Morbidity of Pertussis in Adolescents and Adults

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The effect of age on the clinical presentation of pertussis was assessed in 664 adolescent and adult cases. Complications were more frequent in adults than in adolescents (28% vs. 16%). Pneumonia occurred in 2% of patients <30 years old but in 5%–9% of older patients. Urinary incontinence occurred in 34% of women ⩾50 years old. Duration of cough, risk of sinusitis, and number of nights with disturbed sleep increased with smoking and asthma. The secondary attack rate in other household members ⩾12 years was 11%. Pertussis in secondary case patients was less severe than in index case patients but presented with classic symptoms. The main source of infection in adolescents was schoolmates or friends; in adults it was workplace or their children. Teachers and health care workers had a greater risk of pertussis than did the general population. The burden of disease appears to increase with age, with smoking, and with asthma.

Pertussis was long considered a childhood illness; however, in the last 2 decades, there has been increasing evidence that pertussis affects not only children but adolescents and adults [1–14]. Although the morbidity of pertussis and the frequency of complications are well-known in children, there are fewer data about the changes that occur with increasing age. The 2 largest published pertussis adult case series included 64 and 79 persons ⩾18 years old (mean, 31 and 36 years, respectively), which were insufficient to compare the morbidity by age [6, 7]. This study documents the morbidity of pertussis in 280 adolescent (12–17 years old) and 384 adult (⩾18 years old) case patients and the susceptibility of their adolescent and adult household contacts.

Methods

Setting and outbreak. In Quebec, the second largest Canadian province (7 million people), universal vaccination against pertussis was introduced in 1946. Thereafter, the number of cases steadily decreased and stabilized between 1970 and 1989, when a mean of 318 cases was reported annually. Since 1990, there has been a resurgence of pertussis, with numerous epidemic years (figure 1). During 1998, 4881 cases were reported, the highest number since 1950, and 26% occurred among adolescents or adults. These cases were either culture-positive or met the Canadian surveillance case definition for pertussis: cough ⩾2 weeks with ⩾1 pertussis-related symptom (paroxysms, posttussive vomiting, posttussive apnea, or whoop) and no other apparent cause [15].

Case patients were recruited in 5 of the 18 public heath units where 68% (3302) of all reported cases occurred. In these regions, among the 718 eligible patients ⩾12 years old and whose disease began between 1 July and 30 December 1998, we were unable to contact 51 patients, despite multiple attempts, and 3 refused to participate. We thus evaluated 280 adolescent and 384 adult cases.

Trained nurses of the public health units where the cases were reported completed a standardized questionnaire, first by using data collected as part of the routine investigation for reportable disease immediately after the case was reported. These data included age, sex, immunization history, date of onset of cough, presence of fever, coryza, other classic pertussis symptoms (paroxysmal cough, posttussive vomiting, posttussive apnea, or whoop), medication, hospital admission, and the use of chemoprophylaxis by household contacts. Nurses also called all patients in February, March, and April 1999 to collect more data on immunization history, total duration of cough, duration of paroxysmal cough, other clinical symptoms (pharyngeal pain, fatigue, or sweating episode), complications, previous health conditions, occupation, smoking history, number of medical visits in clinic or at the emergency room, laboratory and radiologic investigations, medication, hospitalization and its duration, number of workdays lost by patients or their relatives, the presence of other case patients in the family and their symptoms, and the use of chemoprophylaxis by household contacts. Medical records were not consulted to verify this information. Information on patient treatment and house-

