MEASLES *update*

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MEASLES IN CANADA, 1994 (as of June 8)

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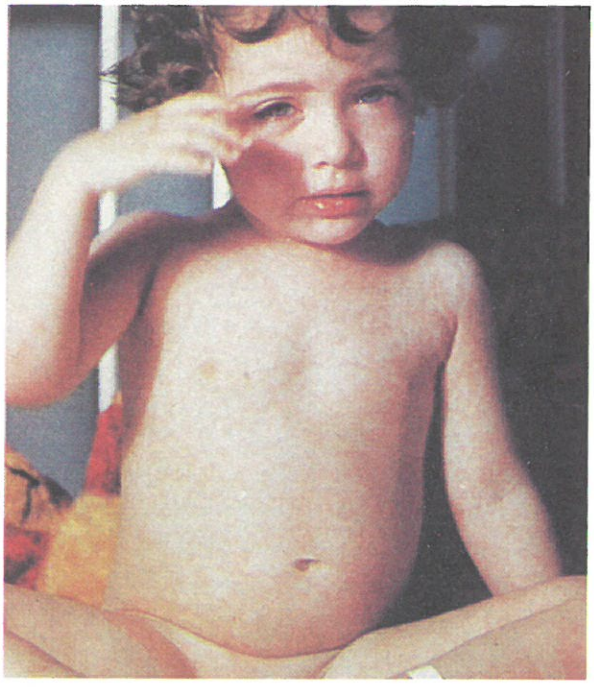
From January 1 to June 8, 1994, a provisional total of 122 measles cases has been reported in Canada. This is higher than the 109 cases reported for the same period in 1993. Over 75% (97 cases) of these cases were reported from Ontario. No cases have been reported from Newfoundland, Prince Edward Island, the Yukon and the Northwest Territories.

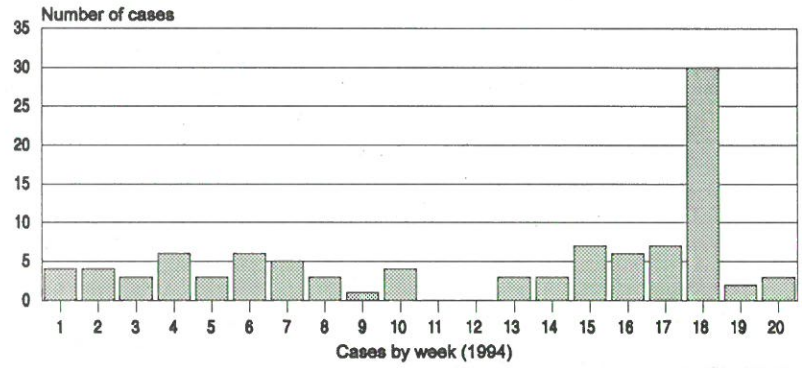
Although several Ontario health regions have reported sporadic cases, the Middlesex-London Health Unit accounted for 45 (46%) of the 97 cases; all 45 were associated with an outbreak in a secondary school (see second article in this issue for details on this outbreak).

Case-by-case information for certain epidemiologic variables is presently available for 103 of the 122 cases. Figure 1 shows the distribution of these cases by week of onset since January 1994. Cases occurred in all weeks, except the last 2 of March. The highest number of cases (30) was recorded for the 2nd week of May. It is likely that, due to the delay in reporting of some cases, the true incidence for the more recent weeks could be higher than is shown in Figure 1. The reported incidence by month for the current period (January 1 to May 30, 1994) is similar to that for the same period in 1993, and is substantially lower than that for 1992. Cases ranged in age from 6 months to 36 years, with the median being 13 years. The highest proportion (38%) of cases occurred among those aged 15 to 19 years; the next highest (21%) in children 5 to 9 years. Infants under 1 year of age accounted for 8 cases (7.8%) (Figure 2). No deaths have been reported.



