

Trends in incidence of invasive pneumococcal disease following introduction of the universal infant immunization program in British Columbia, 2002–2006

Data from the provincial surveillance system and reference laboratories indicate declining rates of infection in children younger than 5 years after routine vaccination with the pneumococcal conjugate vaccine, PCV7.

ABSTRACT:

Background: In 2002 the National Advisory Committee on Immunization recommended routine vaccination of healthy children up to 59 months with a 7-valent pneumococcal conjugate vaccine, PCV7, to prevent disease caused by *Streptococcus pneumoniae*. In 2003 a universal infant immunization program using PCV7 was introduced in British Columbia.

Methods: Data on cases of invasive pneumococcal disease reported from 2002 to 2006 were extracted from the provincial surveillance system and laboratory databases. Annual incidence rates were calculated and trends over time were explored with the chi-square test for trend.

Results: From 2002 to 2006 there was a 70% reduction in the rate of invasive pneumococcal disease among children younger than 5

years. However, from 2005 to 2006 there was a 40% increase in the overall rate for invasive pneumococcal disease. This increase was primarily among 20- to 64-year-olds, who experienced a significant rise in infection caused by strains not covered by PCV7, and was related to an outbreak of serotype 5 invasive pneumococcal disease. There was no significant increase in infections not covered by PCV7 in children, adolescents, or the elderly.

Conclusions: A decrease in the incidence rate of invasive pneumococcal disease for children younger than 5 years is associated with the universal infant PCV7 immunization program introduced in 2003. An increase in invasive pneumococcal disease during 2006 is related to a clonal outbreak in adults rather than to serotype replacement in the immunized population.

Background

Streptococcus pneumoniae causes a range of invasive and noninvasive infections and remains the primary agent of community-acquired pneumonia.¹ Until recently the only licensed vaccine available was the 23-valent pneumococcal polysaccharide vaccine (PPV23), which is protective against

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23 of the 90 most commonly known serotypes² but lacks efficacy in young children. In 2001 a 7-valent pneumococcal conjugate vaccine, PCV7, was licensed for use in Canadian children. PCV7 targets serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F, which are responsible for more than 80% of invasive pneumococcal disease (IPD) in this age group. As with conjugate vaccines against other polysaccharide-bearing pathogens, PCV7 has greatly improved immunogenicity and efficacy in children under 5 years of age. It also prevents carriage, which may contribute to herd immunity.

In early 2002 the National Advisory Committee on Immunization recommended that healthy children up to 59 months of age receive routine vaccination with a four-dose schedule of PCV7.² In BC a universal infant immunization program that was introduced in September 2003 provided children with a four-dose schedule of PCV administered at age 2, 4, 6, and 12 to 15 months.³ In addition, BC authorities continued to offer PPV23 to all persons older than 65 years. The expectation at the inception of the universal infant PCV7 immunization program was that within 4 years the program would prevent 112 cases of pneumococcal meningitis or sepsis annually in children under 5 years of age.³

Methods

IPD is a reportable condition in BC and has been monitored by the British Columbia Centre for Disease Control (BCCDC) since 1999. Invasive pneumococcal disease cases are defined by the isolation of *Streptococcus pneumoniae* from a sterile site, usually blood or cerebrospinal fluid.

For this study data on IPD cases were extracted from two sources: the provincial passive surveillance system (the integrated Public Health Informa-