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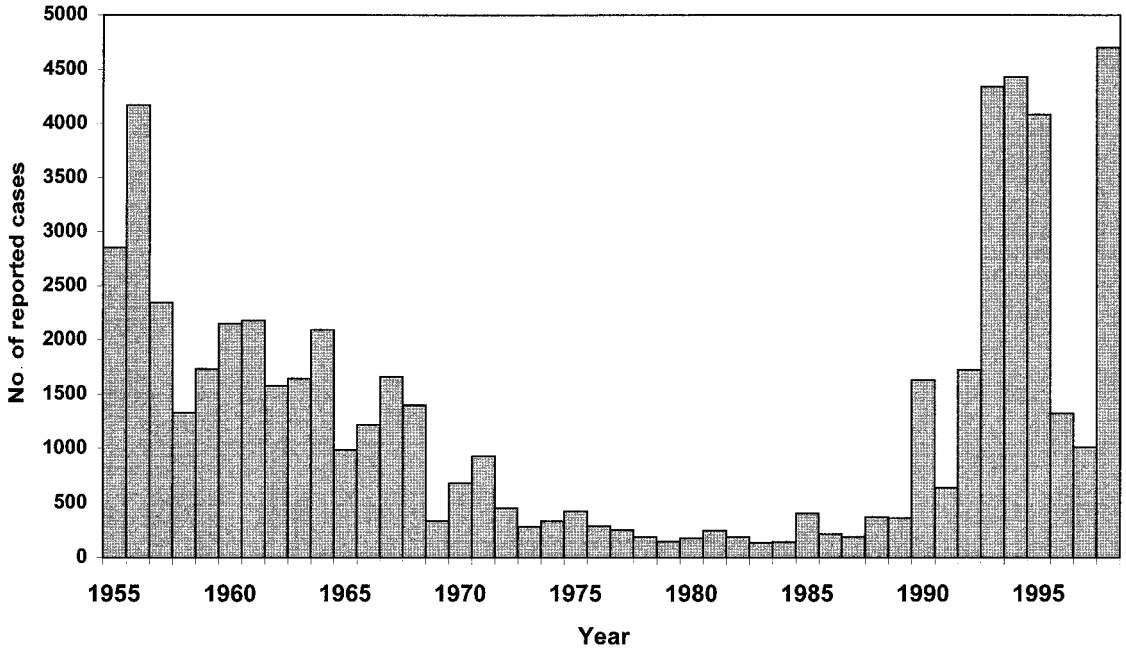

Figure 1. No. of pertussis cases reported in Quebec between 1955 and 1998

hold prophylaxis was augmented when necessary by information from the patients' pharmacists. Patients were asked to rate the severity of their disease on a scale from 1 (very mild) to 10 (most severe). To maintain confidentiality, only denominalized data were sent to the research team.

Analysis. Proportions were compared by Pearson's χ^2 or Fisher's exact tests. The linear trend for age was assessed by the Mantel-Haenszel χ^2 test. To evaluate the secondary attack rate (SAR) in the family, we only used households where the reported case was also the primary case. The primary case patient in the household was defined as the person whose cough developed first. Whereas there could be ⩾1 primary case patient in a household, because the date of onset of disease was based on recall and might involve a greater bias than only the order of the onset of cough, we assumed there was only 1 primary case patient per household. We then excluded the primary case patient and calculated the SAR in the other household members. The case definition for a secondary case was the presence of a cough for ⩾2 weeks.

Results

Females represented 55% of adolescent cases and 70% of adult cases. The average ages of adolescents and adults were 14 and 37 years, respectively. Cigarette smoking was reported by 31% of patients ⩾15 years old, a proportion similar to that in the population (35%; Quebec Ministry of Health and Social Services). Among the 280 adolescents, all but 5 (2%) were students. Among the 384 adults, 86 (22%) were homemakers, 66 (17%) were teachers, 32 (8%) were health care workers, 28 (7%) were students, and 172 (45%) had other jobs. Because education and health care workers represent 4.6% and 5%, respectively, of the adult population of the Province of Quebec, the risk of pertussis for teachers was about 4 times greater than that for the general adult population ($P < .001$); for health care workers it was 1.7 times greater ($P = .03$).

The proportion of patients who had written proof of ⩾4 doses of pertussis vaccine decreased with age; 78% of adolescents had a written record, in contrast with 15% of adults ($P < .001$; table 1). Among adults <50 years old, most reported having been vaccinated, but few had written proof. The proportion of patients with a history of a previous episode of pertussis increased from <1% in adolescents to 18% in those ⩾40 years old ($P < .001$).

Clinical presentation. Overall, 30% of cases were confirmed by culture (table 1). Because clinical findings in cases with and without a positive culture of *Bordetella pertussis* were similar, the results were aggregated. The mean duration of cough was 10 weeks in adolescents and 12 weeks in adults. Overall, 97% of patients coughed ⩾3 weeks, and 52% coughed ⩾9 weeks. A cough for >9 weeks was observed in 47% of adolescents and 55% of adults. Paroxysms (present in 99% of cases) persisted for ⩾3 weeks in 73%. By decreasing order of frequency, the other principal symptoms were posttussive apnea (87%), whoop (69%), and posttussive vomiting (65%). The proportion of cases by number of classic pertussis symptoms was not modified by age; 6% of adolescents and 5% of adults had only 1 principal symptom, and ⩾4 classic pertussis symptoms were present in 50% and 43% of adolescents and adults, respectively. The other

Table 1. Percentage of cases, by vaccination status, history of prior pertussis, symptoms, complications, and investigations.

