# **Pertussis in Rural Populations of** Saskatchewan (1995 to 2003)

Incidence, Seasonality, and Differences Among Cases

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#### ABSTRACT

Background: Few Canadian studies have studied re-emergent pertussis in rural areas. This study described the epidemiology of pertussis in the rural areas of the Saskatoon Regional Health Authority in Saskatchewan, and comparisons were made to the City of Saskatoon.

Methods: Analyses were based on passive surveillance data collected between 1995 and 2003. Estimates of the cumulative incidence (per 10,000 population) measured the occurrence of pertussis. Kaplan-Meier curves were plotted to compare a case's time until disease from their last vaccination by different vaccine types (whole-cell (WCV), or acellular (ACV)) and vaccine histories (complete or partial). Epidemic curves identified peaks in the incidence and checked for seasonal variation in case reporting.

Results: Over the 9-year period, 1,135 cases were reported. Rural areas had higher incidence rates and lower proportions of cases vaccinated than urban areas. Overall, the highest age-specific incidence was observed in people aged 10-19 years. Cases aged 0-9 years vaccinated with the ACV, from both rural and urban areas, presented a shorter time to disease (14 months (95% CI: 13-16) and 17 months (95% CI: 11-21), respectively) when compared to cases vaccinated with the WCV (47 months (95% CI: 40-51) and 36 months (95% CI: 31-41), respectively), or with a combination of the two vaccines (40 months (95% CI: 27-47) and 44 months (95% CI: 36-51), respectively, p<0.01). Epidemic curves revealed that reported cases are occurring earlier in successive years (1997, 1999, and 2003) in rural areas.

Conclusion: Epidemiologic differences among cases from rural areas exist when compared to urban areas. This study further emphasizes the need to better understand age-, vaccine-, and seasonally-related aspects of pertussis epidemiology in rural areas.

MeSH terms: Epidemiology; pertussis; rural communities; surveillance; vaccination

#### La traduction du résumé se trouve à la fin de l'article.

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hile a resurgence of pertussis has been noted,1 few studies have specifically investigated the impact of re-emergent pertussis in rural areas. Because of different population densities, the spread of an infectious disease in rural and urban areas will be dissimilar.<sup>2</sup> This is of concern in the province of Saskatchewan as a large percentage (44%) of the population resides in rural areas.<sup>3</sup> If public health polices are to control the spread of pertussis, we need to improve our understanding of the burden and transmission of pertussis in rural communities.4

The purpose of this paper is to present an epidemiological investigation of pertussis in rural areas in Saskatchewan. The focus is on the occurrence of pertussis across age and gender, as well as the vaccination history among pertussis cases. We also examine the time until cases begin to appear after vaccination, report peaks in the incidence since adopting an acellular vaccine (ACV), and compare rural results with results from an adjacent urban area.

#### METHODS

The former health districts of the Saskatoon Regional Health Authority (SRHA), namely, Central Plains Health District (CPHD), Gabriel Springs Health District (GSHD), Living Sky Health District (LSHD), and the Saskatoon District Health (referred to as the urban area), were studied because of their convenient location to the University of Saskatchewan. The population studied represents approximately 30% of the province's overall population, covers a wide age range, and is socio-economically diverse.5

Passive surveillance data were gathered from January 1, 1995 to December 31, 2003. Physicians reported patients who were presenting pertussis-like symptoms  $(\geq 2 \text{ weeks of paroxysmal cough, post-}$ tussive vomiting, and inspiratory 'whoop').6 Nasopharyngeal samples were collected and pertussis was confirmed by laboratory diagnosis using Polymerase Chain Reaction (PCR) assays.<sup>7</sup> Information about a case's vaccine history and the date of their last immunization was obtained from health records by public health nurses.

