MEASLES *update*

Volume 2 Number 3 August/September 1994

Table of Contents

RELATIVE EFFICACY OF MEASLES VACCINE ACCORDING TO AGE AT ADMINISTRATION

A Case-Control Study in Estrie, Quebec

Jean Drapeau, Philippe De Wals, Département des Sciences de la santé communautaire, Université de Sherbrooke, Sherbrooke, Quebec

Introduction

In 1989, a measles epidemic occurred in Quebec, spreading in Montreal and throughout the province[1]. In the region of Estrie (Eastern Townships), the immunization rate in the population at risk was high and the majority of cases were school-age children known to have received an attenuated live-virus vaccine during infancy. A case-control study, using those cases reported to the Community Health Department (CHD), was conducted to assess the relative vaccine efficacy according to age at administration.

Methods

The analysis was restricted to measles cases occurring in persons living in Estrie in 1989. The population denominators used were those from the 1991 census.

A total of 480 cases notified to the CHD were reviewed. At the beginning of the epidemic in March 1989, active surveillance had been established in the schools to achieve a high level of case finding. Data on clinical symptoms, laboratory tests and vaccination status were obtained through telephone interviews of parents and physicians as soon as possible after notification. Cases were classified as "clinical" or "confirmed", according to the criteria published by the Advisory Committee on Epidemiology[2]. In order to evaluate the effect of age at vaccination, the analysis was restricted to cases in persons aged 5 to 19 years attending a public primary or secondary school and having received a single dose of live-virus vaccine before the age of 25 months (n = 285).

In spring 1992, six controls, matched to each case for age (± 6 months), sex, school and grade during 1988 to 1989, were randomly selected from registry lists provided by the School Boards. Cases in schools unable to provide such lists were excluded (n = 47). The vaccination status of controls was obtained in the registry of the CHD. For 20 cases the vaccination cards for the controls were not available because an immunization program was underway at the school at the time of data collection. Most of the controls had a record of vaccination against measles and it was not possible to contact the parents for assessing the immunization status of children for whom the information was missing. Because the goal of the study was to investigate a potential cause of vaccine failure and not to prove the efficacy of the vaccine, controls were matched for immunization status. Among the six

Upcoming Event

Child Health 2000
2nd World Congress & Exposition

Vancouver, Canada

May 30 – June 3, 1995

controls available, three were selected according to the following criteria: evidence of a single dose of vaccine given before the age of 25 months, no report of measles, and the best match for age. The final analysis was done using 218 cases and 654 controls.

The odds of cases having been vaccinated at different ages relative to the odds in controls [the odds ratio (OR)] is a good estimate of the relative risk of disease and thus of the protection afforded by the vaccine[3]. Data were analyzed with the SAS statistical software. Initially, the age of vaccination was considered as a dichotomous variable: before 15 months and 15 months or more. OR and their confidence limits (CLs) were computed for matched and unmatched data stratified by age at exposure to infection (5 to 9, 10 to 14, and 15 to 19 years)[4]. Because the results of matched and unmatched analyses were similar, only the results of the unmatched analysis are presented. The homogeneity of the OR across age categories was tested according to Breslow and Day[5]. The attributable risk was computed from the OR[6]. Next, the age at vaccination was classified into one-month intervals, for a total of eight sub-categories. Unconditional, multiple, logistic regression was used for computing OR and approximate CL[7]. The existence of a linear trend in the OR according to the age at vaccine administration was tested by the chi-square method[8].

Results

In 1989, 480 cases of measles were notified in Estrie and 71 (14.8%) of these were confirmed by serology. The first case occurred on February 28 and the last one on August 17. The case distribution by age and vaccination status is indicated in Table 1. The largest proportion of cases (41%) occurred in 12 to 14-year-old children attending secondary school and almost all of these had been vaccinated. Twenty-nine cases (45.3%) were unvaccinated children < 5 years: 9 were < 1 year; 6, between 12 to 14 months; and 14, > 14 months.