Generalized measles rash

Figure 1
Reported cases of measles by week, Canada, January 1 to May 30, 1994



Provisional Data; EPIC Data Base

Immunization Status

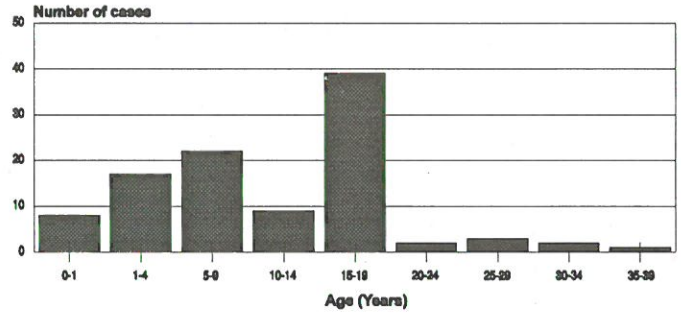
Of the 103 cases, 95 individuals were eligible for measles vaccination, i.e., they were born after 1957 and were older than 12 months of age. Seventy-seven (81%) of this vaccine-eligible group had a documented history of immunization — not surprising because of high immunization coverage with a vaccine with less than 100% efficacy.

Comment

Although remarkable reduction in the incidence of measles has been seen in Canada in recent years, the disease continues to occur in many parts of the country. Occurrence is characterized by sporadic cases, or clusters of cases in small foci or small outbreaks, often involving vaccinated individuals. Examination of available vaccination histories indicates that a few cases had received the vaccine before their first birthday.

Measles rash in an adult

Figure 2
Reported cases of measles by age, Canada, January 1 to May 30, 1994



Provisional Data; EPIC (Data Base)

Because people tend to move frequently, the precise source of infection in many cases is unknown.

Case-by-case information is extremely valuable for understanding the current epidemiology of measles and targeting specific strategies for its prevention and control.

Acknowledgements

The assistance and cooperation of all provincial and territorial epidemiologists, as well as Ms. Carole Scott, Ms. Mary-Jane Garnett and Mr. John Koch from LCDC are greatly appreciated.

MEASLES OUTBREAK AT A SECONDARY SCHOOL, LONDON, ONTARIO
March–June, 1994

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During the spring of 1994, 45 cases of measles occurred at the Sir Frederick Banting Secondary School in London, Ontario. The school has a student population of 1,424, ranging in age from 14 to 20 years. One isolated case (index), initially reported on April 5, was a female student with date of onset of clinical symptoms on March 30. The source of infection for this case was not identified; however, 2 weeks earlier, this student had been travelling in Turkey with other students during the "March Break". On April 18, the Middlesex-London Health Unit became aware of 3 more cases with onset of illness on either April 11 or 12. A meeting was immediately convened by the Medical Officer of Health and an outbreak of measles was declared. A meeting was also held with the Principal of the school and outbreak control strategies were implemented.

A letter, co-signed by the Medical Officer of Health and the Principal, was sent to all families of students to advise them of the situation. Immunization records of all students were screened to identify students at high risk. Students with a history of immunocompromising illnesses were immediately advised of the outbreak.

Screening of measles vaccination status identified 4 (0.3%) students who had no history of MMR and 4 (0.3%) with MMR administration prior to 12 months of age. A school immunization clinic was held on April 21 and MMR was offered to these students plus any others with inadequate information on their health cards to assess MMR status. A total of 28 (2%) students were immunized, including the 8 identified above. Despite these strategies, cases of measles continued to occur at the school, with peak onset occurring between May 6 and May 14 (Figure 1). All cases, including the index case, had been immunized according to the current immunization recommendations.

The last reported onset of a case was on June 8. The overall attack rate in the school was 3.2%.

Figure 1 shows the distribution of cases by date of onset. The highest frequency (8 cases) was reported on May 11. Twenty-three (51.1%) of the 45 cases were females. The ages ranged from 15 to 20 years (mean: 17 years) (Figure 2). Seven of the 45 cases were laboratory-confirmed (IgM positive) and the others were epidemiologically linked.