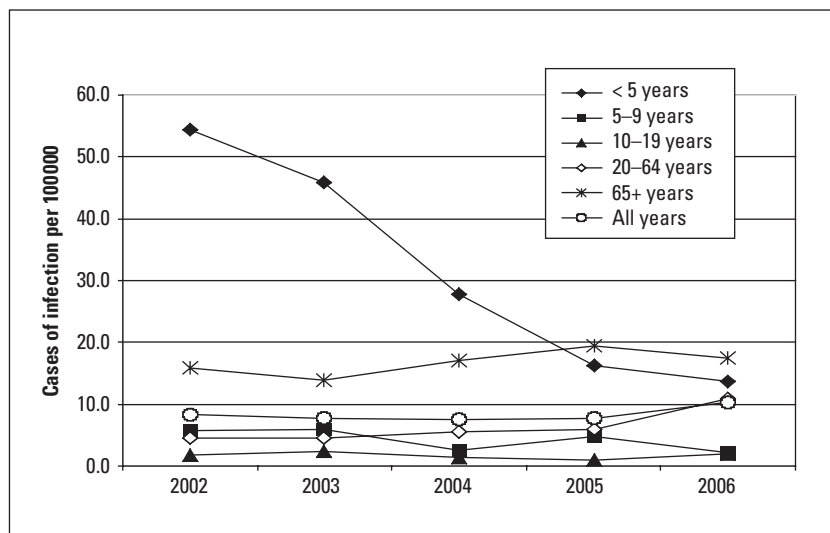


Figure 1. Incidence rates of invasive pneumococcal disease in all age groups in BC, 2002–2006.

Source: iPHIS

tion System or iPHIS) and the provincial laboratory databases. Together these data sources provided information on the demographics (patient age, sex, geographical location), episode date, type of infection, and serotype. Serotype analysis of clinical isolates was provided by both the National Centre for Streptococcus and BCCDC laboratories using MYSIS Healthcare Systems technology.

Annual incidence rates were calculated by obtaining population estimates for the denominators from P.E.O.P.L.E 30 (Population Extrapolation for Organization Planning with Less Error, run cycle 30, BC STATS). Data management and calculations were performed using Microsoft Excel software. Trends over time were explored with the chi-square test for trend, using the StatCalc calculator in EpiInfo 6. Trends were considered statistically significant if the *P* value was less than .05.

Results

Between 2002 and 2005 the rate of IPD reported in the overall population

of British Columbia was relatively stable at between 7.5 and 8.5 cases per 100 000 population (see **Figure 1**). In 2006 the overall rate increased 40% over 2005 to 10.4 cases per 100 000. This increase was seen primarily among those aged 20 to 64 years and was related to an outbreak of serotype 5 IPD in British Columbia. For this age group alone the incidence rate in 2006 was 11.0 per 100 000 (300 cases) compared with 4.6 per 100 000 (117 cases) during 2002—a significant increase ($\chi^2 = 87.1$; $P < .0001$).

From 2002 to 2006 there was an increase in the incidence of cases within the 65+ years group ($\chi^2 = 2.6$; $P = .10$) and the 10 to 19 years group ($\chi^2 = 0.3$; $P = .57$), and a decrease in the 5 to 9 years group ($\chi^2 = 3.6$; $P = .06$).

Between 2002 and 2006 there was a statistically significant decrease in the incidence of IPD among children under 5 years of age (see **Figure 2**) from 54.4 to 13.6 cases per 100 000 ($\chi^2 = 80.8$; $P < .0001$). When individual age categories were examined, significant decreases in the rate of IPD were observed: the rate for infants

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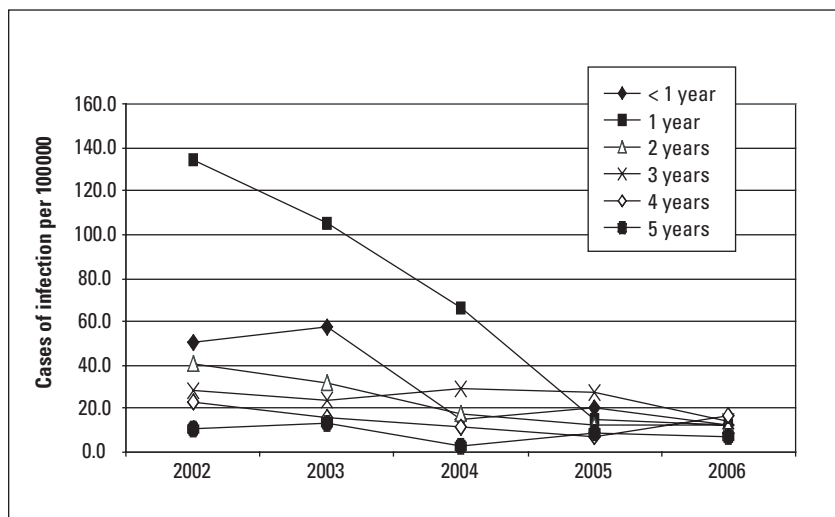


