunized persons of all ages who had unexplained respiratory disease. This included persons with paroxysmal cough accompanied by whoop and vomiting. Children with unexplained respiratory disease were barred from day-care centers and schools until they could be evaluated by a physician.

To prevent transmission, erythromycin or trimethoprim-sulfamethoxazole (14 days) was recommended for patients with suspected pertussis and their close household contacts, regardless of their immunization status. To prevent neonatal disease, which characteristically entails high morbidity and mortality,^{10,14,15} visits to the 12 regional newborn nurseries were restricted to parents, grandparents, and guardians. Since more than 85 percent of the cases of pertussis were in children, the CHMC prohibited all visits by children less than 14 years old and adults with respiratory disease. The CHMC further implemented aggressive measures for preventing nosocomial transmission³⁰.

In September, surveillance increased further; 2097 respiratory cultures yielded 108 confirmed cases ([Table 1](#) and [Figure 2](#)). There were 255 epidemic cases in July, August, and September ([Figure 2](#)); this was 195 excess cases over the maximal base-line rate of 20 per month in the previous 14 years. An end to the epidemic was declared on October 21, after seven weeks, when the number of reported cases for the month had fallen to 13, below the base-line level. The normal DPT immunization schedule was reintroduced, and restrictions on visits to hospitals were lifted.

GEOGRAPHIC DISTRIBUTION

Maps of the location of the 255 epidemic cases of pertussis diagnosed in July through September revealed early clustering within the suburban areas of northwest Cincinnati and early activity in suburban northeast Hamilton County, Ohio. Later maps reflected widespread pertussis activity in Cincinnati, extending outward in all directions through Kentucky, Indiana, and Ohio.

ETHNIC GROUP, SEX, AND INSURANCE STATUS

Of the 255 epidemic cases, 75 percent (191) were in white patients and 20 percent (52) in black patients. Fifty-one percent of the patients were males. Sixty percent (153 patients) had private insurance, 7 percent (17) paid for care out of pocket, 32 percent (82) were covered by Medicaid, and 1 percent (3) had unknown insurance status. Fifty-five percent (139) were referred by pediatricians in private practice, 32 percent (81) presented at the CHMC emergency room or outpatient clinics, and 14 percent (35) were seen in the public health clinics.

AGE

Table 2.

AGE	1979–1992*	1993	P VALUE
	<i>no. (%)</i>		
0–6 mo	285 (53)	122 (35)	<0.001
7 mo–5 yr	178 (33)	153 (43)	<0.002
6–12 yr	27 (5)	40 (11)	<0.001
>12 yr	27 (5)	37 (11)	<0.003
Unknown	25 (5)	0	—
Total	542 (100)	352 (100)	

*Because of rounding, individual age-group percentages do not total 100.

Pertussis Cases in Nonepidemic Years (1979 through 1992) and in the Epidemic Year (1993), According to Age Group.

The 542 cases diagnosed from 1979 through 1992, when the disease was endemic, were compared with the 352 cases in the epidemic year of 1993 in terms of the age distribution of the patients. The median age shifted from 6 months during the 14 years of endemic pertussis to 17 months in 1993. There was a significant shift from a preponderance of young infants among the patients with the 542 endemic cases toward older immunized children, adolescents, and adults among the 352 patients in the epidemic year (Table 2). Sixty-four percent (349) of endemic

cases were in infants less than one year old, as compared with 44 percent (156) of epidemic cases. The age range among the 352 patients in 1993 was 21 days to 51 years; 21 patients were 18 years of age or older.

IMMUNIZATION STATUS

Table 3.

AGE	NO. OF PATIENTS*	NO. OF DPT DOSES APPROPRIATE FOR AGE	NO. OF DPT DOSES RECEIVED†					
			0	1	2	3	4	5
			<i>no. (%) of children</i>					
3–4 mo	16	1	4 (25)	6 (38)	6 (38)	0	0	0
5–6 mo	18	2	2 (11)	6 (33)	8 (44)	2 (11)	0	0
7–18 mo	52	3	3 (6)	5 (10)	5 (10)	37 (71)	2 (4)	0
19–71 mo	74	4	5 (7)	3 (4)	2 (3)	12 (16)	47 (64)	5 (7)
6–12 yr	27	5	1 (4)	3 (11)	0	0	6 (22)	17 (63)

*Of known DPT status. Four patients had unknown DPT status; none had unknown age.

†Because of rounding, percentages do not always equal 100.

Vaccination against Diphtheria, Pertussis, and Tetanus among Infants and Children 3 Months to 12 Years of Age Who Had Reported Cases of Pertussis.