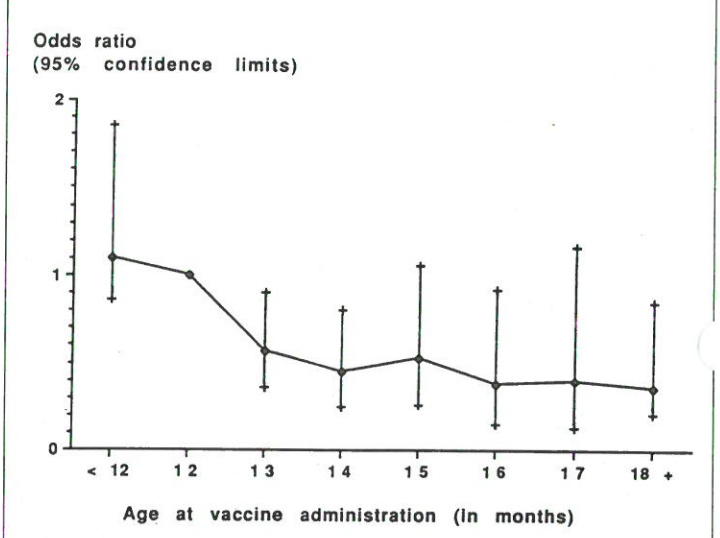
Table 1

Reported incidence of measles in Estrie, 1989

Age group (in years)	Population (1991 census)	Number of cases	Rate per 100,000	% vaccinated
0 – 4	17,630	64	363	55
5 – 9	18,490	68	368	93
10 – 14	20,410	259	1,269	95
15 – 19	18,455	70	379	79
20+	193,415	19	10	21
All ages	**268,400**	**480**	**179**	**84**

Among the 218 cases evaluated for risk factors, 11% had been vaccinated before 12 months of age, 71% between 12 and 14 months, and 18% after 14 months. In the control group, the proportions were 7%, 62% and 31%, respectively. The risk of contracting the disease if vaccinated at ≥15 months of age, relative to the risk if vaccinated before that age, was 0.50 (95% CL: 0.71 - 0.33). There was no indication that the OR varied according to the age of the child at the time of exposure to infection. The OR in children born from 1980 to 1984 (0.47) was similar to that for those born from 1975 to 1979 (0.45). In the school-age population, 42% of the total cases could be attributed to vaccination before 15 months.

Figure 1
Relative odds of contracting measles according to age at vaccination in Estrie, 1989



The relative risk of disease according to one-month intervals of age at vaccination is shown in Figure 1. The trend is highly significant ($p < 0.001$). The shape of the curve suggests that the efficacy of the vaccine increases rapidly up to 14 months of age and stabilizes at 16 months.

Discussion

The results confirm the important effect of age at administration of the measles vaccine[9]. During this epidemic, children who had been vaccinated after the age of 15 months were two to three times less likely to get the disease than those vaccinated at 12 months. A ratio of the same magnitude was observed in Quebec City[10]. The persistence of maternal antibodies to measles virus is a probable mechanism for primary vaccine failures[11,12].

These observations have two public health implications. First, for the cohort of children born between 1972 and 1983, it appears that the one-dose policy to give the vaccine at 15 months of age was more effective than the recommendation to target the first birthday[13,14]. This would have prevented 42% of cases in school children at no financial cost and for a low additional risk of

disease among those aged between 12 and 15 months. More studies are needed to support the hypothesis that the benefit of delaying vaccine administration could be lost with the increasing proportion of births to women who have acquired immunity following vaccination instead of the disease[15]. With a two-dose program, age at administration is less important but the high cost of such a policy must be recognized[16].

Second, if selective revaccination is to be implemented in the event of an institutional outbreak, the most effective measure should be to offer the vaccine to all those who received a single dose before 15 months of age, instead of targetting those vaccinated before 12 months[16]. This has the potential to prevent nine times more secondary cases but it also requires the revaccination of 10 times more children.

Acknowledgement

The authors wish to thank the Public Health Department (Reno Proulx and Serge Déry) and the School Boards of Estrie for their excellent cooperation in carrying out this study, and Jacques Pépin, Eric Frost and Gaston De Serres for their useful comments.

