The Changing Age and Seasonal Profile of Pertussis in Canada

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During the postvaccine era in Canada, most cases of pertussis have been reported in children <5 years of age, with the highest incidence, morbidity, and mortality in infants <1 year old. Population-based data, with very high laboratory confirmation rates and hospital separation and mortality statistics, chronicle the changing age and seasonal profile associated with pertussis over recent successive outbreaks in British Columbia, Canada. A large outbreak during 2000 highlights 2 important changes to the postvaccine profile. For the first time in Canada, the incidence of pertussis among preteens and teens surpassed that of all other age groups. At the same time, a decreasing incidence of pertussis among infants and preschool children highlights reduced susceptibility in the very young. Recent changes in the childhood immunization program (including introduction of an acellular pertussis vaccine), waning immunity, and changes in laboratory methods are considered in explaining these 2 simultaneous but divergent trends in the pertussis profile.

As elsewhere in the world, pertussis activity in Canada demonstrates cyclic peaks every 2–5 years [1, 2]. Although these cycles are asynchronous between provinces, activity generally peaks during the late summer or early autumn. During the postvaccine era, pertussis has primarily been a disease of childhood, with the highest incidence among infants <1 year of age and then among preschool children [3, 4]. Routine childhood immunization programs across Canada have targeted pertussis since the early 1940s [5]. Vaccine doses for the primary series have been given at 2, 4, and 6 months of age, with booster doses at 18 months and again at 4–6 years of age [5, 6]. Adsorbed products replaced older fluid versions in a staggered fashion across Canada during the early 1980s. In 1997–1998, all provinces switched to a 5-component acellular pertussis vaccine for the primary series and first and second booster doses. Controlled trials with infants provide efficacy estimates of 85% for this acellular pertussis vaccine [7]. The whole-cell pertussis vaccine used previously in Canada demonstrated lower efficacy [8–10]. An acellular pertussis vaccine has been licensed recently for use in persons 12–54 years of age in Canada, but its routine inclusion as a booster dose in this age group has thus far been restricted to 1 province (Newfoundland) [3].

Localized and large community outbreaks of pertussis involving adolescents and adults have been described recently, and there is increasing appreciation for pertussis as an unrecognized but important cause of prolonged cough illness in older age groups. Sero-epidemiologic studies and clinical surveys have supported this growing perception [3, 11–27]. A recent large outbreak in British Columbia (BC), Canada, adds further evidence and highlights 2 important changes to the pertussis profile. BC is the western-most province of Canada and has a population of 4.1 million, of whom 12% are <10 years of age and 75% are >20 years of age. Population-based data with very high laboratory confirmation rates and hospital separation and mortality statistics chronicle the changing patient age and seasonal profile associated with pertussis infection over successive outbreaks in BC.

Methods

In BC, pertussis is a notifiable disease to the BC Centre for Disease Control (BCCDC). Cases are reported electronically as confirmed cases (determined by laboratory testing or by an epidemiologic link to a confirmed case) or as clinical cases (>2 weeks of paroxysmal cough, cough ending in vomiting, or apnea or inspiratory whoop for which there is no other known cause). Testing for laboratory confirmation of pertussis is done in 3 laboratories in BC, with BCCDC Laboratory Services responsible for the vast majority of these tests. Specimens submitted to BCCDC Laboratory Services are per-nasal swabs transported in Amies Charcoal Transport medium (Becton Dickinson). Swab samples are cultured at BCCDC on charcoal medium with 20 μg/mL cefalexin, and isolates are confirmed as Bordetella pertussis or B. parapertussis by use of fluorescent antibody conjugates (Difco Laboratories).

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tinely added to the laboratory assessment of all specimens submitted for pertussis testing to BCCDC Laboratory Services. After culturing, swabs are eluted in double-distilled water, and the eluate is lysed using Instagene Matrix (BioRad). The PCR test for *B. pertussis* is carried out on the lysate, using primers described by Glare et al. [28]. The 153-bp pertussis PCR product is detected using standard gel electrophoresis methods and staining with ethidium bromide. PCR has been accepted nationally in Canada as evidence of laboratory confirmation of pertussis since May 2000.