Among the 101 patients 19 months to 12 years old whose vaccination status was known, 74 percent (75 children) had received four or five doses of DPT vaccine. Of those 7 months to 12 years old, 82 percent (126 of 153) had received three or more doses of DPT vaccine. Table 3 shows the immunization status of 187 patients 3 months to 12 years of age. Since the majority of patients with pertussis were appropriately immunized for their age, especially those who were seven months to five years old, the pertussis epidemic cannot be explained by waning immunity among older children.

Of 126 children with pertussis who were 7 to 71 months old and whose vaccination status was known, 103 had received three or more doses of DPT vaccine (82 percent), and information on the vaccine manufacturer was available for 82 (80 percent). For the primary series only, information on the manufacturer was available in 80 cases. For the first three doses, 64 percent (51 children) received three consecutive doses of DPT vaccine manufactured by Connaught Laboratories (Swiftwater, Pa.), 19 percent (15) received vaccine manufactured by Lederle Laboratories (Pearl River, N.Y.), and 17 percent (14 children) received vaccine from both manufacturers. Of 305 total known doses given to children who were 7 to 71 months old, 72 percent were manufactured by Connaught Laboratories and 28 percent by Lederle Laboratories.

HOSPITAL ADMISSION

Of the 255 patients who were given a diagnosis of pertussis in July through September, 80 (31 percent) were hospitalized at CHMC. Sixty-six percent were less than 6 months old, and 84 percent were less than 12 months old. The duration of the hospital stay was 1 to 16 days (mean

[±SD], 3.8 ±2.4). All received erythromycin. Their symptoms included paroxysmal cough (97 percent), post-tussive emesis (78 percent), cyanosis (63 percent), apnea (42 percent), and whoop (22 percent). Many infants presented with gasping and choking spells. Serious complications included pneumonia or atelectasis (11 percent) and seizures (3 percent). Laboratory-confirmed pertussis and toxic shock syndrome occurred concurrently in an adolescent with *Staphylococcus aureus* pneumonia. An infant with *B. parapertussis* infection and prolonged apnea was admitted for intensive care; he required 12 hours of mechanical ventilation. There were no deaths.

MICROBIOLOGIC CHARACTERISTICS

B. pertussis or *B. parapertussis* infection was confirmed by culture or DFA testing in 82 percent of the 352 cases reported in 1993 (Table 1). The rate of positive cultures for *B. pertussis* or *B. parapertussis* was 63 percent, the rate of DFA-positive, culture-negative cases was 18 percent, and hospitalized children with “clinical pertussis” (pertussis diagnosed on clinical grounds but with negative cultures and DFA tests) made up 18 percent. In the 4641 specimens submitted for testing in 1993, the concordance rate for DFA-positive, culture-positive cases was 97 percent, with a kappa value of 0.6 (1.0 indicates perfect agreement)²⁷. Eleven of the 223 culture-positive cases were of *B. parapertussis*, 10 of which were identified during the epidemic months.

Discussion



After two decades of stable rates of pertussis, an epidemic occurred in 1993 in Greater Cincinnati. Among the 352 cases reported during that year, cases that were culture-positive for *B. pertussis* or *B. parapertussis* represented 63 percent, with a combined DFA-positive and culture-positive rate of 82 percent. This is the highest rate of culture-confirmed pertussis in any outbreak reported to the CDC^{7,18,31-33}. Currently, culture and DFA staining are the most practical methods of diagnosing pertussis. Many have shown the DFA test to have low sensitivity (18 percent)^{34,35} and variable specificity³⁶ for pertussis. Moreover, culture itself has less than optimal sensitivity. During 1993, the rate of concordance between DFA tests and culture at our institution was 97 percent²⁷. Although the polymerase chain reaction and serologic methods for diagnosing pertussis are highly sensitive and specific,^{8,19,35} these tests are of limited use in epidemics because of the length of time they require and because of their cost, technical difficulty, and lack of general availability.

This may have been the largest population under microbiologic surveillance for pertussis^{7,18,31-33}. Treatment with erythromycin was recommended at the time of respiratory culture for all those with suspected cases of pertussis in this epidemic. Many cases of clinical pertussis in the community may therefore have been excluded from this report because of our requirement of a supporting laboratory diagnosis or hospitalization.

