MEASLES *update*

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Current News

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Ontario and Quebec Announce a Routine Two-Dose Measles Vaccine Program and a Supplementary Catch-up Program

Ontario

A formal announcement was made by the provincial minister of health on December 5, 1995, for the introduction of a two-dose measles schedule with a second measles-mumps-rubella (MMR) to be given at school entry, starting in 1996, and a mass immunization catch-up campaign with monovalent measles vaccine for school-aged children junior kindergarten through to grade 13 starting in February 1, 1996. The program had been approved at the Community Health Division level earlier, and initial preparations have been in progress for some time.

In preparation for the catch up, physicians were sent a direct mailing of pertinent information throughout the 2nd and 3rd week of December. Fact sheets and consent forms are being distributed through schools to students (beginning in January). School-based clinics delivered by the public health staff will administer measles vaccine. These clinics will run through June in some areas; others will be completed in 1 or 2 months.

For the routine two-dose schedule, immunizations will be given by physicians in conjunction with DPT-Polio given at 4 to 6 years of age. Beginning September 1996, two doses of measles vaccine will be required by provincial law for children > 6 years of age for attendance at Ontario schools (exemptions are allowed for valid medical reasons, or reasons of religion or conscience).

Quebec

On December 18, Quebec officially announced the introduction of a routine two-dose measles schedule, with a second MMR dose to be given at 18 months of age, and a mass catch-up program with monovalent measles vaccine, primarily targeted at school-aged children (primary and secondary school). Both programs are expected to start in February or March, 1996. The objective is to complete the school catch-up program as early as the end of April, 1996. A measles catch-up aimed at preschool children will be carried out only on a 'progressive' basis and could extend up to December, 1996. The campaign is being carried out in collaboration with the Ministry of Education.

Generalized measles rash

Health Canada Santé Canada

Canada

The Yukon and Northwest Territories

Both the Yukon and the Northwest Territories have started (January,1996) a routine two-dose schedule, with a second MMR at 18 months of age.

The two-dose and catch-up programs introduced in some provinces/ territories mark an important milestone in Canada's public health strategy and is in line with the recent National Advisory Committee on Immunization (NACI) recommendations*. With these important steps, Canada now joins the other countries of the Americas in their efforts to eliminate measles in this region of the world. The anticipated Ontario and Quebec catch-up programs immediately will protect over 60% of Canadian school-aged children potentially at risk.

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* *The Supplementary Statement for Measles Elimination in Canada* by NACI follows this article and also appears in CCDR 1996;22:9-15.

Supplementary Statement on Measles Elimination in Canada

*NACI**

Summary

Elimination of indigenous measles by the year 2000 is a highly desirable goal, shared by all countries of the Americas. To achieve it in Canada, a two-dose immunization schedule must be implemented and completed by all children within the next few years. This is best achieved by beginning the routine administration of a second dose of vaccine to a specified cohort of young children and by implementing short-term "catch-up" programs to revaccinate all children over the recommended age for the second dose. Considerable latitude is possible in the design of catch-up programs but common initiation periods among provinces and territories would aid public education activities, facilitate immunization programs and reduce costs through large volume vaccine purchases.

Introduction

Measles is a severe respiratory tract infection frequently complicated by pneumonia, croup, sinusitis, otitis media and febrile convulsions[1]. Nearly one million measles deaths still occur annually in children worldwide[2]. Measles is the most contagious infection of humans, able to spread even when only a small proportion of case contacts are susceptible[3]. The available live, attenuated measles vaccines are safe and effective[4]. Among children vaccinated after the first birthday, about 90% to 95% develop protective immunity.

Experiences of the past decade indicate that outbreaks of measles can occur in populations with virtually 100% vaccination rates[3,5], resulting from spread of virus among the small proportion of children who failed to respond to primary vaccination or, less commonly, who lost protection over time after vaccination. The typical pattern of measles in highly vaccinated populations is one of outbreaks at extended intervals, involving 1% to 5% of school children, with spillover into pre-school children. Control measures, such as exclusion from school and mass revaccination, are disruptive, expensive and of limited effectiveness[6]. The occurrence of outbreaks inevitably causes members of the general public to question the efficacy of measles vaccine.