Characteristic	Age group, years					Total (n = 664)
	12–17 (n = 280)	18–29 (n = 111)	30–39 (n = 129)	40–49 (n = 91)	⩾50 (n = 53)	
Vaccinated						
With written proof of ⩾4 doses	78	32	12	7	2	42[a]
Without written proof	19	49	55	44	26	35
History of prior pertussis	0.4	4.5	8.5	15.4	22.6	6.5[a]
Culture positive	34	22	29	30	38	30
Cough						
Any cough for ⩾3 weeks	97	96	98	99	96	97
Paroxysmal cough for ⩾3 weeks	73	63	80	73	74	73
Classic pertussis symptoms						
Paroxysms	100	100	100	100	94	99
Posttussive apnea	86	87	85	92	85	87
Posttussive vomiting	71	58	64	54	70	65
Whoop	67	68	69	74	74	69
⩾3 of 4 prior symptoms	81	76	80	85	81	80
Sweating episode	24	30	39	46	40	32[a]
Complications						
Sinusitis	11	14	16	13	17	13
Pneumonia	2	2	5	5	9	4[a]
Urinary incontinence in women	0	3	2	13	34	6[a]
Investigations						
Nasopharyngeal aspirate	52	44	37	44	45	46
Chest radiograph	24	23	36	37	60	31[a]
Sinus radiograph	11	12	15	16	23	14[a]

[a] χ^2 trend, $P < .05$.

symptoms were rhinorrhea (49%), pharyngitis (46%), sweating attack (32%), fever (31%), and fatigue (21%). Apart from the sweating episodes, which increased with age (χ^2 trend, 18.3; $P < .001$), the frequency of symptoms and the duration of cough were not modified significantly by age (table 1).

Complications. Reported complications were sinusitis (13%), otitis media (4%), urinary incontinence (4%), pneumonia (4%), weight loss (3%), rib fracture (2%), and fainting (2%) (table 1). The proportion of cases with ⩾1 complication was greater among adults than among adolescents (28% vs. 16%, $P < .001$). Sinusitis increased slightly with age—11% in adolescents and 13%–17% in adults ($P = .16$). Pneumonia occurred in 2% of patients <30 years old but in 5%–9% of adults ⩾30 years old ($P = .004$). Except for 1 patient, urinary incontinence occurred only in women and increased significantly with age, reaching 34% in women ⩾50 years old ($P < .001$). Rib fracture was reported exclusively by women—1% in adolescents and 4% in adults. Fainting occurred only in adults. One 36-year-old woman reported a convulsion. The proportion of patients with otitis media (4%) or weight loss (3%) was similar in every age group.

Medical visits. The mean number of medical visits to establish the diagnosis and the mean total visits for illness did not differ in adolescents and adults (1.6 vs. 1.7 and 2.3 vs. 2.5, respectively). A diagnosis was established at the first visit in 58% of cases, at the second in 27%, at the third in 10%, and at visit 4 or later in 5%. Of the medical visits, 89% were at a clinic and 11% at an emergency room. These proportions were not affected by age.

Investigations. Nasopharyngeal specimens were collected from 306 (46%) of patients (table 1); 202 (66%) were positive for *B. pertussis.* A chest radiograph was obtained for 31% of patients; 27% had only 1 chest radiograph, 4% had 2, and 0.6% had 3. The proportion of patients who had chest radiographs increased significantly with age and was twice as frequent in those ⩾50 years old than in younger patients (table 1). The proportion of patients who had sinus radiographs also increased significantly with age. A single sinus radiograph was obtained in 13% of cases; 1% had 2.

Hospitalization. The mean proportions of hospitalized adolescent and adult patients were 1% and 2%, respectively. Among adults ⩾50 years old, 6% were hospitalized, with a mean duration of stay of 17 days, versus a mean of 3 days for patients <50 years old ($P = .1$).