Figure 2. Incidence rates of invasive pneumococcal disease in children 5 years and younger in BC, 2002–2006.

Source: iPHIS

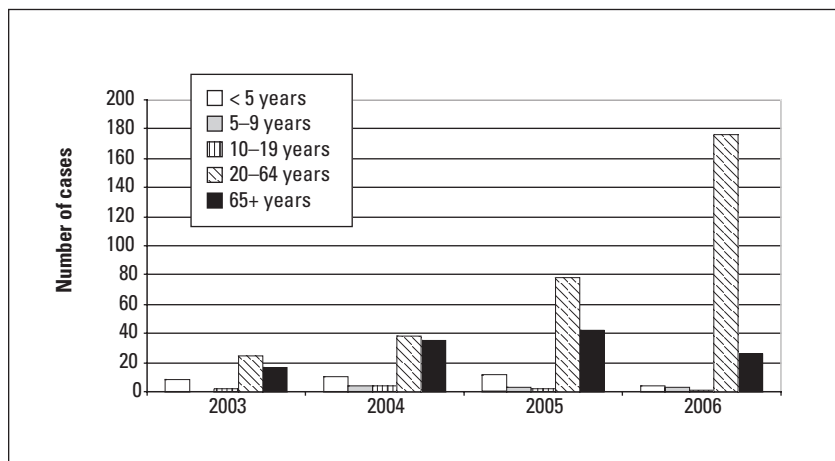


Figure 3. Cases of invasive pneumococcal disease caused by serotypes not covered by PCV7, grouped according to age, 1 January 2003 to 31 December 2006.

Source: MYSIS data.

younger than 1 year fell from 50.6 to 12.4 cases per 100 000 ($\chi^2 = 16.6$; $P < .0001$), while the rate for 1-year-olds fell from 134.7 to 14.9 cases ($\chi^2 = 68.5$ $P < .0001$), and the rate for 2-year-olds fell from 40.4 to 12.2 cases ($\chi^2 = 10.5$; $P < .001$). There were also nonsignificant decreases among 3-year-olds (27.9 to 14.3 cases), 4-year-olds (22.7 to 16.9 cases), and

5-year-olds (10.9 to 7.1 cases), with all having P values greater than .26.

Serotype distribution

Serotype-specific data acceptable for analysis were available for 70% to 83% of case reports in the iPHIS system for each year studied. The only age group with a statistically significant increase in infections with

serotypes not covered by PCV7 was the 20 to 64 years group (see **Figure 3**) where there was a 6.7-fold increase from 25 to 176 cases ($\chi^2 = 145.2$; $P < .0001$). Most of this excess was attributable to 117 serotype 5 cases reported in 2006.

For all other age groups there was no significant increase in cases of IDP associated with serotypes not covered by PCV7. Most importantly, in children younger than 5 years of age there was no evidence of strain replacement and this has continued to date (see **Figure 4**). Strain replacement was not found in those younger than 1 year (7.47 to 4.97 cases per 100 000 population; $\chi^2 = 0.1$; $P = .68$), the 1-year age group (7.53 to 2.44 cases, $\chi^2 = 0.6$; $P = .42$), the 2-year age group (2.43 to 0.00 cases, $\chi^2 = 1.6$; $P = .20$), the 3-year age group (2.36 to 0.00 cases, $\chi^2 = 0.0$; $P = .99$), the 4-year age group (0.00 to 2.41 cases, $\chi^2 = 1.8$; $P = .17$), or the 5-year age group (0.00 to 0.00 cases, $\chi^2 = 0.0$; $P = 1.00$).