The administration of a second dose of measles-containing vaccine has been shown to diminish substantially the proportion of susceptible children[7,8], decreasing the potential for outbreaks from imported cases. Countries that have successfully delivered two-dose programs have virtually eliminated indigenous measles[9]. As more countries reach this goal, it becomes possible to envision global eradication of measles, as was achieved with smallpox and is near with poliomyelitis. A major dividend from aggressive efforts to eradicate measles globally will be the opportunity to discontinue measles vaccination programs altogether, sparing future generations from these costs.

In December, 1992, following large outbreaks of measles in several provinces, a National Consensus Conference on Measles was held in Ottawa[10]. Participants endorsed the goal to eliminate indigenous measles in Canada by the year 2005. It was recognized that this would require near universal uptake of the initial dose of vaccine, as well as new programs to deliver a second dose before school entry. NACI subsequently advocated a routine two-dose measles vaccination schedule[11].

In September, 1994, the Federal Health Minister, the Honourable Diane Marleau, resolved (Resolution CSP24R16) with representatives of other nations at the XXIV Pan American Sanitary Conference to eliminate measles from the Americas by the year 2000. To date, competing developments in childhood vaccination programs have pre-empted the formal introduction of two-dose measles programs in Canada. In provinces with physician-based vaccine delivery, some second doses are being given on an ad hoc basis, but such an approach lacks the benefits of an organized program.

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A "laissez-faire" approach was acceptable in 1993 when Canada enjoyed the lowest level of measles activity ever recorded. Only 204 suspected cases were reported (0.7/100,000 population). Three provinces and the territories reported no cases and four additional provinces reported fewer than 12 cases each. The lull ended in 1994 when reports jumped to 523, a 2.5-fold increase. An additional sharp increase has been evident in 1995, driven in part by renewed outbreaks in Ontario. The provisional total to October 31, 1995, exceeded 2,100 cases. This total is about 10-fold greater than for the United States during the same period and represents over 50% of cases reported in the Western Hemisphere in 1995. Other countries in the Americas have recently conducted highly effective mass measles vaccination campaigns or have already implemented routine two-dose programs[9] and are experiencing few cases in spite of heightened surveillance activities. Consequently, the approach taken in Canada to date is overtly the least effective. Sufficient numbers of unprotected children exist in every province to give rise to outbreaks at any time. Mathematical modelling of the Canadian situation predicts that outbreaks involving upwards of 20,000 true cases nationwide are possible.

Recommendations

1. All provinces and territories should make a commitment to eliminate indigenous measles, as recommended by the Measles Consensus Conference and by NACI.

   To do so by the year 2000 would place Canada in step with other members of the Pan American Health Organization (PAHO).

2. A first dose of measles-mumps-rubella (MMR) vaccine should continue to be given to all eligible children, as soon as practicable after their first birthday.

3. A second dose of MMR vaccine should be offered routinely at least 1 month after the first dose, to raise protection rates as high as possible.

   It would be most convenient to link this dose with other routinely scheduled vaccinations. Options include giving it with the next scheduled vaccinations at 18 months of age, or with school-entry vaccinations at 4 to 6 years of age, or at any intervening age that is practicable (such as at entry to day care). Provinces should determine a preferred time for administration of second MMR doses.

4. For the earliest elimination of measles, a second dose of measles vaccine should be provided, as part of special catch-up programs, to all children and adolescents previously immunized under the one-dose schedule.

   Without a catch-up program, giving a second dose only to young children may not eliminate outbreaks for 10 to 15 years, or until after the year 2005, which is inconsistent with the PAHO target.

   Numerous models exist for carrying out catch-up programs[9]. Many PAHO countries have successfully used mass vaccination campaigns lasting 1 to 7 days. The United Kingdom recently achieved 94% uptake among school children over a 4-week period. Other acceptable options would include programs extending over several months or even a few years. In the latter approach, several grade cohorts are vaccinated annually until all children have been included. With extended programs, efforts may be confounded by the occurrence of outbreaks in children not yet revaccinated. However, the success of similar programs in other countries will likely reduce the frequency of imported cases that ignite outbreaks.

   Nevertheless, the faster catch-up programs are completed, the greater their impact will be in preventing major outbreaks.

5. The necessary infrastructure should be included in the design of two-dose programs to maximize their effectiveness.

   Necessary supportive measures include intensive surveillance and rapid reporting of all suspected measles cases; availability of reliable tests to confirm the diagnosis of measles; achievement and maintenance of documented proof of immunization in the entire population at risk; and prompt outbreak control measures designed to prevent spread to susceptible contacts until all susceptibles have received a second dose.

