A Community-wide Pertussis Outbreak

An Argument for Universal Booster Vaccination

Sean Schafer, MD; Hilary Gillette, RN, MPH; Katrina Hedberg, MD, MPH; Paul Cieslak, MD, MPH

Background: Pertussis incidence has increased in the United States since 1980, punctuated by outbreaks that involve adults and adolescents. We investigated a community-wide outbreak and studied risk factors among adults to identify prevention and control opportunities.

Methods: We analyzed surveillance data, interviewed patients, visited outbreak sites, and conducted a case-control study of risk factors for first-in-household adult infection during a Jackson County, Oregon, outbreak in 2003.

Results: In Jackson County, 135 pertussis cases were reported; the incidence was 71 per 100 000 population compared with 0 to 1 per 100 000 population from 1995 through 2001. Case investigations identified 2658 close contacts (19.7 per case); 1050 (40%) received antibiotic prophylaxis. Older children and adolescents (aged 10-17 years) and adults (aged ≥18 years) accounted for 67% of cases. Five infants were hospitalized (192 hospitalizations per 100 000 infants) compared with 18 in the remainder of the state (33 per 100 000 infants). Many cases occurred among epidemiologically linked clusters of varied composition, such as jail inmates and employees, methamphetamine users, low-income housing residents, school students and employees, and employees in certain work settings. Adult patients were more likely than controls to live with children aged 6 to 10 years (odds ratio, 6.4; 95% confidence interval, 1.8-23.4) and less likely to report a complete childhood vaccination history (odds ratio, 0.1; 95% confidence interval, 0.003-0.9).

Conclusion: The predominance of adolescent and adult cases, appearance of new clusters despite aggressive control efforts, clustering of cases in hard-to-reach populations, and absence of modifiable risk factors for adult disease in this outbreak all suggest that universal booster vaccination of adolescents and adults might offer the only effective means to prevent such events in the future.

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Pertussis persists in the United States despite more than 50 years of routine childhood immunization against the disease. The reported incidence has increased steadily from 0.5 cases per 100 000 population in 1981 to an average annual rate of 3.3 cases per 100 000 population from 1996 through 2003. Although the incidence remains highest in incompletely immunized infants, the reported incidence has increased 5-fold among adolescents aged 10 to 19 years (from 0.3 to 7.7 per 100 000 population) and 4-fold among adults 20 years or older (from 0.3 to 1.1 per 100 000 population) from 1990 through 1993 to 2001 through 2003. Pertussis among adolescents and adults has substantial direct consequences, being the likely cause of 12% to 30% of cases of prolonged cough. The true incidence has been estimated at 507 cases per 100 000 population, 150 times higher than reported, with resultant economic costs of $980 million annually in the United States. More important, adolescents and adults with pertussis frequently transmit infection to vulnerable infants, who experience more severe morbidity and nearly all pertussis-related mortality. Increased pertussis morbidity and mortality among US infants since the 1980s suggest that at least some of the recent rise in reported cases is real rather than solely an artifact of increased surveillance. Large outbreaks have punctuated the resurgence of pertussis. These events often involve hundreds of cases and extend for many months. They tax public health resources and highlight the need for more effective means to interrupt transmission. We investigated one community-wide outbreak that lasted for most of 2003 in Jackson County, Oregon (2000 population, 181 269; county seat, Medford), to iden-
identify transmission patterns, risk factors for first-in-household adult infection, and opportunities for improved prevention and control.

METHODS

CASE DEFINITIONS

Oregon law requires laboratories and physicians to report suspected cases or laboratory results indicative of pertussis to the local health department. A confirmed case of pertussis was defined in a Jackson County resident during 2003 as a cough illness of any duration with coughing paroxysms, “whoop,” or posttussive vomiting; or a cough lasting 2 or more weeks and (1) laboratory evidence of Bordetella pertussis infection or (2) close contact with a patient who had a laboratory-confirmed case within 7 to 14 days of onset. Acceptable laboratory evidence included isolation of *B pertussis* by culture or identification of its DNA in nasopharyngeal specimens by the polymerase chain reaction. Close contact was direct contact with respiratory, oral, or nasal secretions; direct, face-to-face contact; or sharing a confined space in close proximity for more than 1 hour. This case definition varied slightly from the more restrictive one recommended by the Council of State and Territorial Epidemiologists. The Council of State and Territorial Epidemiologists defines cough illness of any duration as a confirmed case with a positive culture result but requires a symptom duration of 2 or more weeks with paroxysms, whoop, or posttussive vomiting for confirmation by polymerase chain reaction or through close contact with a laboratory-confirmed case.