All pertussis reports to the BCCDC between 1981 and 2000 were compiled and analyzed according to incidence by age, sex, and seasonal distribution. The 3 most recent outbreaks during the 1990s were specifically compared. Specimen test results from BCCDC Laboratory Services were compared during successive outbreaks for patient age distribution and positive findings. Hospital separation and mortality statistics were also compared over these successive outbreaks, using ICD-9 codes 330 and 339 for pertussis.

**Results**

There was a gradual resurgence in reported pertussis activity in BC throughout the 1990s, including notable increases in the size of successive peaks. The most substantial outbreak was observed in 2000 (figure 1). Of pertussis reports overall in 2000, 51% of cases were among females, but the patients’ sex varied significantly with age \((P < .01)\); for example, 66% of cases in the 20–44-year-old age group were among women.

The number of requests for pertussis testing was similar in 1993 and 1996 but increased substantially \((\geq 4\text{fold})\) during 2000. During 2000, there were 1811 pertussis notifications to BCCDC, of which 1549 (85.5%) were laboratory-confirmed cases (BCCDC Laboratory Services provided 94% of these confirmations). Of the 1456 confirmations of pertussis by BCCDC Laboratory Services, 778 were determined to be positive by PCR alone, 68 by culture alone, and 610 by both culture and PCR. The overall proportion of positive tests remained constant at 10%–15% during each of these outbreaks; the proportion of specimens positive by culture varied from 7% in 2000 to 12% in 1996. In 2000, the proportion of specimens positive by PCR was double that which were positive by culture; this ratio was constant across all age groups.

There was a shift in patient age distribution for specimens submitted for pertussis testing to BCCDC Laboratory Services. Preteens and teens aged 10–14 years represented a larger proportion of all requests for pertussis testing in 2000, increasing from 12% in 1993 and 1996 to 20% in 2000. Conversely, the proportion of specimens decreased between 1993 and 2000 from 19% to 6% for infants and from 29% to 16% for preschool children. Although the proportion of specimens from 10–14-year-old children who tested positive by culture was comparable across outbreaks in 1993, 1996, and 2000 (9%, 16%, and 12%, respectively), it decreased in infants (11%, 19%, and 4%, respectively) and in preschool children (11%, 11%, and 2%, respectively). PCR results were positive for 25% of specimens submitted for 10–14-year-old children during 2000; this figure is nearly 3-fold higher than the proportion positive among infants (10%). The proportion of tests positive by culture for 10–14-year-old children (12%) was also 3-fold higher than that for infants (4%).

The incidence and proportionate age distribution of pertussis cases during successive outbreaks in BC has changed (figure 2). The incidence in children aged 10–14 years, as well as the proportion they comprise of all cases, increased across successive outbreaks. In contrast, the proportion of all cases occurring in infants (<1 year old) or preschool children (1–4 years old) has decreased despite the persistent high incidence in infants overall. The most dramatic changes were observed between the outbreaks of 1996 and 2000: the proportion of cases in preteens or teens increased from 12% to 34%, whereas the proportion among preschool children and infants decreased from 24% to 8% and from 12% to 5%, respectively.

In 2000, for the first time, 10–14-year-old children not only represented a larger proportion of all reports (34%) than did infants or preschool children (13%), but they also experienced the

![Figure 1](image-url)  
**Figure 1.** Annual incidence of pertussis notifications, by age group, in British Columbia, Canada, 1981–2000
highest incidence. Although previous patterns of pertussis incidence by age have shown the highest rates to be among infants, with a gradual decrease with increasing age, the most recent outbreak in 2000 has altered this pattern (figure 2A). At present, rates for infants (197/100,000) still exceed those for preschool children, but the highest incidence now appears in preteens and teens (230/100,000). This is the first time this age effect has been observed in nearly 2 decades of pertussis surveillance in BC.

Although a high pertussis rate persists among infants overall, an age effect exists within this category. The rate of pertussis per 100,000 live births among infants 6–12 months of age decreased by 35% during the 2000 outbreak (38 cases/100,000), compared with 1996 or 1993 (52 and 58 cases/100,000, respectively), but it increased by the same number of cases among infants 3–5 months of age (53, 38, and 34 cases/100,000 during 2000, 1996, and 1993, respectively). The rate among infants <3 months of age was 2-fold higher than that among older infants during outbreaks in 2000, 1996, and 1993 (101, 134, and 69 cases/100,000, respectively).