References

1. McLean ME, Walsh PJ, Carter AO et al. *Measles in Canada, 1989.* CDWR 1990;16:213-18.
2. Advisory Committee on Epidemiology. *Canadian communicable disease surveillance system: disease-specific case definitions and surveillance methods.* CDWR 1991;17S3:23.
3. Orenstein WA, Bernier RH, Hinman AR. *Assessing vaccine efficacy in the field.* Epidemiol Rev 1988;10:212-41.
4. Schlessman JJ. *Case-control studies.* New York: Oxford University Press, 1982:144-226.
5. Breslow NE, Day NE. *Statistical methods in cancer research. Vol. 1: The analysis of case-control studies.* Lyon: International Agency for Research on Cancer, 1980:142-46.
6. Hennekens CH, Buring JE. *Epidemiology in medicine.* Boston: Little, Brown and Company, 1987:87-96.
7. Hosmer DW, Lemeshow S. *Applied logistic regression.* New York: John Wiley and Sons, 1989:307.
8. Mantel V. *Chi-square test with one degree of freedom; extension of the Mantel-Haenzel procedure.* J Am Stat Assoc 1963;58:690-700.
9. Orenstein WA, Markowitz L, Preblud SR et al. *Appropriate age for measles vaccination in the United States.* Develop Biol Standard 1985;65:13-21.
10. De Serres G, Boulianne N, Joly JR. *Étude sur les déterminants de l'efficacité du vaccin antirougeoleux dans la région de Québec.* Québec : Département de Santé Communautaire, Centre Hospitalier de l'Université Laval, 1990.
11. Albrecht P, Ennis FA, Saltzman EJ et al. *Persistence of maternal antibody in infants beyond 12 months: mechanism of measles vaccine failure.* J Pediat 1977; 5:715-18.
12. Sato H, Albrecht P, Reynolds DW et al. *Transfer of measles, mumps, and rubella antibodies from mother to infant.* Am J Dis Child 1979;133:1240-43.
13. CDC. *Measles prevention: recommendations of the Immunization Practices Advisory Committee (ACIP).* MMWR 1989;38:(no. S-9):1-18.
14. Advisory Committee on Epidemiology. *Guidelines for measles control in Canada.* CDWR 1991;17:35-40.
15. Pabst HF, Spady DW, Marusyk RG et al. *Reduced measles immunity in infants in a well-vaccinated population.* Pediatr Infect Dis J 1992;11:525-29.
16. LCDC. *Consensus conference on measles.* CCDR 1993;19:72-79.

EPIDEMIOLOGIC INVESTIGATION OF A MEASLES OUTBREAK IN QUEBEC

L Alain, Field Epidemiology Division, Bureau of Communicable Disease Epidemiology, LCDC, and Public Health Protection Branch, Quebec Ministry of Health and Social Services; S Bernier, Hôtel-Dieu de Lévis and formerly with Public Health Department, Chaudière-Appalaches, Quebec

The last major measles outbreak in Quebec was in 1989, with 10,184 cases reported (152.2 per 100,000). In the three subsequent years, the incidence reached the lowest levels ever, with rates of 1.4, 4.1 and 0.6 per 100,000, respectively. During the first half of 1993, 50 cases were reported, for an annualized rate of 1.4 per 100,000; 22 of these were concentrated in the Chaudière-Appalaches region. This report summarizes findings of the epidemiologic investigation of the outbreak that occurred in this region.

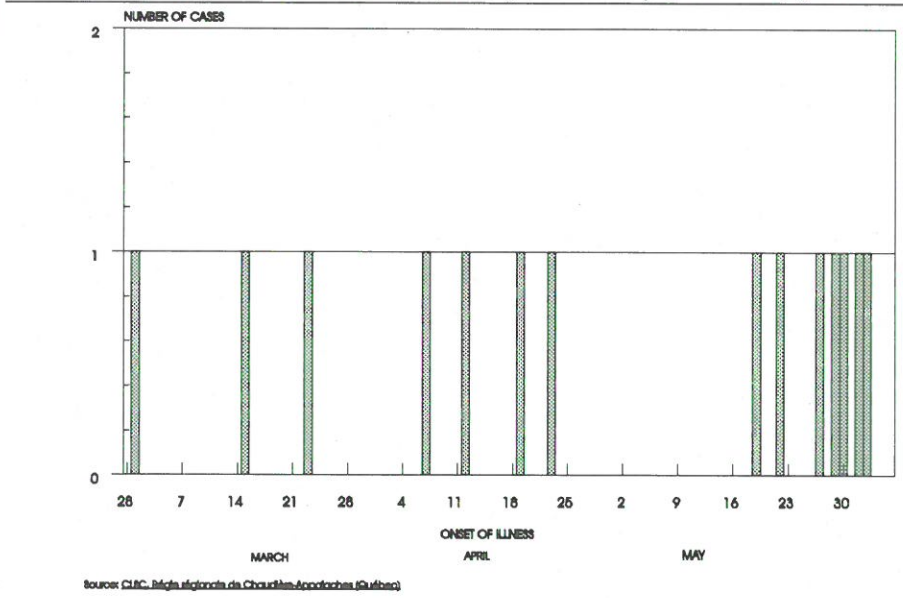
During the first week of March 1993, a 17-year-old male student who attended village B secondary school was diagnosed with measles. Following the review of the immunization records, measles vaccine was offered to unimmunized students, siblings and other contacts. A total of 48 students were vaccinated on March 12. Two additional cases from a primary school were notified the weeks ending March 20 and 27, respectively. Immunization status of primary school and pre-school children was reviewed. One of three unimmunized primary students was vaccinated on April 22; one could not be vaccinated due to illness