Fifty-two exchange students from France were at the school in April. To the knowledge of school authorities, none of these visitors became ill. Two Sir Frederick Banting students became ill with measles during a school trip to Washington, D.C. Another student became ill during a weekend camp for military cadets, all from London. To the knowledge of their leader, none of the other 30 cadets attending the camp became ill.

During this same period (March 30 to June 8), one case of measles occurred at the H.B. Beal Secondary School (student population — 2,270), located approximately 6 km from the Banting School. This case had exposure to a case in the Banting School.

Figure 1

Distribution of measles cases by date of onset, London, Ontario, March 30 to June 8, 1994

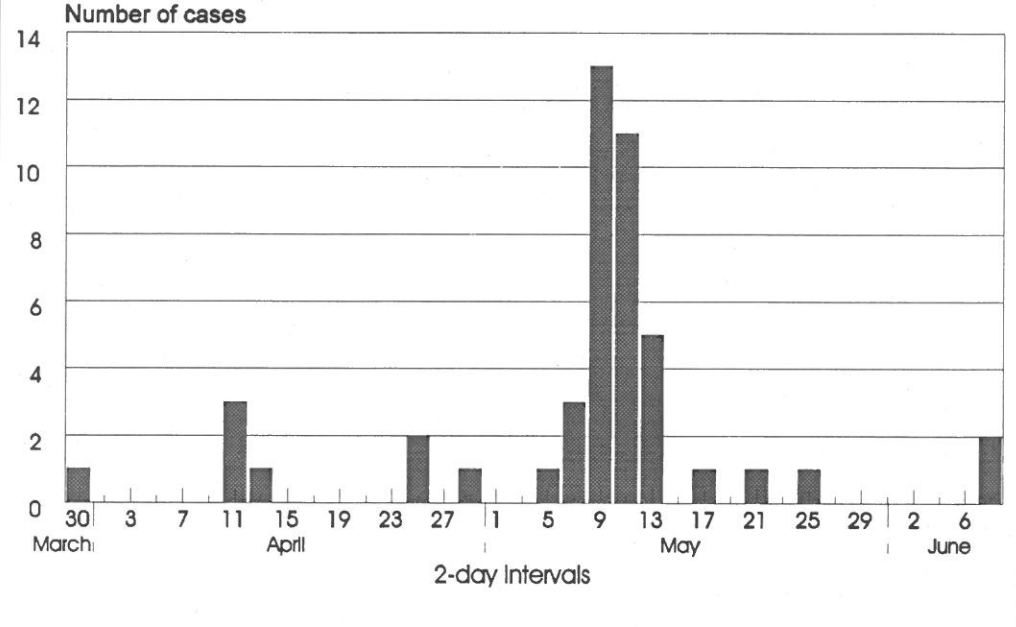
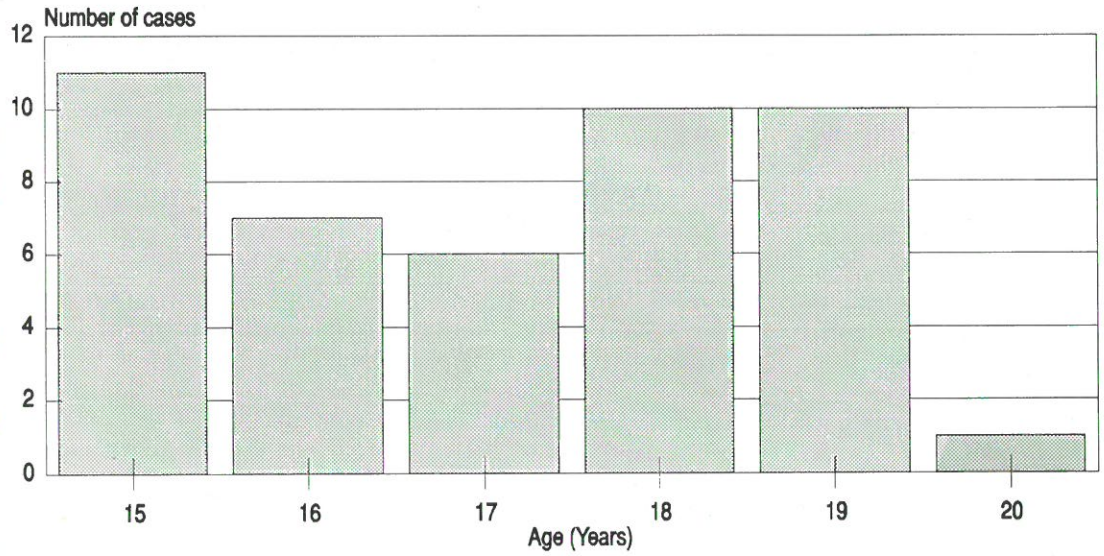