The crude cumulative incidence rate (CIR) was calculated as the number of new

#### TABLE I

Comparison of Average Yearly Cumulative Incidence (per 10,000 population), Gender, Age, Immunization History, and Vaccination Coverage Across Cases in Each Rural (CPHD, GSHD, and LSHD), Combined Rural, and Urban Areas of the Saskatoon Regional Health Authority (1995 to 2003)

CPHD (N=23,424*)	GSHD (N=13,272*)	LSHD (N=15,447*)	Combined Rural (N=52,143*)	Urban (N=300,046*)
117	91	101	309	826
6.2	8.5	8.2	7.5†	3.8
(2.8-9.6)	(3.3-13.9)	(3.4-12.9)	(4.9-9.9)	(3.1-4.7)
12.9	13.9	16.1	14.3	14.7
(10.8-15.0)	(11.1-16.8)	(12.9-19.3)	(12.7-15.8)	(13.8-15.6)
58 (49.6)	47 (51.6)	58 (57.4)	163 (52.8)	406 (50.8)
59 (50.4)	44 (48.4)	43 (42.6)	146 (47.2)	420 (49.2)
91 (77.8)	34 (37.4)ࠠ	79 (78.2)	204 (66.0)‡,‡‡	633 (76.6)
90 (76.9)	23 (25.3)	75 (74.2)	188 (60.8)	575 (69.8)
1 (0.9)	11 (12.1)	4 (4.0)	16 (5.2)	58 (7.0)
22 (22.6)	57 (62.6)	22 (21.8)	105 (34.0)	192 (23.2)
	CPHD (N=23,424*) 117 6.2 (2.8-9.6) 12.9 (10.8-15.0) 58 (49.6) 59 (50.4) 91 (77.8) 90 (76.9) 1 (0.9) 22 (22.6)	CPHD $(N=23,424^*)$ GSHD $(N=13,272^*)$ 916.2 $(2.8-9.6)$ 8.5 $(3.3-13.9)$ 12.9 $(10.8-15.0)$ 13.9 $(11.1-16.8)$ 58 (49.6) 59 (50.4)47 (51.6) 44 (48.4)91 (77.8)34 (37.4)ࠠ90 (76.9) $23 (25.3)$ $1 (0.9)$ 23 (25.3) $11 (12.1)$ $22 (22.6)$	$\begin{array}{c c} \textbf{CPHD}\\ \textbf{(N=23,424*)}\\ 117 \\ \textbf{(N=13,272*)}\\ 91 \\ \textbf{(N=15,447*)}\\ 101 \\ \textbf{(S=15,417*)}\\ ($	$\begin{array}{c c} \textbf{CPHD} \\ \textbf{(N=23,424*)} \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 117 \\ 111 \\ 117 \\ 111 \\ $

The average population for the time period 1995-2003

p<0.01 Kruskal-Wallis test compared differences among the age of the cases

Normal Theory test comparing rural health districts (combined) with urban areas<sup>31</sup>

Percentage is based on those cases with either partial or complete immunization histories

Pearson's chi-square compared gender by area of residence

†† Binomial comparison between proportion of cases vaccinated in the CPHD and GSHD

## Binomial comparison of proportion of cases vaccinated between the rural health districts (combined) with urban region

cases reported over a specified period of time divided by the known population of residents, and expressed as cases per 10,000 population.8 Age was categorized into three groups: 0-9 years, 10-19 years, and  $\geq 20$ years; age-specific incidence rates were calculated similarly to crude rates. Vaccination history was categorized as 'complete' (≥4 vaccinations, or were up-todate for their age), or 'partial' (vaccination records indicated partial or lapsed vaccination for their age) regardless of the type of vaccination that was received. The proportion of cases vaccinated were all cases with a vaccine history.