and the other could not be reached. An information program targeted the schools, local physicians and pharmacists. Despite these actions, new cases appeared. Figure 1 shows the distribution of cases by date of onset. By June 4, 1993, a total of 14 cases had been notified in the area served by one Centre local de santé communautaire (CLSC) (population 26,663). An investigation of the outbreak was initiated and control measures were reviewed to select the most appropriate intervention to limit the outbreak.

Information on cases and contacts had already been gathered by the CLSC nurses using a standardized questionnaire.

Figure 1

Reported measles cases in one of the CLSCs in the Chaudière-Appalaches Region of the Province of Quebec (n = 14) — February 28 to June 5, 1993



By June 4, 8 of the 14 cases were laboratory confirmed; others were epidemiologically linked. Thirteen of the 14 attended school or pre-school: 11 at the primary level and two at the secondary level. All but the index case, who came from village B, lived in village A. Age of cases ranged from 3 to 17 years (average: 8 years; median: 7). None of the cases suffered from severe complications and none required hospitalization.

Based on the date of onset, there has been three generations of measles infections since the index case, from late February to June 5, 1993 (Figure 1). Case distribution within these three periods reflects the incubation period, but no precise explanation can be given for the time lapse between generations two and three. It is most likely that some cases that occurred during this period were either not identified or not diagnosed, or both.

Immunization Status of the Cases

Twelve (86%) of the 14 cases had a history of measles vaccination. The 13th case received a dose of measles-mumps-rubella vaccine (MMR) on April 22 during the outbreak; the vaccination history could not be obtained for the 14th case. The average age for immunization of the 12 cases was 15.8 months. However, only one of four cases in the first grade had been immunized at the recommended age (12 months). The remaining three cases were vaccinated at 7 months, 5 years and 7 years of age, respectively (the latter two during the outbreak).

The average immunization coverage at the beginning of the school year for the two schools combined was 95.6% (97.8% for the primary/pre-school level and 95.3% for the secondary level).

Spread of the Disease

It was not possible to trace the source of infection for the index case. Available information indicates that the brother of the index case (aged 13 years) and the mother had attended a hockey tournament from February 5 to 7, 1993 at Nashwa (a small city near Boston, Mass., USA). According to the mother, none of the players on her son's team, or on the opposing teams was sick at that time, nor was any other person travelling with them. The index case appears to have been in contact with his cousins in village A where the outbreak occurred, before he was symptomatic. Household contact was traced in four cases.

Intervention Strategies

Further action plans and intervention strategies were discussed with provincial and federal experts on June 8, after a meeting with the staff from the CLSC. It was decided not to proceed with a second dose of measles vaccine. It seems that the necessity for the second dose was not made sufficiently clear and, because the school year was coming to an end, it was automatically anticipated that the outbreak would end.

It seems, upon examination of the 1993 data that the Chaudière- Appalaches Public Health Department experienced a particularly marked increase in measles activity compared to the previous 2 years and eight compared to the rest of the province. In addition to the 14 cases, eight other cases had occurred in other CLSCs of this Public Health Department, for a total of 22 cases in 1993 and an incidence rate of 6.5 per 100,000 population, compared to 0.5 in 1992, zero in 1991, and 7.4 during the epidemic period in 1990. A total of 59 cases were notified in 1993 in the province of Quebec (0.8 per 100,000).

Intervention

The interventions used in this outbreak followed the recommendations for control of measles epidemics made at the Consensus Conference on Measles in May, 1993[1]. The immunization campaign strategy was well organized, considering it was getting near the end of the school year.

Conclusions

This investigation revealed that there was increased measles activity in a specific area of the Chaudière-Appalaches region, despite a high level of vaccine coverage. It also pointed out the importance of prompt and concerted action in the field, and the significance of an effective epidemiologic surveillance system.