Figure 2

Age distribution of measles cases, London, Ontario, March 30 to June 8, 1994



Maculopapular, haemorrhagic and confluent measles rash

Acknowledgement

The assistance and cooperation of Middlesex-London Health Unit staff and officials at the Sir Frederick Banting and the H.B. Beal Secondary Schools, and the Ontario Ministry of Health are appreciated.

Editorial Comment

The occurrence of this outbreak in a population having 99.7% vaccine coverage with one dose of measles vaccine emphasizes that similar incidents can happen any place in Canada with the current routine 1–dose schedule. It is noteworthy that all cases in the current outbreak, including the index case, had a documented history of measles vaccination and there were no cases among children less than 14 years of age.

This outbreak probably was linked to an imported case, although the precise source is not known. The threat of importation will continue as long as measles virus is circulating in other parts of the world. Such importations and import-related cases have been documented as a continuing source of reported measles in the United States. Similar documentation on imported cases is lacking in Canada. In order to minimize the impact of importing the disease, it is essential that all Canadians are immune.

The National Advisory Committee on Immunization recommends that travel to areas with high measles incidence is an opportune time to review immunization status and to ensure travellers have adequate measles immunization according to the current recommendations[1].

We welcome reports like the one above — whether they involve small or large numbers of cases or whether the investigations are preliminary or final. Such information is valuable information for all public health practioners across Canada.

Reference

1. National Advisory Committee on Immunization. *Measles vaccine*. In: *Canadian immunization guide*. 4th ed. Ottawa, Ont: Health Canada, 1993:70-77. (Supply and Services Canada, Cat. No. H49-8/1993E).

CHILDREN'S VACCINE INITIATIVE*

Ad Hoc Committee on an Investment Strategy for Measles Control
Bellagio, Italy
March 15-19, 1993

Measles, a viral exanthem of childhood, is the most contagious infection of man. Global vaccination coverage with live attenuated measles vaccine in children less than 1 year of age is currently estimated to be 78%. Immunization programs worldwide now prevent over 1.5 million deaths from measles in developing countries. Yet over 1.1 million children continue to die each year from measles - a preventable and potentially eradicable disease. Measles and its complications are responsible for more children's deaths worldwide than from all other childhood vaccine-preventable diseases combined, and more than from any other single, specific, infectious agent.

In developing country settings, particularly those with the highest rates of infant mortality, the case-fatality rate of acute measles infection ranges from 3% to 15%. In a given area, this rate is affected by age (highest in children when they contract measles early in life) and socioeconomic status. Socioeconomic status encompasses a number of potentially interacting risk factors: heavy disease burden in the community from a number of other infectious diseases, nutritional status (especially marginal vitamin A levels) of the infected person, crowding and intensity of exposure, and access to appropriate supportive care. In addition to the substantial morbidity and mortality from an acute measles infection, morbidity and mortality continue to occur after the acute measles infection has resolved. This stems from measles involvement of the respiratory and gastrointestinal tracts and cells of the immune system and may predispose to pneumonia and diarrhea, which often further contribute to underlying malnutrition.