On July 1st, 1997, Saskatchewan underwent a vaccine transition from a whole-cell vaccine (WCV, Penta<sup>TM</sup>, Sanofi Pasteur Canada) to a five-component ACV vaccine (Pentacel<sup>TM</sup>, Sanofi Pasteur Canada). Information on the type of vaccination was inferred using the information about the date of a case's last immunization, the date of diagnosis, and their age at diagnosis. Cases were considered to have received: the WCV, if the date of their last immunization was before July 1st, 1997; the ACV, if cases were estimated to have been born after May 1st, 1997; or a combination of the two vaccines (WCV/ACV) for the remaining cases with the date of their last immunization recorded. All descriptive analyses used SPSS Statistical Software for Windows (SPSS Inc., Chicago, IL, version 12.0). Appropriate statistical tests (see footnotes in Table I) were used for statistical comparisons.

Because vaccine-induced protection is thought to be the most important through childhood,<sup>2,6</sup> we were able to assess a case's 'time until disease' as the difference (in months) between the individual's last recorded vaccination and the date they were diagnosed with pertussis among children aged 0-9 years. Kaplan-Meier (KM) curves were plotted to compare the influence of vaccination type and history on a case's time until disease in both urban and rural areas. KM curves stratified by vaccine type only included those cases with complete vaccination. Since immunogenesis and anamnestic responses of pertussis vaccines have been measured 4 weeks postvaccination,<sup>9-11</sup> cases were also excluded if their time until disease from the last vaccination was <1 month. Inferences were based on PROC LIFETEST (SAS Institute, Cary, NC, version 8.0).

Data on pertussis incidence in the SRHA was not available prior to 1995, making it difficult to estimate the endemic level of pertussis. Therefore, the average yearly CIR was used to estimate endemic levels. Years with a CIR above the average yearly CIR were identified as peaks in the incidence, and were plotted individually to

determine the months with the largest number of cases.

#### RESULTS

A summary of the 1,135 reported cases in the CPHD, GSHD, LSHD, combined rural, as well as the urban health district is given in Table I. The average yearly CIR in the urban area was lower than in the combined rural areas (3.8 per 10,000 population (95% confidence interval (CI): 3.1-4.7) and 7.5 per 10,000 population (95% CI: 4.9-9.9), p=0.04, respectively).

Annual age-specific CIRs in the combined rural areas experienced similar fluctuations (Figure 1a). Cases aged 0-9 years reported incidence rates that peaked at 73.79 per 10,000 population in 1999. Cases aged 10-19 years followed a similar trend with a peak incidence of 51.79 per 10,000 population also in 1999. Cases aged ≥20 years reported the lowest, leastfluctuating incidence rates that peaked at 4.47 per 10,000 population (in 2003). Unlike rural areas, the age-specific incidence rates of urban residents demonstrated that cases aged 10-19 years consistently reported the highest incidence after 1999 (Figure 1b).

Immunization history was recorded among 204 rural cases, of which 188 (92.2%) reported complete vaccination

<sup>÷</sup> p<0.05







(b) Urban area



Figure 2. Time until disease for cases in the Saskatoon Regional Health Authority (1995 to 2003) stratified by vaccine type: Whole-cell (WCV), a combination (WCV/ACV), and the acellular (ACV) aged <10 years with complete vaccination

histories (Table I). Among rural health districts, the proportion of cases vaccinated was the lowest in the GSHD (Table I). The proportion of cases vaccinated in the combined rural areas was also lower than the urban area (Table I).

The median time until disease was shorter for rural cases vaccinated with the ACV compared to those cases vaccinated either with the WCV or WCV/ACV (14 months (95% CI: 13-16), 47 months (95% CI: 40-51), and 40 months (95% CI: 27-47), respectively, p<0.01, Figure 2a), as well as for those urban cases vaccinated with the ACV compared to those vaccinated with WCV or WCV/ACV (17 months (95% CI: 11-21), 36 months (95% CI: 31-41), and 44 months (95% CI: 36-51), respectively, p<0.01, Figure 2b). No differences were found between WCV and WCV/ACV in either rural or urban areas. KM plots by vaccination history, for both the combined rural and urban areas, revealed no statistical differences (p=0.12 and p=0.85, respectively, Figure 3).

