Health Canada Santé Canada

Update: Vaccine-Preventable Diseases

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Vaccine Safety Notes

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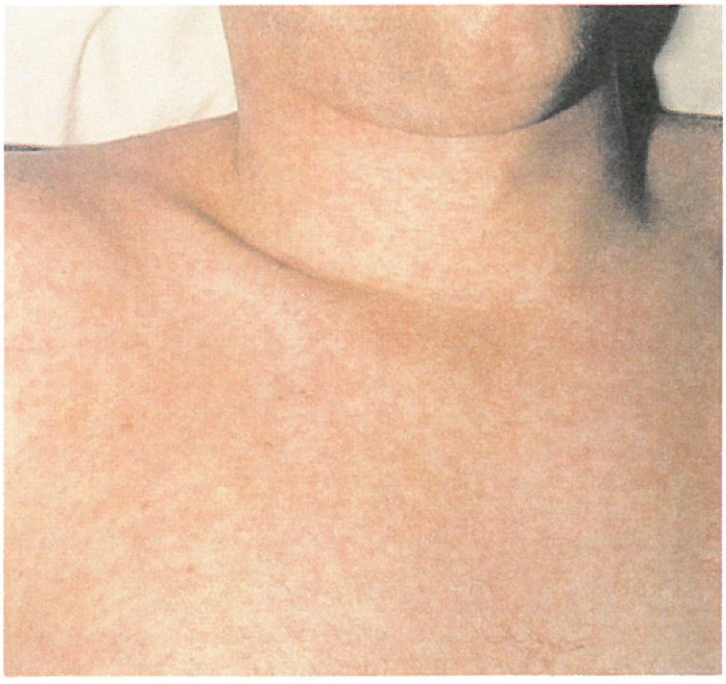
This column is being introduced as a regular feature in the *Update: Vaccine-Preventable Diseases*. Its purpose will be to highlight news and issues of significance regarding the safety of vaccines in routine use in Canada. All vaccines available in Canada have undergone rigorous evaluations for safety and efficacy, and of all drug products approved in this country, vaccines are among the safest. However, by their very nature, vaccines can have side effects. In addition to those that are expected from pre-licensure clinical trials and by experience with similar products already in use, vaccines are continually monitored while on the market for any emerging safety concerns. Public health nurses, physicians, patients and provincial and territorial authorities are monitoring vaccines. Case reports of events thought to be related to a vaccination are submitted through each province and territory for aggregation and analysis at the national level, as part of routine postmarket surveillance activities similar to those in place for other drug products in Canada and internationally. Canada also has an active surveillance project through pediatric hospitals to detect the rare serious adverse reactions that may occur from time to time. Partners around the world are involved on a regular basis, in surveillance efforts regarding the safety of immunizing agents. Each partner contributes to the global monitoring of vaccine safety with similar as well as more specialized surveillance activities.

Ensuring vaccine safety is the concern and responsibility of both vaccine providers and consumers. At the same time, communicating any vaccine safety concerns and suggested actions and remedies is vital. The *Update* can only reflect on prior experience and bring news on events that have already taken place. Any serious concerns will already have been dealt with and information disseminated as appropriate. However, this new column can serve to bring news and updates from programs monitoring vaccine safety and provide an ongoing forum for discussion of emergent safety issues that affect immunization programs at an operational level. The scope of issues covered will include the following:

- Vaccine-Associated Adverse Events database
- Immunization Monitoring Program Active (IMPACT) surveillance project



Generalized rubella rash. The diffuse maculopapular rash can be difficult to differentiate from a measles rash and may occur in other viral infections.
Courtesy of Dr. Noni MacDonald

Canada

- Issues from case report evaluations by the Advisory Committee on Causality Assessment
- Issues of current interest from international partners
- Issues of major interest and impact from the literature

Naturally, contributions for this column are most welcome, as they are for the *Update* in general. Of special interest are notes about the challenge of vaccine risk communication – an area that is receiving more and more attention. The book *Your Child's Best Shot - A parent's guide to vaccination*[1] published by the Canadian Paediatric Society was, among other reasons, intended to fill a major gap in the information on vaccination available to parents and patients. Immunization information to this point was either too simplistic (brochures and handouts), too complex or too difficult to obtain (literature). This book, however, is not the end point. The onus is still on all parties involved in immunization delivery to make sure that information on vaccination is provided in a balanced, timely and appropriate manner.