Recommendations

- Assess immunization status of newly admitted students periodically throughout the school year.
- Ensure that the monitoring system will detect all measles cases.
- Maintain epidemiologic follow-up of cases after diagnosis and after public health intervention.

Acknowledgments

We are particularly grateful to the Executive Director of the CLSC and his team; Dr. François Desbiens, Director and Dr. Gabrielle Vermette, consulting physician of Chaudière-Appalaches Public Health Department; Dr. Philippe Duclos, Chief of the Childhood Immunization Division, LCDC; Dr. Marc Dionne and Dr. Odette Laplante, Director and consulting physician from the Public Health Protection Branch (Quebec Ministry of Health and Social Services); Dr. Gilles Delage, Chairman of the Quebec Immunization Committee; and Dr. Jamie Hockin for his assistance in the preparation of this paper. Our thanks also go to all of the school authorities for their cooperation in the immunization campaign.

Reference

1. LCDC. *Consensus conference on measles*. CCDR 1993;19:72-79.

MEASLES IN CANADA, 1994 (as of September 14)

Paul Varughese, Childhood Immunization Division, Bureau of Communicable Disease Epidemiology, LCDC, Ottawa

From January 1 to September 14, 1994, a provisional total of 358 measles cases have been reported in Canada. This is 108% higher than the 172 cases reported for the same period in 1993. Over 65% (258 cases) of these cases were reported from Ontario, followed by Quebec with 25% (98 cases). No cases have been reported from Prince Edward Island, New Brunswick, the Yukon, and the Northwest Territories.

The province of Quebec recently reported two outbreaks, one of which involved a group of people who oppose immunization for religious reasons (a full report will appear in the next issue). Although several Ontario health regions have reported sporadic cases, only two have reported outbreaks, both in May: Middlesex-London with 43 cases (peaking in the 2nd week of May) and Haliburton, Kawartha, Pine Ridge District with 147 cases (peaking in the last week of May). A brief report follows in this issue on the latter outbreak.

Figure 1 shows the distribution of cases by month of onset for the period January 1 to July 31, 1994. The highest number of cases (145) was recorded in May, followed by June (89 cases).

Ages of the cases ranged from 5 months to 57 years (median: 13). The highest proportion (38%) of the cases was among those aged 15 to 19 years with the greatest incidence occurring among those 16 years of age, followed by those 5 to 9 years old (22%). Infants < 1 year of age accounted for 14 cases (4%) (Figure 2). No deaths have been reported.

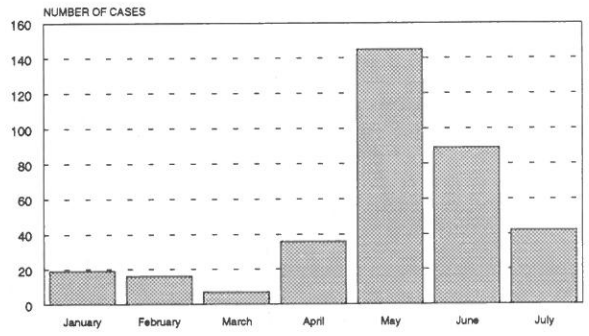
Immunization Status

Of the 358 cases, 339 were eligible for measles vaccination, i.e., they were born after 1957 and were older than 12 months of age. Two hundred and ninety-two (86%) of this vaccine-eligible group had a documented history of immunization — a pattern expected due to the high immunization coverage of a vaccine with < 100% vaccine efficacy. Immunization history was not known for 32 of the cases (8.9%).

Comment

In 1994, measles activity in Canada has been characterized by sporadic cases, clusters of cases, or small outbreaks, often involving vaccinated individuals, or those not vaccinated for religious reasons. Despite these outbreaks and the potential for transmission of the virus, the overall attack in the affected regions has still been low, suggesting that most individuals are

Figure 1
Reported cases of measles by month, Canada, January 1 to July 31, 1994*



* Provisional data

immune. Examination of those records available indicated that, although most children were vaccinated after their first birthday, a few had received the vaccine before 12 months of age.

Acknowledgement

The assistance and cooperation of all provincial and territorial epidemiologists, medical officers of health and other health care personnel, as well as Ms. Carole Scott, Ms. Mary-Jane Garnett, and Mr. John Koch from LCDC is greatly appreciated.