Vaccine Considerations

For routine second doses, MMR vaccine is preferred because a proportion of children will also derive protection against rubella and mumps. In serosurveys carried out at various intervals following routinely administered first doses of MMR vaccine, about 1% to 6% of children vaccinated after the first birthday lacked antibody to rubella[12,13,14] and 3% to 19% lacked antibody to mumps[12,14,15], in addition to the 2% to 12% lacking antibody to measles[12,15,16]. Component-specific failures to respond seldom co-exist in individual children. Most non-responders make and retain protective antibody responses upon revaccination[17], regardless of the antigen in question. Measles vaccination remains highly cost effective even with the addition of a second MMR dose (unpublished observations).

Use of monovalent measles vaccine is acceptable for special catch-up programs, although some benefits would be derived by including rubella and mumps vaccines. Because special catch-up programs involve large target populations, the choice of vaccine is influenced by cost considerations, the limited range of licensed combination vaccines and the age of the population targeted. In Canada, only monovalent measles vaccine and MMR vaccine are currently licensed, although a measles-rubella (MR) vaccine could shortly become available. Monovalent measles vaccine is substantially cheaper than MMR vaccine.

MMR or measles vaccine can be given concurrently with other routinely used childhood vaccines[18], such as diphtheria toxoid, pertussis vaccine and tetanus toxoid (DPT)-based combination vaccines. Separate injections are required, in opposite limbs. The minor adverse effects of co-administered MMR and DPT-based combination vaccines are not additive

because they occur at different intervals following administration. Co-administration of MMR and DPT-based combination vaccines does not overtax the child's ability to mount a normal immunologic response to each component.

Special Considerations for Catch-Up Programs

The principal target group for a catch-up campaign is school children because they had the highest rates of measles in recent Canadian outbreaks and are most readily identified and served. Ideally, all children in grade schools would be included. The upper and lower age limits should be set taking into consideration local disease epidemiology. All age groups through early adulthood contain persons at risk of measles but too few outbreaks in Canada have involved college and university students to recommend their routine inclusion in such programs.

Children who have already received two doses of a measles-containing vaccine at appropriate ages can be exempted if documentation is readily available. When immunization records are incomplete or unavailable, there is no concern about proceeding with immunization because no harm is done by administering measles vaccine to immune individuals.

Catch-up campaigns require extensive education of health professionals and the general public. Promotional activities would be most efficient if uniformity existed among the programs offered by the provinces and territories. Coordination of starting dates may be more crucial than similarity of other program parameters, such as scope and duration. An additional advantage of coordinated programs is the opportunity to reduce vaccine costs through combined large volume purchases.

Adverse Effects of Second Doses of Measles Vaccine

The adverse effects of a primary dose of measles vaccine are described in the *Canada Immunization Guide*[11]. Only 5% to 15% of persons receiving a second dose will experience a "primary take", with the potential to cause the same minor adverse effects seen after primary doses. Older children appear to have less risk of high fever 7 to 10 days following measles vaccination than infants. Older children may complain of transient stinging at the injection site. School-wide vaccination campaigns are unlikely to result in illness symptoms that would increase absenteeism or disrupt academic or athletic programs.

The risk of rubella vaccine-associated arthralgia or acute arthritis, although present, is very low in the age group 5 to 19 years. Acute arthritis is rarely seen in persons vaccinated prior to 16 years of age and affects only occasional vaccinees aged 17 to 25 years, after which it becomes more frequent, particularly in women. Only 1% to 6% of revaccinated children will experience vaccine-induced primary infection with the attendant possibility of adverse effects.

Precautions and Contraindications to a Second Dose of Measles Vaccine

Administration of live, attenuated measles vaccine is contraindicated in persons of any age whose immune system is impaired by disease or medication.

Measles vaccination is, nevertheless, indicated for most infants infected with the human immunodeficiency virus (HIV), whose immune function at 12 to 15 months of age is compatible with safe MMR vaccination[19]. Second doses of measles vaccine should also be safe later in the second year of life and are recommended. The safety of doses at later ages is uncertain because immune function can be expected to decline with age.