The communication of vaccine risks and benefits is a difficult but essential task. All those involved in immunization delivery programs have a genuine desire to prevent suffering from vaccine-preventable diseases while avoiding side effects of vaccination. At the same time, any information on risks associated with vaccines must be made available to the public in a format that can be used to make an informed decision about vaccination. For providers of vaccines, this can be a difficult task. Despite the fact that the risk of disease, if not in Canada then in other parts of the world, far overshadows the risks associated with vaccination, groups who oppose immunization openly, challenge the wisdom of vaccinating and disseminate misleading and sometimes incorrect information to a public that has little access to more balanced readings. In a growing spirit of openness, all parties should subscribe to high moral and ethical standards in the dissemination of vaccine safety information. These standards are vital to the continued success of vaccination programs in reducing or eliminating vaccine-preventable diseases.

Reference

1. Canadian Paediatric Society. *Your child's best shot - A parent's guide to vaccination.* Ottawa: Canadian Paediatric Society, 1997.

Preliminary Report

Childhood Vaccination Coverage Levels in Canada, 1994-1997: Progress Towards National Targets

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Since 1994, the Division of Immunization, at the Laboratory Centre for Disease Control, has assessed vaccination coverage among 2-year-old children in Canada through annual mail surveys which have previously been described[1,2]. In 1997, in addition to coverage among 2-year olds, the first coverage assessment by the seventh birthday was carried out to evaluate the progress towards national targets for childhood vaccination coverage. National targets for up-to-date vaccination have been set for each of diphtheria, tetanus, poliomyelitis, mumps and rubella as 97% coverage by the second birthday and 99% coverage by the seventh birthday by 1997[3]. Additional targets have been set for *Haemophilus influenzae* type b (Hib) conjugate vaccine (97% coverage by the second birthday by 1997), measles (97% coverage by the second birthday by 1997 and 99% coverage by the seventh birthday by 2000) and pertussis (95% coverage for pertussis for both age milestones by 1997). This report summarizes the results of the 1997 National Vaccine Coverage Survey. Two sets of coverage estimates for the eight routinely recommended childhood vaccines are provided for 2-year olds (1994-1995 birth cohort) surveyed in 1997; coverage *at 2 years of age* for comparison with previously surveyed cohorts, and coverage *by the second birthday* for assessing the national targets for vaccination by the second birthday (Table 1). Estimates for 7-year olds (1989-1990 birth cohort) are only based on vaccinations received *by the seventh birthday* (Table 2).

Coverage among 2-year olds: For most vaccines, coverage levels *at 2 years of age* in the 1994-1995 birth cohort are similar to levels previously reported for the 1993-1994 cohort[2]. However, the coverage for polio is lower than for all four cohorts previously surveyed. As well, the current polio coverage level is comparable to that for diphtheria, tetanus and pertussis contrary to higher polio coverage levels previously documented. A likely explanation for the current finding is the general switch from oral polio vaccine (OPV) to inactivated polio vaccine (IPV) in 1994-1995 in almost all the provinces and territories. In most cases IPV is formulated and administered with pertussis-containing vaccines and therefore its uptake is influenced by uptake of the latter. As with previous cohorts, the highest coverage is for one-dose measles vaccination, along with mumps and rubella. However, approximately 2% of children in the 1994-1995 cohort received their first-dose measles vaccination prior to their first birthday, contrary to current recommendations and similar to previous findings. Coverage for the Hib conjugate vaccine has only increased marginally from that for the 1993-1994 cohort. Possible contributing factors to the low level of up-to-date coverage include the effect of low pertussis uptake as well as poor or inaccurate record keeping of Hib vaccination at least in the early stages of its introduction into the infant schedule.