Conclusions

Our findings support conclusions about two important and largely unrelated trends. First, a decrease in the incidence of IPD for children under 5 years of age is almost certainly related to the increase in vaccination coverage provided by the universal infant PCV7 immunization program in British Columbia. Second, an increase in IPD in those 20 to 64 years is most likely not an example of serotype replacement connected to the program because the increase occurred in a nonoverlapping age group.

The 2003 immunization coverage rate for the first group of infants offered the pneumococcal conjugate vaccine was 64%, a rate that increased to 77.6% in 2006.³ This increase in coverage may be improving herd immunity.⁴ It is of note that the impact of PCV7 on the prevention of IPD else-

where has been greater than expected from original clinical trials,⁵ which were used for approval of the vaccine and to guide the initial recommendations for the infant immunization schedule.⁶ However, in BC we are not yet seeing herd immunity in age groups older than 5 years as described in the USA.⁷ In British Columbia the IPD rate among those aged 65 years and older has not changed significantly in the past 4 years. This group continues to receive PPV23.

Regarding the increase in the rate of IPD in those 20 to 64 years, this trend can be adequately explained by the well-documented introduction of a clonal outbreak of serotype 5 IPD among indigent urban dwellers during 2006. The hospital and health authority involved in identifying the outbreak will soon be publishing an article describing the outbreak (personal communication with Dr Mark Romney, medical microbiologist, Providence Health Care, 16 August 2007).

This study had at least two limitations. First, while passive reporting of IPD by laboratories is generally fairly complete, there may be some underreporting. Second, not all isolates associated with a diagnosis of IPD were referred to reference laboratories for serotyping, which means that the serotype-specific trends are derived from the large subset of cases where such data were available.

This study highlights the success of the universal infant PCV7 immunization program in British Columbia, where there has been a significant reduction in the incidence rate of IPD in children younger than 5 years. Since January 2007 BC has moved to a three-dose schedule of PCV7 administered at 2, 4, and 12 to 15 months. In order to evaluate this change, authorities will continue to monitor invasive pneumococcal disease in children under 5 years of age.

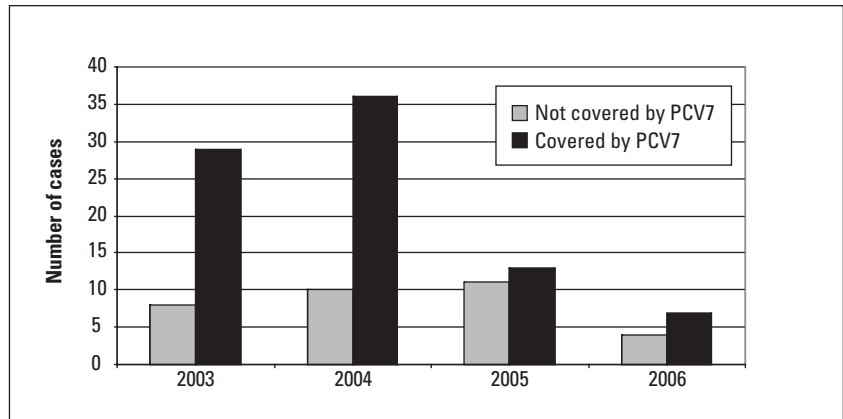


Figure 4. Cases of invasive pneumococcal disease in children younger than 5 years, grouped according to whether the serotypes identified were not covered by PCV7 or were covered, 1 January 2003 to 31 December 2006.

Source: MYSIS data

Acknowledgments

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Competing interests

None declared.

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