The greatest increase in the incidence of pertussis during 2000 was among those ≥8 years of age (figure 3), in whom a >2-fold increase was observed relative to 1996. Peak incidence (>300/100,000) occurred among those 9–11 years of age and dropped rapidly after that age (figure 3). The shift in age distribution is also reflected in an increase in the median age of those reported to have pertussis in BC: median age increased from 5 years in 1993 to 6 years in 1996 to 11 years during the outbreak of 2000.

Despite a more substantial outbreak of pertussis during 2000, the overall rate of related hospitalization was half that observed during each of the 3 previous outbreaks in the 1990s (2 vs. 4/100,000). Infant hospitalization rates dropped by nearly half during the 2000 outbreak, compared with 1990, 1993, and 1996.

Figure 2. Incidence (A) and proportion (B) of pertussis notifications, by age group, during outbreak years 1990, 1993, 1996, and 2000, in British Columbia, Canada.
Hospitalization rates for preschool children dropped to one-quarter of those previously witnessed (4/100,000 vs. 15, 16, and 17/100,000, respectively). Although hospitalization rates in older groups remained low, relative increases were seen. Persons ≥10 years of age represented 2% of all hospitalizations in 1996, but this increased to 14% in 2000. In those ≥20 years of age, the rate of hospitalization per 100,000 increased from 0.04 in 1990 and 1993 to 0.07 in 1996 and 0.23 in 2000.

There were 2 deaths due to pertussis during the 1996 outbreak (an infant and a 3-year-old child). There were no deaths due to pertussis during the 2000 outbreak.

The shift in age distribution has also been accompanied by a change in the seasonality of reported pertussis cases (figure 4). In the past 10 years in BC, during outbreak and nonoutbreak periods, pertussis reports began increasing in July, peaked between the end of August and November, and substantially decreased by January. During the outbreak of 2000, however, pertussis reports began to increase in March, peaked in June, dropped markedly in July, and were much lower by October (figure 4). This profile reflects the predominance of pertussis activity in preteens and teens. Pertussis in infants and preschool children continued to demonstrate typical seasonality, with rates peaking in August and September.

Discussion

In the prevaccine era, the peak incidence of pertussis was in children 1–5 years of age. Less than 20% of cases were in infants, and almost all children had pertussis by 12 years of age [2, 22]. In the postvaccine era, there was a decline in overall incidence, but epidemics continued, and peak incidence switched to infants <1 year of age, followed by preschool children. The proportion of cases occurring in adolescents and young adults increased [2, 3, 11–27]. Two new, simultaneous but divergent trends have emerged recently in the postvaccine profile of pertussis in Canada. During the outbreak of 2000 in BC, the peak incidence of pertussis was in preteens and teens, highlighting greater susceptibility in older age groups. At the same time, the incidence in infants and preschool children decreased, highlighting reduced susceptibility in the very young.

The 2000 outbreak in BC is particularly noteworthy, not only because of its intensity and altered profile but also because of the very high proportion of reports that were confirmed by culture or PCR. Other investigations documenting intense pertussis activity in older age groups relied largely on serologic identification. Per-
Pertussis in older age groups is easily missed because its milder presentation generally places it below the threshold of clinical detection. Prolonged cough, which may be the only symptom, may eventually prompt a clinical visit, but by then the organism may no longer be detectable by standard culture methods. Infant disease is more readily identified, investigated, and reported because its progression is readily characteristic and severe [2, 4, 5].