Children who had a true anaphylactic reaction to their first dose of MMR vaccine should not be revaccinated. Persons with anaphylactic hypersensitivity to hen's eggs may rarely react to the small quantity of ovalbumen-like protein in measles vaccine[20]. Allergy to eggs is often outgrown and is rarely reported as a life-threatening condition among school-aged children. Children who safely received a first dose of MMR vaccine in spite of having evidence of being allergic to eggs at the time should be at minimal risk of anaphylaxis with a second dose. Similarly, "egg-allergic" children who tolerate small quantities of egg in foods are at minimal risk of anaphylaxis with vaccination. Therefore, skin testing for MMR allergy is not required for second doses of the vaccine. Whenever vaccines are administered, it is prudent to ensure that all children are supervised for at least 15 minutes afterward and that treatment can be instituted promptly if signs of anaphylaxis develop[21,22].

Fever $\geq 39.4^{\circ}$ C occurs in 5% to 15% of young children following measles vaccination and a small proportion of these children have febrile seizures. Fever as a result of vaccination is restricted to susceptible subjects so the risk of seizures with a second dose of measles vaccine is very low. The risk is further reduced when the second dose is given to children of school age because susceptibility to simple febrile convulsions subsides after 5 years of age.

Immunization should not be delayed because of minor illness, with or without mild fever. This is particularly relevant for school-based campaigns, when a proportion of children will inevitably have cough or cold symptoms. The response to vaccination is not impaired in subjects with concurrent mild infections[23,24].

A consideration in targeting adolescents and young adults for vaccination with live virus vaccines is the possibility of pregnancy, a contraindication to vaccination. Pregnant persons should be given the opportunity to refuse vaccination. In the event that measles vaccination is administered to someone subsequently found to be pregnant, it is reassuring to know that no clear evidence of teratogenicity exists in spite of 25 years of experience with this vaccine[25]. Active screening for pregnancy prior to administering monovalent measles vaccine in large campaigns is not essential. The teratogenic potential of RA27/3 rubella vaccine is of more concern, but studies in accidentally exposed women indicate an observed risk of fetal injury of 0%

and a theoretical maximum risk of 2%[26]. Pregnancy screening protocols should be developed if MR or MMR vaccine is targeted for use in age groups likely to be sexually active.

Large-scale catch-up campaigns inevitably attract public and media attention, warranting careful explanation of benefits and risks. NACI and the Laboratory Centre for Disease Control pay close attention to reports of rare, serious adverse events following administration of vaccines. No substantiated evidence exists to support speculation that measles vaccine can cause Crohn's disease or Guillain-Barré syndrome (GBS). None of 63 cases of GBS reported in Canadian children since 1991 had been vaccinated within the previous 30 days. The Institute of Medicine in the United States[27] concluded that evidence was inadequate to accept or reject a causal relationship between measles vaccination and encephalitis, subacute sclerosing panencephalitis, optic neuritis, transverse myelitis, GBS, and diabetes mellitus.

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An Outbreak of Measles in a Secondary School/Day-Care Complex, York Region, Ontario, May-June, 1995

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The York Region Public Health Department received notification on May 18, 1995, from a secondary school of a student's absence reportedly due to measles infection. Investigation by the Health Department revealed that the case had been ill 4 to 5 days prior to the onset of the rash, but attended school for 1 1/2 days before the rash appeared on May 17. At that time the case presented to her family doctor with a rash, fever, cough, conjunctivitis, and coryza. She had no known contact with a case of measles, but was aware of a case in track and field athlete a week earlier at the school, that was widely publicized.

Upon notifying the school of the outbreak control process which would be undertaken by the health department, it was revealed that there was knowledge of a case that had occurred the previous week. Follow-up revealed that this case, later determined to be the Index Case, had been clinically diagnosed on May 3, 1995, and had been mistakenly reported to a neighbouring public health unit causing a delay in the follow-up at York Region Public Health Department. The case had no known contact with a case of measles, but lives in the area of Nobleton where an outbreak in a local elementary school from April 15 to 20, 1995, involved nine cases. Only one other outbreak in the region had been reported at another secondary school, involving one student who developed measles on April 24, 1995. These two cases were laboratory-confirmed IgM present and had been immunized after their first birthday.

By the end of the outbreak, which spanned 6 weeks and three generations of cases, a total of eight cases of measles occurred in the school. Five were laboratory-confirmed. Everyone had been immunized with measles-mumps-rubella (MMR) after their first birthday.