Rates of pertussis that graphically qualified as peaks in rural areas occurred in 1997, 1999, and 2003 (Figure 4a). In 1997, the majority of reported cases were initially occurring in the late summer to early fall (Figure 4b). However, during subsequent peaks (1999 and 2003), reported cases began to occur during the late spring to early summer months (Figure 4b). The peak number of cases reported also appears to have increased from 1997 to 2003 (Figure 4b).

#### DISCUSSION

Passive surveillance data provides an excellent source of descriptive information about notifiable infectious diseases.<sup>12,13</sup> However, such data often do not contain sufficiently detailed information and are therefore limited.13 This study used routinely collected data on pertussis to carry out a descriptive analysis of rural and urban differences in the epidemiology of this disease.

The average yearly CIR of pertussis over the 9-year period was higher in rural areas compared to the urban area. Because these rates are derived from surveillance data, they are likely underestimated. However, these results support previous studies that rural inhabitants have a greater incidence

of disease than their urban counterparts.<sup>14</sup> The higher rates in the rural areas may be due in part to the very low proportion of cases vaccinated. This is an interesting finding as previous research in the United States has shown that children are just as likely to receive appropriate vaccine coverage in rural areas as urban areas.<sup>15,16</sup> The proportion of cases vaccinated in the GSHD seemed to be much lower than that in the urban area.

Older children and adolescents in urban areas possessed the highest incidence rates, while rural areas demonstrated a pattern consistent with 'classic' pertussis epidemiology. These findings in the urban area may likely be the result of waning immunity combined with a higher likelihood of exposure to *B. pertussis* – a function of living in an urban area. Although 'shifts' in the age-specific incidence is the main impetus of re-emergent pertussis, and is widely reported, this is one of few published Canadian studies that have demonstrated an age-specific shift in the incidence of this disease.<sup>17</sup>

Although ACVs are less reactogenic and comparatively immunogenic as WCVs, both will yield variable efficacy.6,9,10 Currently, little understanding about the period of protection from pertussis, conferred through either infection or vaccination, exists.<sup>18-20</sup> We used the case's time from last vaccination until diagnosis with pertussis as a proxy measure for the duration of vaccine-induced protection. These results suggest that protection from the ACV may fail earlier than the WCV or the WCV/ACV. Although this is consistent with findings elsewhere,<sup>19,21</sup> this is a new finding in Canada. Therefore, further research is needed to corroborate these results, as well as investigate how vaccine type might be affecting the incidence of pertussis in the SRHA.

KM curves stratified by vaccination history demonstrated no statistical differences within the SRHA. However, cases in rural areas with partial vaccination demonstrate a notably (and expected) shorter time until disease than cases with complete vaccination (23 months (95% CI: 4-35), and 39 months (95% CI: 35-46), respectively, Figure 3a). The lack of statistical significance might be due to the small numbers of cases included in the survival analysis among the rural areas ( $n_{\text{partial}} = 8 \text{ vs. } n_{\text{complete}}$ 





= 91), and should be reexamined with additional data to verify if this trend remains. In the urban area, however, a case's time until disease did not demonstrate this distinction. Urban areas are likely to have higher contact between susceptible and infectious individuals than rural areas.<sup>2</sup> In the presence of high vaccination rates, high contact rates might favour polymorphisms of bacterial virulence factors among circulating strains of *B. pertussis*. As a result, antigenic components in current vaccines and of circulating bacteria may differ considerably. This has been speculated to have decreased vaccine effectiveness elsewhere,<sup>22-24</sup> and may be partly responsible for the similar time until disease between 'partially' and 'completely' vaccinated cases. Conducting an antigenic surveillance of the circulating B. pertussis isolates in the province of Saskatchewan (as in other Canadian provinces<sup>25-27</sup>) might clarify the observed results of vaccine history from the urban area.