DATA SOURCES

In the current outbreak, index cases of all ages were typically diagnosed and reported to local public health authorities by community-based health care professionals and confirmed by laboratory testing. Epidemiologically linked cases, many also laboratory confirmed, were subsequently identified through public health investigation. Jackson County health department nurses interviewed patients and potentially exposed persons, collecting demographic and epidemiologic information, results of laboratory testing, and lists of contacts. They ensured that symptomatic case patients and asymptomatic close contacts were appropriately treated with antibiotics. In addition, the nurses vaccinated children who had inadequate vaccinations or referred them to private physicians for vaccination.

DESCRIPTIVE EPIDEMIOLOGIC FEATURES

Using case reports and midyear population estimates from the US census, we calculated Jackson County’s 2003 pertussis incidence and hospitalization rate and compared these data with statewide rates for Oregon, similarly calculated from case reports from all local health departments. We also calculated incidence and proportional morbidity by age group during the outbreak. To elucidate transmission patterns in Jackson County, we reviewed case reports, visited the sites of case clusters, and interviewed some patients and contacts to identify kinship or congregation among clusters of cases. Case clusters were defined as groups of 2 or more epidemiologically linked cases that were part of a discrete physical setting, shared activity, or social network.

CASE-CONTROL STUDY OF FACTORS ASSOCIATED WITH ADULT ILLNESS

We undertook a case-control study to investigate risk factors for reported disease in adults in Jackson County. Risk factors under investigation were collected via telephone-administered questionnaire in December 2003, 3 to 6 months after symptom onset for most cases. They included age, race, sex, occupation, number of daily personal contacts, use of public transportation, attendance at large meetings or gatherings, socioeconomic status (income and education), cigarette use, exposure to second-hand tobacco smoke, illicit drug use, household composition and crowding, type of housing, home use of air conditioning, personal vaccination history, vaccination history of children, and other health conditions (such as asthma, chronic lung disease, or diabetes). Patients 18 years or older with a reported case of pertussis were included if they experienced the first confirmed case in their household during 2003. No additional exclusion criteria were applied. We enrolled 2 controls per case, frequency matched by broad age group (≤35 or >35 years) and sex. We identified controls by pairing random 4-digit numbers with the 3-digit exchanges of telephone numbers of contacted cases. This method yielded numbers to cellular telephones, institutions, businesses, and residences. Controls were told how the telephone number was generated and asked whether an eligible person in their household or business was available. We made at least 3 different attempts to reach someone at different times of day and days of the week at all numbers, unless a number was clearly not working. The telephone interview included questions about personal, socioeconomic, and demographic characteristics and health conditions. We calculated response rates as completed interviews divided by eligible telephone numbers.

Data were exported using Microsoft Access (Microsoft, Redmond, Wash) and SAS statistical software, version 8.2 (SAS Institute Inc, Cary, NC) for analysis. Mantel-Haenszel–stratified univariate odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each exposure. We used unconditional multiple logistic regression to estimate adjusted ORs, forcing the model to include the 2 matching factors.

The Program Managers Committee of the Oregon Office of Disease Prevention and Epidemiology and the associate director for science of the Office of Workforce and Career Development at the Centers for Disease Control and Prevention reviewed the protocol before implementation. Both the committee and the director determined the investigation to be evaluation and control of a public health problem rather than human subjects research. Nevertheless, informed consent was obtained from all participants before interview.

RESULTS

OVERALL INCIDENCE AND PROPORTIONAL MORBIDITY

During 2003, Jackson County reported 135 confirmed pertussis cases compared with 0 to 3 cases per year from 1995 through 2001. Countywide incidence was 71 per 100 000 population, and statewide incidence was 12.5 per 100 000. Jackson County incidence was 695.1 per 100 000 infants, 190.3 among children aged 1 to 4 years, and 104.2 among children aged 5 to 9 years, 183.5 among those aged 10 to 17 years, and 38.6 among persons 18 years or older. Older children and teens aged 10 to 17 years accounted for 28% of all cases, and adults accounted for 39%. Five infants were hospitalized for pertussis in Jackson County in 2003 (192 hospitalized per 100 000 infants) compared with 18 in the remainder of the state (33 hospitalized per 100 000 infants). The state’s single death from pertussis was outside Jackson County. A total of 2658 close contacts (19.7 per case) were identified through case
investigation; 1050 (40%) of these were known to have received prescriptions for prophylactic antibiotics (erythromycin or azithromycin).