Table 1
National estimates of vaccination coverage at 2 years of age, Canada, 1994-1997

Vaccine (# of doses)	Percent coverage by birth cohort*					
	1990-1991	1991-1992	1992-1993	1993-1994	1994-1995	1994-1995 (by 2nd birthday)
Diphtheria (4)	84.7	84.0	84.4	87.1	86.8	84.2
Pertussis (4)	80.1	81.6	82.9	84.8	85.2	83.0
Tetanus (4)	82.0	82.5	83.9	85.9	85.1	82.9
Polio (≥ 3)	89.7	89.0	87.4	89.9	85.8	85.3
Measles (≥ 1)§	96.1	97.2	96.2	97.0	96.0	95.1
Measles (≥ 1)¶			91.4	93.3	94.1	93.0
Mumps (≥ 1)	92.8	93.6	96.0	96.8	95.9	95.1
Rubella (≥ 1)	93.0	94.4	96.0	96.7	95.9	95.0
Hib (4)			54.6	69.3	73.7	71.5

* 95% confidence limits range between ± 1% to 5%.
§ Coverage based on measles vaccine dose(s) received at any time.
¶ Coverage based on measles vaccine dose(s) received **on or after the first birthday.**

Table 2
National estimates of vaccination coverage by the seventh birthday, Canada, 1997

Vaccine	# of doses	Percent coverage*	# of doses	Percent coverage*
Diphtheria	4	94.5	5	78.7
Pertussis	4	90.9	5	74.9
Tetanus	4	93.1	5	76.8
Polio	≥ 3	95.4	≥ 4	85.1
Measles§	≥ 1	98.8	2	55.9
Measles¶	≥ 1	97.6	2	50.2
Mumps			≥ 1	96.7
Rubella			≥ 1	97.2
Hib			≥ 1	86.2

* 95% confidence limits range between ± 1% to 5%.
§ Coverage based on measles vaccine dose(s) received at any time.
¶ Coverage based on measles vaccine dose(s) received **on or after the first birthday.**

Coverage assessment based on only those vaccines received *by the second birthday* results in slightly lower levels for all vaccines. Overall, none of the national targets for vaccination coverage by the second birthday have been met. However, coverage levels for first dose measles, mumps and rubella are just slightly below the targeted levels. Current coverage levels for diphtheria, pertussis, tetanus and polio range between 12% and 14% below the national targets. The vaccine program for which current levels are furthest from target is Hib vaccination starting at 2 months of age, also the most recently introduced program for routine immunization for infants. Although surveys of two previous cohorts indicated an increase in four-dose coverage among 2-year olds that increase has not been sustained.

Coverage among 7-year olds: The highest coverage levels by the seventh birthday are for first dose measles, mumps and rubella, all of which are slightly improved over the already high levels documented in the 2-year-old cohort. Surprisingly two-dose measles coverage by the seventh birthday was estimated in this survey as only 55.9% (50.2% for both doses received after the first birthday) although most of the children in this cohort were targeted through school catch-up programs in 1996. One or more of the following factors may explain the low coverage documented: on average catch-up reached only 90% of children where implemented, catch-up programs have not been implemented in three provinces (representing about 7% of the population), catch-up campaigns were not completed in two medium-sized provinces at the time of the survey, catch-up of preschoolers was limited in some provinces, incomplete recording of catch-up doses in regular immunization records during school-based programs in some provinces, and lack of immunization monitoring and updating at school entry. Up-to-date coverage levels for diphtheria, pertussis, tetanus and polio in this cohort are very low although primary immunization levels (four doses) show improvement over recent levels documented for 2-year olds. The higher Hib coverage for this cohort (86.2%) is based on a single-dose coverage with the polysaccharide vaccine available for use in the cohort and therefore should not be compared to the coverage levels for the 2-year-old cohort. As with the 2-year-old cohort, current vaccination coverage levels by the seventh birthday are below national targets. In particular, coverage for diphtheria, pertussis and tetanus is very poor, being up to 22% below target.