Source of infection. The source of infection was unknown by 31% of patients, and this proportion was slightly higher in patients <30 years old (34% vs. 26%). Adolescents reported that they acquired pertussis from schoolmates (39%), friends (12%), and household contacts (9%). Adults reported that they acquired pertussis most frequently from household contacts (32%). Household contacts and relatives were the source of infection for 41% of patients ⩾40 years old (table 2). The

Table 2. Source of infection, by age group.

Age group, years	No. of patients	Source of infection, %					
		Household contact	Relatives	Friends	Work or school	Other	Unknown sources
12–17	280	9	5	12	39	2	34
18–29	111	25	7	5	25	2	35
30–39	129	44	4	5	17	5	26
40–49	91	33	8	2	22	8	27
⩾50	53	13	28	6	25	2	26
Total	664	22	7	8	29	3	31

sources of infection for adult patients who were the primary case patient in their household were as follows: unknown sources, 42%; workplace, 32%; relatives, 14%; friends, 6%; and other, 6%. For adolescents the proportions were as follows: school, 43%; unknown, 36%; friends, 14%; relatives, 5%; and other, 2%.

Treatments. No medication was given to 3% of patients, 33% received 1, 31% received 2, 17% received 3, 9% received 4, 4% received 5, and 3% received 6–9 different medications. The mean number of medications used by patients was 2 and was similar among age groups. Antibiotics were given to 602 (91%) patients; 76% received 1, 13% received 2, and 1.4% received ⩾3 antibiotics. Half the antibiotic treatments or prophylaxis were with the newer macrolides, with a predominance of clarithromycin. Erythromycin, clarithromycin, and azithromycin were given to 42%, 42%, and 8% of the patients, respectively. Bronchodilators were prescribed for 27% of the patients. A β_2-adrenergic aerosol was prescribed for 17%, and a corticosteroid aerosol for 21%. Only 2% used an oral corticosteroid.

Previous medical conditions. Cardiac disease was reported by 7 patients, 6 of whom were ⩾50 years old. Asthma was present before pertussis in 24% and 13% of adolescents and adults, respectively ($P < .001$). The proportion of adolescents with asthma in Canada is estimated to be ~12% (Childhood Asthma in Sentinel Health Units: Findings of the Student Lung Health Survey, 1995–1996; Health Canada, National Population Health Survey [available at http://www.hc-sc.gc.ca/hpb/lcdc/publicat/asthma/index.html]). Chronic obstructive pulmonary disease (COPD) affected only 1% of the patients, all of whom were adults >40 years old. Among the 139 patients with previous pulmonary disease, 52% already were using a bronchodilatator aerosol, and 93% had to increase their medication because of pertussis. One patient reported an exacerbation of his cardiac problem but did not increase his medication.

Severity. Patients ranked the severity of their disease from 1 (very mild) to 10 (the most severe disease). The mean rating was 6.9, but 94 (14%) rated it 10, and 44% rated it ⩾8. The ratings were similar in the different age groups.

Clinical presentation by smokers and persons with asthma. The number of symptoms, their duration, the risk of complication and hospitalization, the mean number of nights disturbed by pertussis, and the assessment of the severity of disease by patients was not modified by sex or by a positive nasopharyngeal culture for *B. pertussis.* However, smoking or asthma increased the mean duration of paroxysmal cough (smoking, 5 vs. 4 weeks, $P = .006$; asthma, 5 vs. 4 weeks, $P = .004$), risk of sinusitis (smoking, 19% vs. 11%, $P = .008$; asthma, 16% vs. 12%, $P = .4$), and the mean number of nights disturbed by pertussis (smoking, 25 vs. 20 nights, $P = .04$; asthma, 26 vs. 20 nights, $P = .03$). However, the assessment of the severity of disease did not vary with smoking or asthma (mean, 7 in all groups).

Social impact. The social impact of pertussis in terms of loss of workdays and nights of sleep and workdays lost by relatives was not modified significantly by age. Adolescents lost a mean of 5 school days; 22% lost no school days, 53% lost 1–5 days, 17% lost 6–10 days, and 9% lost ⩾11 days. In adults, the mean number of workdays lost due to pertussis was 7; 33% lost no work, 36% lost 1–5 days, 13% lost 6–10 days, 7% lost 11–15 days, and 12% lost ⩾16 days. For 10% of cases, relatives of the patients lost 1–5 days of work. It took 1–9 days to resume regular activities in 18% of cases and ⩾10 days in 24%. The mean number of nights disturbed by pertussis was 14: 1–7 nights, 25%; 8–14 nights, 19%; 15–21 nights, 18%; 22–28 nights, 4%; 29–59 nights, 18%; and ⩾60 nights, 9%.