Preliminary Report

MEASLES OUTBREAK — WARKWORTH, ONTARIO April – July, 1994

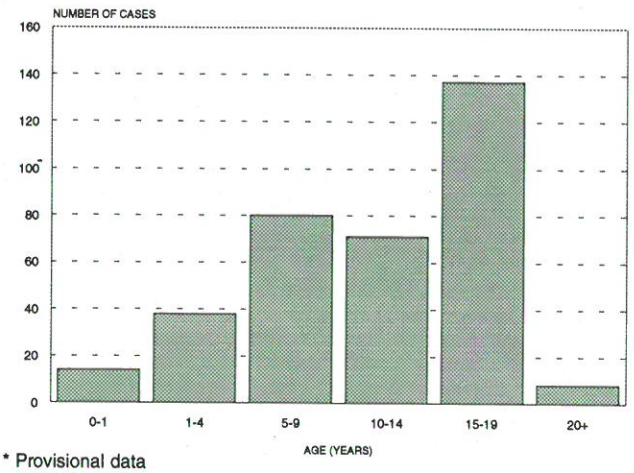
A. Hukowich, Haliburton, Kawartha, Pine Ridge District Health Unit, Warkworth, Ontario

On April 26, 1994, the Haliburton, Kawartha, Pine Ridge District Health Unit received notification of four suspect cases of measles in students at a Warkworth elementary school. The children had been on a trip to the Skydome in Toronto approximately 10 days earlier. The Medical Officer of Health and a Public Health Nurse arranged to visit three of the children at their homes that afternoon. All were found to be slightly ill with no fever but each had a generalized, non-pruritic, papular rash. There was mild hyperemia of the buccal membranes but no Koplik spots and no significant findings of cough, conjunctivitis, or photophobia. All of the affected children did have a history of measles-mumps-rubella (MMR) immunization.

While none of the intial cases fully met the case definition for measles, consideration was given to the fact that prior immunization could have resulted in less severe and less typical symptoms. All children were epidemiologically linked within the incubation period for measles and that particular area had escaped a previous measles outbreak that had occurred within Northumberland County approximately 3 years earlier. Arrangements were made for serologic testing to confirm a presumptive diagnosis of measles. A meeting was held that afternoon with the school principal, and the local hospital in Campbellford was advised of the possibility of a measles outbreak. Parents of children at the school who were unimmunized due to medical or philosophical exemptions were contacted. They were advised that school exclusion orders would be issued the following day and that they might wish to keep their children out of school voluntarily pending the formal serving of such orders. A parent information letter was updated and provided to the school the following day for distribution. Similarly, a physician fact sheet was distributed to all local physicians.

Figure 2

Reported cases of measles by age group, Canada, January 1 to July 31, 1994*



* Provisional data

A news release was also prepared for the local media. Fortunately, by the time of the most intense media interest, positive IgM antibody titres from initial cases confirmed measles in two of the initial four suspect cases.

Publicity to parents and physicians stressed the value of measles immunization in children between 6 months and one year of age. A health unit-operated clinic was organized following a request for assistance from local physicians. No school-based or health unit-based clinics were undertaken for re-immunization of children already having satisfactory proof of measles immunization. Some school activities were cancelled including a planned trip to the province of Quebec and the participation fo children in some county-wide activities. There was one case reported the following week and 23 one week later. The outbreak peaked in its sixth week with 41 cases reported. The last cases were reported the week of July 2. In total, 147 cases of measles were confirmed. As anticipated, no cases developed in any adjacent areas of the county that had experienced the previous measles outbreak.

Submissions of pertinent reports/epi notes are welcome and success of this endeavour depends upon the readers' interest and cooperation. Priority for inclusion in the newsletter is determined by the article's relevancy. This is not a formal publication, and the views and interpretation may not necessarily reflect Health Canada's position. Distribution is free of charge. Anyone wishing to receive a copy on a regular basis should contact the Childhood Immunization Division, Bureau of Communicable Disease Epidemiology, LCDC, Ottawa, Ontario, K1A 0L2; telephone (613) 957-1340; Fax (613) 998-6413.

Editors:
Philippe Duclos
Paul Varughese (613) 957-1344
Childhood Immunization Division
FAX: (613) 998-6413

Preparation:
Editorial and Production Division

Bureau of Communicable Disease Epidemiology
Laboratory Centre for Disease Control
Health Canada
Tunney's Pasture, Ottawa, Ontario K1A 0L2