Conclusions: The data presented reveal good up-to-date coverage levels for only some of the recommended childhood vaccines. There is still a lot of work to be done by both vaccine providers and parents to ensure that optimum levels are achieved and maintained for all recommended vaccines at the appropriate age. The slow progress in achieving target levels for pertussis,

and other antigens with which it is administered, has been largely attributed to negative attitudes towards pertussis immunization in Canada. The data for the 7-year olds also reveal that children are considerably delayed in all school entry booster vaccinations. Children with such delayed vaccinations are at risk of remaining inadequately immunized. Continued monitoring of coverage at this age will be required to assess if the availability of acellular pertussis vaccine for primary immunization in Canada will have the expected positive impact on up-to-date coverage with these antigens by the seventh birthday. Although the national level of two-dose measles coverage by the seventh birthday documented in this survey is unexpectedly low, additional information about activities relating to the recent catch-up campaigns and routine two-dose immunization is needed to fully explain the low coverage documented. With all provinces and territories now implementing a routine two-dose schedule the target level for this age should be reached by the year 2000. Assessment of vaccination coverage at the national, provincial/territorial, and local health region levels remains an essential part of immunization delivery programs and should be conducted in a timely manner in order to have the best impact on improving immunization programs.

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Upgrading Cold Chain Equipment in Ontario Health Departments: An Initiative to Reduce Vaccine Waste

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(Adapted from Public Health and Epidemiology Report Ontario, Vol 8, No 10, October 1997)

Background

The Vaccine Utilization Review (VUR) project was undertaken by the Disease Control Service (DCS), Public Health Branch beginning in 1992. In addition to promoting proper vaccine storage and handling, the VUR project focused its attention on the issue of excess vaccine waste. The World Health Organization's (WHO) goal for acceptable vaccine waste is 5%. In 1992, it was estimated that Ontario's provincially funded program has vaccine waste of approximately 20% to 30%, based on population requirements. In response to these findings, several interventions were implemented by DCS to reduce excess waste. Two of the initial interventions included were annual reviews of vaccine utilization for each health department for commonly used vaccines, and the elimination of multiple vaccine formats.

One component of the VUR project is the Ontario cold chain study, which highlighted the existing risks for cold chain breaks, both in vaccine storage and transport. Cold chain breaks are known to contribute to vaccine waste as products exposed to temperatures outside the +2° C to +8° C range often require replacement. In Ontario, health departments are the primary vaccine depots for physicians in their jurisdictions and frequently have inventories valued in excess of $30,000 in a single refrigerator. Records maintained by DCS indicated that, in 1994, cold chain failures in health departments resulted in approximately $300,000 worth of vaccines being wasted. Most of these incidents were due to poorly functioning equipment or mismanagement of vaccine exposures. Also, of concern, are unrecognized cold chain incidents because vaccines that are stored outside at +2° C to +8° C may not adequately protect the vaccine recipient.

WHO recommends that domestic (kitchen style) refrigerators should not be used for bulk vaccine storage. They are not designed to maintain the temperature range required and they warm up quickly following a power failure. WHO also recommends the use of alarms for bulk vaccine refrigerators. A 1994 survey indicated that many of Ontario's health departments were using either domestic or bar-style refrigerators for vaccine storage, most without alarms. The survey also indicated that more than 20% of the vaccine refrigerators were > 10 years old and unreliable.

In response to these concerns, DCS undertook an initiative to ensure that Ontario health departments store vaccines in reliable refrigerators. A proposal was presented to Public Health Branch senior management requesting 100% of ministry funding for the purchase of refrigerators and refrigerator alarms. Prior to this, all cold chain equipment in health departments was purchased with cost-shared money, with the municipal commitment of funds considered a significant barrier to the purchase of high-quality refrigeration equipment.

Objectives were set for equipment purchases for health departments:

1. Laboratory refrigerators (with alarms) for health department main vaccine depots where unreliable or kitchen-style refrigerators were used; and
2. Kitchen refrigerators in those sub-offices with smaller vaccine inventories or for inventory overflow in any office.