Secondary cases. The SAR in the 482 households where the index (or reported) case was also the primary case was 15%. The SAR was not modified by the presence of a positive culture in the index case. SARs were similar in adolescents and adults (12% vs. 11%) but were higher in children 0–4 (29%) and 5–11 years (25%). Among the 7 infants <1 year old, 3 (43%) acquired pertussis. Among adolescent and adult secondary case patients, 85% had paroxysmal cough, 67% had posttussive apnea, 31% had posttussive vomiting, 35% had whoop, and 56% had cough lasting ⩾5 weeks. Adolescent patients were more likely to have all 4 classic pertussis symptoms than were adult patients (32% vs. 17%, $P = .2$). Posttussive vomiting declined with age, from 42% in adolescents to 17% in adults ⩾50 years old (χ^2 trend, 2.4, $P = .12$). When secondary case patients 12–29 years old were compared with those ⩾30 years old, younger patients were more likely to consult a physician (76% vs. 69%, $P = .5$), to be diagnosed by a physician (62% vs. 42%, $P = .07$), and to be reported as a case (49% vs. 12%, $P = .001$).

Disease in secondary case patients was milder than in index case patients of these 482 households. All symptoms were significantly less frequent in secondary case patients than in index

case patients. Posttussive vomiting and whoop were about half as likely to occur in secondary case patients as in index case patients (31% vs. 68% and 35% vs. 69%). Paroxysmal cough and posttussive apnea were also less frequent but remained common (85% and 67%, respectively). The duration of cough was almost half as short in secondary case patients as in index case patients (6 vs. 10 weeks). Only 19% of secondary case patients had all 4 pertussis symptoms, compared with 47% of index case patients ($P < .001$). The SARs in adults were similar by sex, in contrast with adult index case patients, who were predominantly female. The average number of medical visits for index case patients was greater than that for secondary case patients (2.5 vs. 1.1, $P < .001$).

Use of prophylaxis. The proportion of households where prophylaxis was given to prevent secondary spread increased with the number of household members—20% of households with 2 members, 36% with 3, 46% with 4, 50% with 5, 58% with 6, and 82% with ≥ 7 (χ^2 trend, 34.2, $P < .001$). Erythromycin was the antibiotic used most frequently (55%), followed by clarithromycin (36%) and azythromycin (9%).

Discussion

Our adolescent and adult cases were identified by the passive reporting system. Because the diagnosis of pertussis is poor in children and is not expected to be better in adolescents and adults, only patients who presented with classic symptoms were likely to be diagnosed by clinicians and only a fraction of them reported [16]. Our high proportion of culture-positive adult cases likely has a reporting bias because most culture-positive cases are reported, whereas many nonconfirmed cases are not. Thus, our case series probably represents the most severe part of the clinical spectrum. Our analysis of the secondary cases may be more representative of the clinical picture of pertussis in adolescents and adults because these represent an active surveillance process. Secondary case patients had milder disease than did the index case patients, but most had the classic symptomatology. It is possible that our secondary household case patients still represent a more severe disease than do the average case patients infected during community contacts, because of the intensity of their contact with the primary case patient. Our case definition for secondary cases, which required a cough for ≥ 2 weeks, also excluded the mild cases that are found in prospective studies [17–19]. Despite these caveats, our case series and the secondary cases likely represent the most clinically significant cases. Moreover, the number of subjects in each age group was large enough to evaluate the effect of age on clinical manifestations of pertussis, something that was not possible in previously published studies on adults.