This highlights the need to re-examine current tools and strategies and to identify areas where investments will most effectively strengthen measles immunization programs and provide the knowledge base that will increase the effectiveness of measles control efforts.

The undersigned, experts in measles epidemiology, virology, immunology, health economics and measles control, having considered available approaches to achieve the containment and ultimate global elimination of measles, recommend the following balanced program of activities.

1. Improve and expand the use of current live-attenuated measles vaccines in children for measles control

This recommendation is based on the recognition of the safety record of these vaccines, given to millions of children around the world over the past 30 years. They are demonstrated to be effective when administered at an age when neutralizing maternal antibodies acquired in utero no longer render the vaccine ineffective. In settings where 90% or more of children at 9 months of age and older have been immunized against measles, measles morbidity and mortality have been reduced to very low levels. The impact of the measles vaccine also extends beyond the vaccine recipients. In communities where these high rates of coverage have been achieved, infants younger than this scheduled age of immunization have also been protected from measles, the result of the reduction of measles transmission in the community. Furthermore, as measles infections predispose to a number of secondary infections that add substantially to infant and childhood morbidity and mortality, the full impact and cost effectiveness of measles prevention extend well beyond that of the acute measles infection alone.

2. Support the development of a new measles vaccine — from basic and applied research to product development

While it appears technically feasible to achieve country-by-country elimination of measles using currently available vaccines, the extreme contagiousness of the measles virus, its ubiquitous distribution, and the barrier to early vaccination posed by maternal antibody make measles eradication a more difficult challenge than the smallpox eradication effort was or the poliomyelitis eradication effort is likely to be. Needed is a vaccine that is safe for young infants, is not neutralized by maternal antibody, and induces immunity equivalent to the currently used live-attenuated vaccines. A measles vaccine that is effective earlier in life can close the "window of susceptibility" — the interval between the waning of transplacentally acquired, maternal anti-measles antibody and successful vaccine-induced immunity. Since administration of vaccines closer to birth facilitates achievement of higher coverage rates in immunization programs, the availability of such a vaccine for measles will further the goal of improved measles control. In addition, if new measles vaccines are less dependent upon the cold chain, they will also facilitate global measles immunization program goals by reducing both the complexity and cost of vaccine delivery and administration.

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* *Children's Vaccine Initiative (CVI) is sponsored by The United Nations Children's Fund, The United Nations Development Programme, The Rockefeller Foundation, The World Bank, and WHO.*

3. Implementing a balanced investment strategy

Achievement of this balanced strategy will require the mobilization of new resources — financial and personnel — to strengthen and rebuild an evaluation, research and development capacity for measles control. Needed are operations research and cost-effectiveness analyses on vaccination strategies, which are appropriate to specific country and epidemiologic situations, that will guide the optimal use of these vaccines. Special emphasis should also be focused on the most vulnerable groups in developing countries: infants and children with the severest manifestations of measles.

Also needed is a sharp increase in the scientific understanding of the molecular biology and immunology of measles to explain the acute and delayed effects of natural measles infection. Defining the underlying immunopathological mechanisms responsible for the adverse effects of previous alternative measles vaccines should preclude these adverse effects in a new vaccine. An animal model has recently reaffirmed that a measles-like illness in monkeys can be caused by wild-type, but not vaccine, strains. Animal models coupled with the recent advances in immunology and virology offer the potential to unravel the immunological effects of both measles infection and measles vaccines. They will also provide experimental systems to evaluate more rapidly the safety and efficacy of new measles vaccine candidates developed in partnerships with industry. Currently, a candidate-vectored, measles vaccine approach that may bypass the barrier of maternal antibody is being tested. Other vaccine researchers and developers are also actively exploring the feasibility of a variety of alternative approaches to early measles immunization.