The goal of this initiative was to significantly reduce the cost of vaccine losses due to cold chain failures in health departments by equipping all of them with high-quality refrigerators. It was

Table 1
Summary of cost of vaccines lost in cold chain incidents at health departments and cold chain equipment purchases

Fiscal year	Projected costs to ministry with no interventions		Actual costs to ministry with project interventions	
	Projected vaccine losses* ($)	Equipment costs ($)	Vaccine losses ($)	Equipment costs ($)
1995/1996 (Year 1)	286,119.00	0.00	137,610.00	328,024.00**
1996/1997 (Year 2)	286,119.00	0.00	23,344.00	69,392.00
Subtotal	572,238.00	0.00	160,954.00	397,416.00
Total	**572,238.00**		**558,370.00**	

* Projected cold chain losses based on 1994 vaccine losses ($286,119).
** Includes 1994 expenditures.

estimated that expenditures for refrigerators and alarms would be recovered by reduced vaccine losses within 3 years. Vaccine storage and handling guidelines for health departments were also produced. These provide guidance about refrigerator monitoring and response to refrigerator failures. The results for the first 2 years of the 3-year refrigerator purchasing project are summarized below.

Overall Project Results

The baseline data (1994) indicated that losses due to cold chain failures in health departments were close to $300,000 per year. Over 3 fiscal years (FY 1994-1995 to FY 1996-1997), a total of $397,416 was invested by the ministry in cold chain equipment purchases for health departments (Table 1). These purchases included laboratory grade refrigerators, alarms, domestic refrigerators and portable electronic coolers (Koolatron®). The data in Table 1 reflect 2 years of health department cold chain incidents following initiation of equipment upgrades in 1994. Projected losses were determined by assuming that baseline losses in 1994 ($286,119) would continue at the same rate if no interventions were put in place.

It was assumed that the 1994 data reflected an "average" year of health department cold chain incidents, totalling $286,119 in losses. The VUR project had focused on improving vaccine handling since 1992; therefore, it is assumed that health department cold chain losses had either remained constant or decreased slightly by 1994 from previous years. Therefore, total projected cold chain losses for the 2 fiscal years (Year 1 = 1995-1996 and Year 2 = 1996-1997), without additional intervention, were estimated to be $572,238. Although spending was initiated in 1994, the bulk of purchases and improvements were not in place in health departments until 1995, therefore results were tabulated beginning in fiscal year 1995. Consequently, in the 2-year period, the net savings to the ministry due to reduced cold chain incidents in health departments is $13,868.

Another significant factor in the reduction in losses in the health departments is the introduction of Vaccine Distribution, Storage and Handling Guidelines (April 1995). Health departments have made considerable efforts to comply with the requirements for vaccine handling, which we strongly believe contributed to the reduction in the losses due to cold chain incidents. In 1994 health departments reported a total of 13 incidents to the ministry with an average loss of $22,000 per incident. In the 1996-1997 fiscal year, a total of 16 incidents were reported to the ministry, with an average loss of $1,459 per incident. Quick response in the event of a refrigerator failure (due to alarm notification after office hours), plus appropriate handling of exposed vaccines following an incident are likely contributors to this significant decrease in value of losses per cold chain failure.

Conclusion

Beginning in 1994, the ministry undertook several initiatives to reduce vaccine waste and minimize costs in recognition of the approximately $300,000 annual loss due to cold chain failures in health departments. It was assumed that annual losses would continue at this rate unless interventions were implemented. As a result, a 100% ministry-funded program for cold chain equipment purchases for health departments was initiated. At the same time, the DCS developed and distributed a vaccine storage and handling manual for health department staff.

In the first 2 years of the project, the net savings to the ministry was $13,868. The savings from this project are being used in part to fund cold chain equipment purchases and to help pay for new vaccines.

In spite of 100% municipal funding of health departments beginning January 1998, the ministry has announced a commitment to continue providing provincially funded vaccines for immunization programs. The DCS will continue to provide advice on maintaining the cold chain and plans to continue funding health department cold chain equipment purchases.