FOCAL OUTBREAKS AND ROUTES OF TRANSMISSION

In 2003, cases were reported in Jackson County from March through December, with notable peaks in May and late July through early August (Figure 1). We identified 2 groups of overlapping clusters of cases, both beginning in April. The first began with a cluster among an extended family, which spread to an elementary school classroom and a mail order supply company and eventually involved 20 cases.

The index case in the second group of overlapping clusters (Figure 2) was a 1-month-old infant living in a low-income apartment complex. Subsequently, 23 more cases were diagnosed during April and May among residents of the housing complex and their friends and relatives. These were linked to a cluster of cases among hotel housekeepers, 1 of whom babysat for the child with the index case. Several additional cases occurred in the household of another housekeeper and afterward in the elementary school of a child in this household. A second cluster was recognized in the elementary school classroom of a child with pertussis from the housing cluster of the index case.

In September, a new and apparently unrelated cluster of cases among inmates and deputies of the Jackson County jail was linked to methamphetamine users. When not incarcerated, these inmates lived in 3 adjacent “meth houses” across town from the housing complex cluster with approximately 20 other adults. Four additional adults among this group also had pertussis. Unexpectedly, the mother of the index case infant in the apartment complex cluster was recognized among these 4 adults. Having refused an offer of prophylaxis in the spring, she reported a prolonged cough in September. Although a nasopharyngeal culture result was negative, she had a confirmed pertussis case by virtue of clinical illness and an epidemiologic link to other laboratory-confirmed cases. Her diagnosis established a plausible route of transmission between springtime cases in the low-income apartment complex and summer and fall cases among jail inmates and methamphetamine users, and this enabled a total of 44 cases to be linked to this second group of epidemiologically linked clusters.

FACTORS ASSOCIATED WITH ADULT INFECTION

Among 53 adults with reported pertussis in Jackson County during 2003, the median age was 34 years (range, 18-55 years) and 32 (60%) were female; 28 (53%) had the first reported case in their household and were eligible for inclusion in the case-control study. Among these, 4 (14%) had laboratory-confirmed cases, 17 (61%) were female, and median age was 33 years (range, 18-55 years). We interviewed 20 (71%) of 28 eligible patients and 40 age- and sex-matched controls. The 40 controls were interviewed from 84 telephone numbers where an eligible person was clearly present (response rate, 48%). However, 40% of all randomly generated telephone numbers were unanswered after 3 or more tries or answered by a respondent who hung up before eligibility was determined.

Compared with controls (Table), after stratified analysis, patients were more likely to live with children aged 6 to 10 years (OR, 5.4; 95% CI, 1.3-22.1), less likely to report completion of college (OR, 0.03; 95% CI, 0.003-0.4), less likely to have an income of $25 000 or more per year (OR, 0.2; 95% CI, 0.1-0.7), and less likely to report having received all recommended childhood vaccinations (not necessarily limited to pertussis vaccines) (OR, 0.1; 95% CI, 0.01-1.0). In addition, they were more likely to smoke cigarettes (OR, 3.2; 95% CI, 1.0-10.1). Factors not significantly associated with illness included institutional residence, illicit drug or alcohol use, air conditioning in the home, having asthma or other chronic illness, number of housemates, household crowding (persons per bedroom), reported vaccination status of household children, number of household children aged 2 to 5 years and 11 to 18 years, estimated daily personal contacts, and work with children. In multivariate analyses, patients remained 6.4 times as likely (95% CI, 1.8-23.4) to live with children 6 to 10 years old and one tenth as likely (OR, 0.1; 95% CI, 0.003-0.9) to report having received all recommended childhood vaccinations (not restricted to pertussis-containing vaccines).
COMMENT

We investigated a community-wide pertussis outbreak, focusing on adult disease and tracing the progression of the outbreak across numerous distinct case clusters within the community. Several convergent lines of evidence argue that universal adolescent and adult pertussis booster vaccination offers the only effective means of preventing such events in the future. Most cases occurred among adolescents and adults, and although significantly fewer case patients than controls reported complete childhood vaccination, in our study most adult case patients (80%) reported having received a primary pertussis vaccination series. Current evidence indicates that B pertussis infection is many times higher than reported, meaning that most people with pertussis cannot be reached by a conventional, reactive “identify and prophylax” approach to interrupting transmission.7,8 This may be the reason that in our outbreak many new epidemiologically linked cases and clusters appeared despite aggressive treatment of reported cases and prophylaxis of contacts. Cases sometimes cluster in populations, such as the methamphetamine users in our outbreak, that public health nurses find difficult to reach. Such groups would likely be equally difficult to vaccinate if a targeted booster vaccination approach were to be attempted for control of future outbreaks. Achievement of significant herd immunity would reduce both the risk of introduction of disease into these hard-to-reach groups and secondary transmission to the broader community when such events occur.