In the adult and adolescent cases evaluated, the proportion with classic symptoms of pertussis (paroxysm, whoop, posttussive apnea, and posttussive vomiting) was greater than in children [20] but did not change with age. However, age increased the risk of pneumonia, fainting, urinary incontinence, and hospitalization. This is an important finding because, although in childhood pneumonia decreases with age [21], this study demonstrates that it rises again in adulthood. Pertussis was very disruptive and distressing: Nearly half the case patients rated the severity of their disease as 8 on a 0–10 scale, they lost a median of 14–21 nights of sleep, and 3% of adult case patients fainted because of their cough. The main risk factors for acquiring pertussis were sex (females represented 55% of adolescent and 70% of adult case patients) and working in education or in the health care system. However, it is possible that part of the increased risk among these 2 groups is due to their enhanced awareness of pertussis, which they shared with their consulting physicians. Smoking and asthma increased the severity of disease. Because there were few case patients ≥ 65 years old or with prior history of cardiac disease or COPD, it was not possible to assess the effect of these factors on the severity or complications of pertussis. However, when one considers that 2% of adults choked and/or fainted, it is possible that pertussis could have serious implications for those with severe cardiac or pulmonary disease.

The resources spent for adolescent and adult pertussis do not differ greatly from those used for children. The mean number of medical visits to establish the diagnosis was comparable to that for children [16]. It is likely that the high incidence of pertussis in Quebec between 1990 and 1998 has enhanced the diagnostic skills of physicians, and the numerous publications about pertussis in adolescents and adults may also have increased their awareness. Investigation was a little more extensive in older adults than in younger case patients. The higher proportion of case patients ≥ 50 years old who had a chest radiograph is likely due to the desire of clinicians to eliminate serious conditions, such as lung cancer, in their investigation of this unusual cough episode. The shift from erythromycin to new macrolides like clarithromycin and azythromycin, which were used to treat half the case patients and for prophylaxis in half the contacts, has a major impact on the financial burden of this disease. The new antibiotics cause less gastrointestinal intolerance than erythromycin but are ~3 times more expensive. While preliminary studies suggest that clarithromycin and azythromycin may be effective for the treatment of pertussis [22], there are no data on the effectiveness of these antibiotics for prevention.

Nearly 70% of case patients reported the source of their infection. We do not know the validity of this information, but it is likely to be more reliable when it is for a household contact or a close friend than when it is more vague, such as "school." The frequency of different sources of infection is a function of the number and distribution in the population of infective cases, of vulnerable subjects, and the mixing pattern of both groups. Adolescents were infected mainly by people in their age group (51%), which suggests that prevention of pertussis in adolescents should target children before they enter high schools. In adults, pertussis was acquired mostly from household contacts.

This source was reported by 44% of case patients 30–39 years old and probably reflects transmission from younger children, with the consequence that the reduction of incidence in children is likely to decrease the burden in adults.

In Canada, pertussis vaccination was implemented during the mid-1940s, and most people born since then likely were vaccinated. Most adolescents had written proof of vaccination, but few adults could provide documentation even if they claimed to be vaccinated. Immunity against the disease in both adolescents and adults cannot be measured, because of the lack of a reliable serologic marker of protection. Because there is no herd immunity within a household, the SAR provides a good estimate of the vulnerability of its members. The SARs were strikingly similar in adolescents (12%) and adults (11%). This is the opposite of what would be expected with a waning vaccine immunity [23, 24], which normally would lead to an increasing proportion of vulnerable subjects with age. However it is consistent with an endemic transmission that decreases the proportion of susceptible subjects with age and with a long-lasting natural immunity. Natural immunity does not appear to last for life, as is evidenced by the fact that 18% of adult case patients had a history of prior pertussis. This is lower than the 34% reported in Germany by Postels-Multani et al. [6] and Schmitt-Grohé et al. [7]. The discrepancy may be explained by the lower level of pertussis vaccination in Germany than in Canada, which allows a greater proportion of adults to have sustained a prior episode of pertussis. Among adults who had no memory of prior pertussis, 12% developed the disease after household exposure. Thus, 88% were protected. Because this protection is unlikely to come from vaccination, it is probable that they in fact sustained an unidentified episode of pertussis. It should be concluded that a negative history of prior pertussis has low validity (negative predictive value) in our context.

The availability of an adolescent and adult formulation of the acellular pertussis vaccines is promising. It is safe and immunogenic, although efficacy has not yet been demonstrated. Adolescent immunization programs are logistically feasible, whereas adult programs present questions about both feasibility and acceptability (cost). In this study, the burden of pertussis appeared to increase with age, which may point to a need for programs that provide lifelong prevention of pertussis. Assessment of the implications of potentially postponing cases of pertussis into adulthood should be part of the planning of adolescent pertussis immunization programs.

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