The years identified as peaks in the incidence among the rural areas demonstrate a changing seasonal profile that has been observed elsewhere in Canada.<sup>17</sup> Each of the respective rural peaks, since 1997, has

occurred earlier in the calendar year and recorded more cases. Previous studies have reported that, in temperate climates, pertussis infections will typically peak in the fall and winter months, and will experience changes in seasonality on a regular basis.<sup>6,28,29</sup> Therefore, these results may simply represent a localized, cyclic pattern and not a changing seasonal profile, as similar results were not observed for the urban area studied (not shown). Given that seasonal changes in the peaks of pertussis incidence have been acknowledged previously, it may prove useful to monitor this seasonality more closely, as it might help public health officials to identify cyclical trends before they emerge and consequently help create public health practices to interrupt pertussis transmission.17

Despite the availability of routine childhood immunization, pertussis still remains an endemic and epidemic disease.<sup>30</sup> Our results reinforce the role of adolescents in pertussis epidemiology. They also indicate that rural areas experience higher incidence, and a shift in the seasonal profile when compared to their urban counterparts. Although it is possible that the results presented here are localized, they do



(b) Epidemic curves for the peaks in the incidence (i.e., 1997, 1999, and 2003) in the combined rural areas of the Saskatoon Regional Health Authority



**Figure 4.** Graphical identification and characterization of the peaks in pertussis incidence in the Saskatoon Regional Health Authority (1995-2003)

inform us that epidemiologic differences among cases exist and further research is still needed to monitor pertussis and the impact of our prevention efforts.

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#### RÉSUMÉ

**Contexte :** Peu d'études canadiennes portent sur la réapparition de la coqueluche en milieu rural. Nous décrivons ici l'épidémiologie de la coqueluche dans les régions rurales couvertes par l'office régional de la santé de Saskatoon, en Saskatchewan, par opposition à la ville de Saskatoon.

**Méthode :** Nos analyses sont fondées sur les données de surveillance passive recueillies entre 1995 et 2003. Nous avons mesuré la fréquence de la coqueluche d'après les estimations de son incidence cumulative (pour 10 000 habitants). En traçant des courbes de Kaplan-Meier, nous avons comparé le temps écoulé entre la dernière vaccination et l'apparition de la coqueluche, selon les différents types de vaccins reçus (à cellules entières ou acellulaire) et selon les antécédents vaccinaux (complets ou partiels). Des courbes épidémiques ont permis de déceler les pics d'incidence et de vérifier la présence d'écarts saisonniers dans les cas déclarés.

**Résultats :** Au cours des neuf années de l'étude, il y a eu 1 135 notifications de coqueluche. En milieu rural, les taux de fréquence étaient plus élevés et les proportions de cas vaccinés étaient plus faibles qu'en milieu urbain. Dans l'ensemble, la plus grande fréquence par âge a été observée chez les personnes de 10 à 19 ans. Dans les régions rurales comme dans les agglomérations urbaines, les enfants de 0 à 9 ans ayant reçu le vaccin acellulaire ont contracté la maladie plus rapidement (après 14 mois [IC de 95 % = 13-16] et après 17 mois [IC de 95 % = 11-21], respectivement) que les sujets ayant reçu le vaccin à cellules entières (après 47 mois [IC de 95 % = 31-41], respectivement), ou que les sujets ayant reçu une association des deux vaccins (après 40 mois [IC de 95 % = 27-47] et après 44 mois [IC de 95 % = 36-51), respectivement, p<0,01). Les courbes épidémiques montrent que les cas déclarés se sont produits de plus en plus tôt chaque année (1997, 1999 et 2003) dans les régions rurales.

**Conclusion :** Il existe des écarts épidémiologiques entre les cas des régions rurales et ceux des agglomérations urbaines. L'étude souligne aussi le besoin d'approfondir notre compréhension du rôle de l'âge, des vaccins reçus et des cycles saisonniers dans l'épidémiologie de la coqueluche en milieu rural.



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