Apart from insufficient childhood immunization in a few, we found no specific, modifiable risk factors for first-in-household infection among adult cases that would allow for targeted prevention efforts. For these reasons, we agree with the Advisory Committee on Immunization Practices’ recent recommendation of routine pertussis booster vaccination of adolescents and adults.20

Most cases in this outbreak occurred among adolescents and adults. Several clusters included infants and children and specific instances of bidirectional transmission among children, adolescents, and adults. Clusters occurred in congregate settings where outbreaks have previously been reported, such as the workplace and schools, and other perhaps predictable but previously unreported settings, such as among methamphetamine users and jail inmates and employees.15-17 The number and diversity of settings in which clusters occurred suggest widespread adult susceptibility and abundant disease transmission when a case is coincidentally introduced into a congregate setting.

Until adolescent and adult booster vaccination became available, early identification and antibiotic treatment of cases as well as isolation and prophylaxis of at-risk contacts were the only available methods of preventing secondary cases and interrupting outbreaks. Evidence from other studies that only a minority of pertussis cases are recognized suggests that this traditional approach has, at best, modest impact.7,8 In this outbreak, despite aggressive application of these conventional control methods, new cases and clusters continued to occur, often in congregate settings where successful antibiotic treatment and prophylaxis could be thwarted by cost, limited health care access, and chaotic or impoverished lifestyles (eg, jails, crowded housing, or communities of illicit drug users). Similar barriers hinder vaccination of exposed children. In addition, isolating exposed contacts in such settings is often impractical. Consequently, prolonged transmission within and between focal clusters persists.

Our case-control study attempted to identify specific characteristics of adults at greatest risk who might be targeted for prevention or control efforts, such as intensified contact tracing and treatment or booster vaccination. However, we identified only 2 significant, independent risk factors: having school-aged children in the household and incomplete childhood vaccination. Although we limited enrollment of cases to adults whose infection was thought to be primary within their household, we suspect that school-aged children in the home—many with immunity beginning to wane from earlier vaccination—might acquire subclinical cases of pertussis and transmit infection to household adults who lack natural immunity and have even less residual vaccine-induced protection than their children.21 Consistent with this scenario, one previous study14
found the presence of adolescents in a household to be associated with reported infection, another study22 found that primary cases were most frequent among children in household clusters, and a more recent study23 found that household composition, including the presence of children aged 6 to 11 years, was associated with pertussis in preschoolers. Insufficient immunity is the obvious explanation for the association between incomplete childhood vaccination and infection. However, 16 of 20 patients in our study had been fully immunized, substantiating the influence of waning immunity.24

Our investigation has several limitations. First, reported cases are not likely to be representative of all cases. Milder cases, sporadic cases, and those occurring in adults or other persons with a comorbid cough illness or limited access to care are probably underrepresented among reported cases. Second, ascertainment bias is a possible alternative explanation for observed associations in a case-control study. A child who has pertussis after an initially undetected primary adult case in a household might have the condition diagnosed more readily, leading to belated recognition of the antecedent adult case. Third, recall bias might have contributed to the observed association between case status and incomplete childhood vaccination. Finally, a low response rate (48%) threatens the interpretation of our case-control study of adult risks. A random digit–dialing approach permitted us to reach and interview controls through methods comparable to those used for cases (eg, home telephones, cellular telephones, businesses, and institutions such as jails and dormitories), perhaps at the cost of a more desirable response rate.

After approval by the Food and Drug Administration and recent demonstration of 92% vaccine efficacy among adults, booster vaccination of adolescents and adults has been recommended by the Advisory Committee on Immunization Practices.25 An economic analysis estimated that vaccination of adolescents might save $1.6 billion a year.26 Although our investigation suggests that adults and adolescents with incomplete or unrecorded childhood vaccination histories and those with school-aged children in the home might be ushered to the front of the booster vaccination line, prevention of future outbreaks will likely rely on universal periodic vaccination of adolescents and adults, with limited roles for more targeted approaches.

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Correspondence: Sean Schafer, MD, Oregon State Public Health, HIV/STD/TB Program, 800 Oregon St, Suite 1105, Portland, OR 97232 (sean.schafer@state.or.us).

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