Immunization Coverage and Action Taken

This secondary school has a total of 1,152 students ranging from 14 to 21 years of age. The overall MMR coverage was 95.5%. Five students had documented exemptions to immunization because of prior immunity and there were no religious or conscientious exemptions. The remaining 47 students were classified in the exclusion category because no documented immunization records or evidence of prior immunity were on file for them with the health department. All the students in this category were over 18 and records were not sought due to the age restriction dictated by the Immunization of School Pupils Act.

Under the York Region Health Department Policy and Section 22 of the Health Promotion and Protection Act, exclusion was enforced affecting students and any school staff born after January 1, 1957, who could not provide documentation of immunization or immunity. Eleven students and 38 staff members were eligible for exclusion.

Of the 11 students, five (45%) provided documented dates of MMR immunization and six (55%) received immunization at their physician's office. Only 10 of the original 11 students were excluded, eight losing one school day and the other two losing 2 and 4 days, respectively, for a total of 10 student days lost.

Of the approximately 107 staff, 38 were born after January 1, 1957, and were required to submit proof of immunity. Thirty (79%) of those evaluated were able to provide documentation of MMR history, and seven (18%) received MMR at their physician's office. Only one staff member chose to have her immunity assessed serologically rather than be reimmunized. Of the original 38 staff members, a total of seven were excluded for 1 or more days with a loss of 18 work days, the most being 8 days lost by the staff member who had measles antibody levels done.

A day care is also located on the same property, and housed within the same building as the secondary school affected. A total of 49 full and part-time children attend this day care with 10 full-time staff running the facility. Of the children attending the day care, two children belonged to teachers and two to students of the secondary school. It was, therefore, established that there was significant contact between the student population and the day care.

Evaluation of the immunization status of the children revealed five babies < 1 year of age who had no measles immunization, and five toddlers of the remaining 44 who did not have proof of immunization on file. Monovalent measles vaccine was used to immunize these five infants. The immunization history of the five toddlers was individually reviewed by the day-care supervisor and all were assessed to be up-to-date.

Of the 10 staff members, all provided proof of immunization.

No exclusions took place in the day care, and no days were lost by either staff or children. By June 16, no cases of measles had developed in the day-care population.

We estimate that a total of 45 hours of professional nursing staff time was required to investigate and manage this small outbreak.

Measles in Canada, 1995 (as of December 27)

Paul Varughese, Division of Immunization, Bureau of Infectious Diseases, LCDC, Ottawa

From January 1 to December 27, 1995, a provisional total of 2,301 measles cases (7.9/100,000 population) has been reported in Canada. This is 4.4 times greater than the 517 cases reported for the same period in 1994, and 11 times greater than the number reported for 1993 (204). Following remarkable increases in the number of cases in April and May, the incidence peaked in June with 854 cases, followed by a sharp decline in July with 260 cases. Data since July show a downward trend, although the reporting is less likely to be complete. Only 16 cases were reported in November, followed by an additional eight cases as of December 27. Sixty-nine percent of the cases were reported as outbreak-associated.

During the past 12 months, seven of the 12 provinces/ territories reported measles activity and the number of cases has ranged from one to 2,253. Ontario has accounted for the majority of cases (98% or 21/100,000 population) reported in Canada. No deaths linked to measles have been reported in 1995.

In Ontario, measles activity has been wide spread: 36 (86%) of the 42 health units have reported cases, ranging from one to 438, the highest number being reported from the Peel Health Region — population approximately 788,000. The Peel Region has experienced measles transmission since mid-January. Four Health Regions (Peel, Sudbury, Hamilton, and Haldimand), representing 15% of the population, accounted for 61% of the cases, with the highest incidence (205/100,000) being reported from the Sudbury Region (population 209,000).