A commitment to a balanced investment strategy for measles control should not, in any way, be construed as weakening the global community's resolve to optimally use available measles vaccines in an all-out effort to control measles. Dedication to this overall effort is a trust held by this generation. Success will benefit generations of children for all time to come.

Recommendations from Bellagio: The measles agenda for the next decade

The CVI Ad Hoc Committee on an Investment Strategy for Measles Control strongly recommends that national and international agencies increase investments in measles research and control efforts according to the following priorities.

Basic science

Immunology

- Define the components and mechanism of durable protective immunity.
- Define the mechanism of the immune response to the measles virus.

Virology

- Define the structure function of measles virus, in particular, the genetic characteristics and attributes distinguishing attenuated and wild (virulent) types of measles virus.
- Achieve infectious clone technology.
- Define and characterize the cellular receptor(s) for measles virus.

Clinical studies

- Define the mechanism of post-measles immunosuppression.
- Define the role of co-factors in enhancing or protecting against severe measles (e.g., nutritional status, concurrent infections, intensity of exposure).
- Assess the immunological effects of early administration of licensed measles vaccines.

Animal studies

- Establish models for study of
  - Measles virulence and pathogenesis
  - Post-measles immunosuppression
  - Atypical measles
  - Existing vaccines and vaccine candidates.

Vaccine development

- Test existing vaccine candidates in animals (see above) and, when appropriate, human subjects.
- Explore the feasibility and efficacy of alternate routes of vaccine administration.
- Develop new vaccine candidates that
  - Bypass maternal antibody
  - Can be given by oral route
  - Are safe and highly efficacious
  - Are heat stable.

Epidemiology and Operational Research on Control Strategies

- Assess the full contribution of measles infection to overall infant and childhood mortality and the impact of measles vaccination on children's health, especially in developing countries.
- Establish global surveillance on measles strains, including surveillance of the molecular changes of measles virus strains over time.
- Establish prospective studies to identify risk factors for severe measles and post-measles immunosuppression.
- Strengthen operations research in diverse settings to establish cost-effective strategies for measles control and/or elimination.

- Assess the hypothesis that individuals who are immune (due to prior vaccination or wild-type measles infection) may contribute to the chain of measles transmission.
- Monitor the effect of HIV infection on measles control efforts.
- Support seroepidemiological studies, including the development of a simple, rapid, and accurate field diagnostic test.
- Promote multidisciplinary field studies at developing country sites.

Suggested Reading

The following is the abstract from an excellent article in a recent issue of the ***American Journal of Epidemiology*** *(1994;139:77-90).*

Outbreaks in Highly Vaccinated Populations: Implications for Studies of Vaccine Performance

Paul E.M. Fine and Elizabeth R. Zell

Most of the factors associated with the failure of a vaccination to provide protective immunity are not distributed uniformly or randomly within populations. This paper explores the extend to which a nonrandom distribution of vaccination failures and the selection of exceptional situations for investigation may influence estimates of vaccine performance. The authors show that outbreak investigations will tend to underestimate vaccination efficacy, and that the extent of underestimation will be related directly to the size of the epidemic triggering an investigation, the vaccination coverage in the community, and the extent of clustering of vaccination failures in the population; it will be related inversely to the size of and contact intensity within the investigated community. These potential sources of bias are not the only problems that arise in estimating vaccine efficacy, but they should be taken into consideration when analyzing and interpreting outbreak situations. The fact that outbreak investigations carried out within the United States during the past decade have provided estimates of measles vaccination efficacy on the order of 95% is consistent with a somewhat higher overall "true" efficacy of current vaccines and procedures in the total population. It is important to understand better the frequency, distribution, and risk factors for vaccination failures in populations.

Upcoming Event

National Conference on

IMMUNIZATION IN THE 90s CHALLENGES AND SOLUTIONS

The Hilton Hotel, Quebec City, Quebec

For information and registration packages, please contact:

Chuck Schouwerwou
Conference Coordinator
Childhood Immunization Division
Tel.: (613) 957-1352
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Financial aid is available.

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