The Cincinnati system of regionalization of pediatric care permitted the efficient education of the public and physicians in the community about pertussis. The media provided the public with regular updates on the epidemic, allaying parental anxiety and facilitating diagnosis. Early diagnosis, early use of erythromycin for case patients and contacts, and accelerated DPT immunizations may have helped to contain the epidemic. The availability of positive DFA results five days before culture results became available may have limited secondary transmission by allowing the early use of erythromycin. Restrictions on visits to hospitals, surveillance for pertussis and case containment in schools and day-care centers, and the use of aggressive measures to prevent nosocomial transmission in this hospital³⁰ may have assisted in limiting the epidemic to seven weeks. In contrast, in the 10 pertussis outbreaks in the United States in the 1980s, each involving more than 100 persons, transmission was sustained for 6 to 12 months⁷.

This epidemic did not follow traditional sociodemographic patterns, since cases of pertussis were reported among members of the suburban white middle class, who had private insurance and excellent access to medical care. These observations may be partially explained by surveillance bias. A similar reversal in historical epidemiologic trends has been described for acute rheumatic fever³⁷ and measles³⁸. Our rate of hospitalization was low⁷ and disease was mild. In hospitalized patients, most of whom were infants, complication rates were low^{1,2,7}. None of the patients died. This lack of severity may have been due to the frequency of “breakthrough” pertussis in immunized persons, which has a relatively mild course^{8,31}. Surveillance bias may have contributed to the mildness of disease, since case patients and contacts were promptly treated with erythromycin, which ameliorates the clinical features of pertussis when given early in the course of disease³⁹. The only patient who required assisted ventilation had *B. parapertussis* infection; this illness is usually less severe than *B. pertussis* infection, however⁴⁰.

In the 1993 pertussis epidemic in Cincinnati there was a dramatic shift in the age distribution of patients from infants toward older immunized children, adolescents, and adults. Most disturbing was the occurrence of epidemic pertussis among children who were appropriately immunized for their age. Seventy-five percent of infants three to four months old who had pertussis had received one or more doses of the DPT vaccine, as compared with 67 percent in the United States as a whole⁷. In Cincinnati 55 percent of the 5-to-6-month-old infants with pertussis had received two or more doses of the DPT vaccine, 75 percent of the 7-to-18-month-old children had received three or more doses, and 70 percent of the 19-to-71-month-old children had received four or more doses. These rates are in stark contrast to the rate of less than 30 percent for these age groups in the national statistics⁷. Eighty-five percent of the children 6 to 12 years old who had pertussis had received four or more doses of the DPT vaccine.

There are a number of possible reasons for the dramatic resurgence of pertussis among older immunized children. First, there appears to have been intense circulation of *B. pertussis* in the community. Second, reported vaccine efficacy has wide confidence limits (65 to 95 percent⁶), which could mean that there is a substantial number of susceptible children among those who have been immunized. Third, increased

surveillance for pertussis in an informed community may have contributed to increased case finding during the epidemic year. Fourth, the efficacy of whole-cell pertussis vaccines may have declined in recent years. All these factors may have contributed to the resurgence of pertussis.

Over 70 percent of the doses of the DPT vaccine given to children who had pertussis were manufactured by Connaught Laboratories. The Lederle whole-cell pertussis vaccine is known to produce a 46-fold increase in antibody to pertussis toxin, as compared with a 2.4-fold increase with the Connaught product⁴¹. Yet antibody to the toxin is not an adequate measure of protection. We cannot claim that one vaccine is less efficacious than the other, since a properly designed efficacy study has not been performed. Eighty-one percent of the children with pertussis who were 7 to 71 months old had received their primary series of DPT vaccinations -- a rate higher than those previously reported^{7,18}. This finding requires investigation of the failure of the whole-cell pertussis vaccine.

Ongoing laboratory diagnosis and epidemiologic surveillance are essential in controlling the spread of pertussis and in detecting possible changes in the efficacy of vaccines. Our experience suggests that outbreaks can be halted efficiently with increased education of the public and of physicians in the community, a lower threshold of diagnostic suspicion, and careful microbiologic surveillance. The accelerated schedule of DPT vaccination and prompt use of erythromycin for therapy and prophylaxis may also help to contain epidemics. Our study highlights recent national data that emphasize the continuing challenge posed by pertussis. The efficacy of the vaccine cannot be taken for granted, and periodic formal efficacy studies are still needed.

The estimated direct cost of this pertussis epidemic was \$500,000, of which \$85,000 was attributed to containment of pertussis in this hospital alone. Adults and adolescents remain susceptible and may be candidates for booster doses of acellular pertussis vaccines in order to further reduce the cost and clinical consequences of respiratory diseases in infants and children in the future.

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