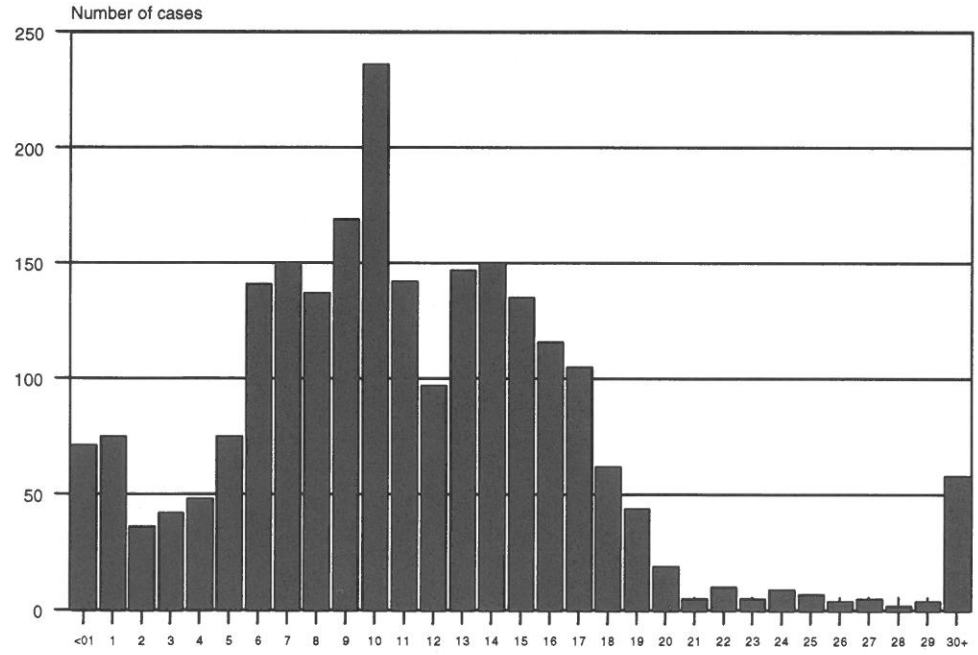
Confirmation Status

Of the 2,242 case records reviewed, 1,177 (52.5%) were laboratory-confirmed: 577 of these were specified as "positive for IgM" and the remaining cases as "laboratory-confirmed". Other cases were reported as "clinically compatible"; almost half of the cases in this group were also reported as "epidemiologically linked to laboratory-confirmed cases".

Age Distribution

Cases were distributed in all age groups (Figure 1); the median and mean ages were 10 and 11.1 years, respectively. School-aged children (5 to 19 years) accounted for 83% of the cases. Among this group, the highest proportion of cases was represented by those 10 to 14 years old (33.2%), followed by those 5 to 9 (29.5%) and those 15 to 19 (20.6%). Children aged 10 years accounted for the highest proportion of cases (9.8%), followed by 9-year-olds (7.4%). Seventy-one cases were infants < 1 year of age. Nineteen cases were > 38 years of age (born before 1957).

Figure 1
Reported Cases of Measles by Age, Canada, 1995*



* Provisional data to December 27

Vaccination Status and Preventability

Almost 90% of the 2,092 cases reviewed had a documented history of measles vaccination with one dose of vaccine; over 91% of these cases received their vaccination between 1980 and 1994.

The vaccine refusal group was small. Of those in the vaccine-eligible age group, but unvaccinated, the reported reason for "no vaccination" included "personal exemption" (17 cases) and medical contraindication (two).

Based on age only, 90 cases (3.9%) were not eligible for vaccination, i.e., they were born before 1957 (19 cases) or were < 12 months of age (71). Immunization status was "unknown" or "unavailable" for 101 cases (4.5%).

Comments

Ongoing circulation of measles virus in 1995 was confined to Ontario — population approximately 10.9 million — with fairly extensive spread in some health regions.

Over 83% of the cases have occurred among school-aged children (5 to 19 years). Median age for the cases during the year remained constant, around 10 years. No college- or university-based outbreaks were reported in Ontario or elsewhere in Canada.

In 1995, Canada has accounted for over 52% of the cases reported in the Americas, although it represents only 3.6% of the total population.

Experience in Canada and other countries strongly suggest that *one-dose* measles strategy is inadequate to protect all children; an alternative universal two-dose strategy, supplemented by a catch-up immunization program, is necessary for efficient and cost-effective measles control and elimination in Canada.

Over the years, demand for necessary alternative strategies has escalated, and increased more recently, especially in view of the epidemiology of current measles outbreaks in Canada. Consequently, NACI recently issued a *Supplementary Statement for Measles Elimination in Canada*, which is found in this issue of *Measles Update*.

Acknowledgment

The assistance and co-operation of all provincial and territorial epidemiologists, medical officers of health and other health care personnel, and staff from LCDC, is greatly appreciated.

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 Division of Immunization, Bureau of Infectious Diseases, LCDC, Ottawa, Ontario, K1A 0L2; telephone (613) 957-1340; Fax (613) 998-6413.

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