Apart from the introduction of PCR, there has been no change in the detection/reporting system for pertussis that could explain the differential changes in incidence or age distribution. Similar trends were found by culture or PCR. The proportion of positive tests in 10–14-year-old children was 3 times that of infants during the outbreak of 2000, whether confirmation was by culture or PCR. Although the rate of positive culture results among young children in 2000 dropped, compared with the rate in earlier outbreaks, the rate among preteens and teens was maintained. PCR increased the rate of positive ascertainment across all age groups, but the greatest proportion of positive tests by either method (culture or PCR) was in preteens and teens. This argues against large-scale indiscriminate testing of older age groups or the introduction of PCR into routine testing as the sole reason for the shift in age profile to older groups. Nevertheless, part of the increased reported incidence is certainly due to the diagnostic improvement after the introduction of PCR. In fact, PCR may reveal a more complete picture of pertussis by identifying cases that were otherwise undetectable by standard culture, including cases that are milder or partially treated [2].

Changes in the seasonal profile of pertussis during the outbreak in 2000 were driven by the predominance of activity in older age groups. The peak in June may reflect differences in social interaction and the greater importance of and opportunity for mixing during the academic year for older children, compared with infants and preschool children. The typical profile of pertussis in BC of peak August and September activity was maintained in the very young. Because this seasonal profile is based only upon 1 outbreak, it is unclear if this will become a permanent feature of the pertussis epidemiology affecting school-aged children and adolescents.

Protection from pertussis vaccination wanes with time [4]. This may explain increased pertussis cases among preteens and teens during the post-vaccine era. However, it does not explain the increasing rates among these same age groups across successive outbreaks in BC or the steady decline in incidence beginning at 12 years of age during the outbreak of 2000. With waning immunity, one would expect incidence rates to increase with longer delay following the last dose.

Although greater detection (i.e., through use of PCR) and awareness may partially explain increases in pertussis activity among adolescents, other factors should also be considered. Pertussis incidence rose dramatically in BC in the early 1990s, particularly among infants and preschool children, and this increase has been sustained. A similar trend has been noted elsewhere in Canada. It is compelling to observe from the BC outbreak that, 10 years later, substantial and peak incidence is occurring in 9–11-year old children. Introduction of a persistent cohort effect related to a poorly protective vaccine could have caused this changing epidemiology. This hypothesis deserves further exploration through surveillance data in other provinces.

Acellular pertussis vaccines are more efficacious than their whole-cell counterparts that were used previously in Canada [6–10]. Their introduction into the childhood immunization program in BC in August 1997 seems to have decreased the vulnerability of infants and children. Their introduction coincides well with a subsequent decline in the proportion and absolute incidence of infant and preschool pertussis cases relative to 1996, despite other evidence of much more substantial transmission among the population in 2000. Routine immunization does not begin until 2 months of age, and full protection is achieved only after the final 6-month dose of the primary series. Persistent elevated activity in infants <5 months of age, despite substantial decline in those ≥6 months of age, is consistent with an improvement in protection due to the acellular pertussis vaccine, relative to the adsorbed whole-cell vaccine previously used [6–10].

We may anticipate this positive impact of the acellular vaccine to slowly spread among childhood and reduce the incidence of pertussis among school-aged children. The administration of a single booster dose of this vaccine in children primed with the whole-cell vaccine has been shown to improve protection against the disease [29]. The fact that in 2000 the incidence increased among children ≥8 years of age supports this previous report. School children who are 5–7 years old attend the same schools as those who are 8–11 years old, but the younger children received acellular vaccine as their preschool booster, and the older children received whole-cell vaccine. Thus it is likely that the incidence of pertussis in Canada will further decrease with the expanding impact of the introduction of acellular vaccine into the routine program and as children who received it constitute an increasing proportion of all school children.

Population indicators of pertussis morbidity are driven by disease in the very young, in whom complications have historically been more frequent and more severe [2, 4, 5]. In 2000, compared with 1996 and 1993, hospitalizations and deaths due to pertussis declined overall and particularly in infants and preschool children. A relative, albeit modest, increase in hospitalizations due to pertussis was observed among adolescents and adults. As independent markers, hospitalization and mortality data provide important corroboration of trends witnessed via the passive surveillance system, particularly the decreasing incidence in infants and preschool children.

The BC outbreak in 2000 depicts an absolute incidence of pertussis for preteens and teens that surpasses that for infants and preschool children. The essential public health question that follows is whether the recently licensed adult-formulation acellular pertussis vaccine, which has been shown to be safe and immunogenic, should now be directed toward the control of pertussis in expanded age groups, particularly in preteens and teens [30].
References