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Genotyping of Measles Virus

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The Pan American Health Organization (PAHO) has set the goal to eliminate measles in the Americas by the year 2000[1]. An important component of this elimination strategy is the tracking of measles transmission using molecular techniques. The purpose of this article is to briefly describe the method used for measles virus genotyping at the Laboratory Centre for Disease Control (LCDC) and the usefulness of molecular epidemiological studies.

A detailed description of specimen collection and measles virus isolation procedures can be found in *Measles Surveillance: Guidelines for Laboratory Support,* which will be available from LCDC in the near future. Briefly, measles virus can be isolated from urine, nasopharyngeal aspirates, and nasopharyngeal swabs within 4 days after rash onset. Proper processing of clinical specimens is essential for successfully obtaining viable isolates due to the fragility of the measles virus lipid envelope. Processed clinical specimen is used to infect a transformed lymphoblastoid cell line, and measles virus growth is monitored by observing the development of syncytium formation and giant-cell cytopathogenic effect (CPE). As measles virus is predominantly cell associated, infected cells are harvested and RNA is extracted at maximal CPE. The appropriate region of the measles virus negative-sense, single-stranded RNA genome, and/or the viral messenger RNA, is then amplified by reverse transcription followed by polymerase-chain reaction (RT-PCR). Double stranded DNA amplicons are sequenced and compared with a measles virus sequence database. Alternatively, RT-PCR can be performed on RNA extracted directly from the clinical specimen. However, initial virus isolation prior to RT-PCR is preferred to allow flexibility for further studies of the isolate.

Phylogenetic analysis of measles virus is most commonly done using nucleotide sequence information from the most variable regions of the measles virus genome: the hemagglutinin (H) gene, and the carboxy-terminal of the nucleocapsid (N) gene. Similar measles virus phylogenetic groups are found for H and N gene analyses. Although the 456 base carboxy-terminal end of the N-gene is the most variable region in the measles virus genome, the most divergent measles virus genotypes are still approximately 90% similar in this region.

Unfortunately, at the present time there is no single, standard genotyping nomenclature. Two of the measles genotyping systems that are presently used are those of Rota and Rima. Rota uses genotype groups 1 through 7, whereas Rima uses genotype groups and subgroups A through G. Phylogenetic analyses show that the final groupings of isolates are essentially the same regardless of the nomenclature used. Examples of these measles virus genotypic groups include Rima-A/Rota-1, which are the vaccine strains; Rima-B/Rota-6, which are African strains; Rima-C2/Rota-5, which are European strains; Rima-D3/Rota-4, which are also European strains; and Rima-D2/Rota-2, which includes the strain responsible for the 1989-1992 resurgence of measles in the U.S. A more detailed description of the distribution of measles virus genotypes has been published[2,3].

Recent genetic analysis of several Canadian measles isolates indicates that they are similar to Rima-D3/Rota-4 strains previously isolated in 1994 (Spain), and 1993 (England). The original source of this chain of transmission into Canada is therefore likely to be an importation from Europe. Similarly, recent molecular epidemiological studies in the U.S. show that all measles cases in 1995-1996 resulted from importations[4]. Future cases of measles in regions undertaking measles elimination programs, such as Canada and the U.S., are likely to be due to importations from regions without an elimination program.

Stringent surveillance of measles cases is critical for measuring the success of an elimination program. Molecular epidemiological studies are a valuable tool which, in combination with traditional epidemiological methods, enhance the ability to determine measles virus transmission pathways. Specimen collection for measles virus isolation and genotyping is an important component of measles elimination programs and should not be overlooked.

Acknowledgements

The cooperation of the Provincial Health Laboratories in Newfoundland, Ontario, Alberta, and British Columbia for sending measles virus isolates to LCDC is greatly appreciated.

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Twelfth Meeting of the Pan American Health Organization's Technical Advisory Group: Conclusions and Recommendations

Adapted from EPI Newsletter Vol 19, No 5, 1997 [Pan American Health Organization (PAHO), Washington, DC]

The Twelfth Pan American Health Organization (PAHO) Technical Advisory Group (TAG) Meeting on Vaccine-Preventable Diseases was held in Guatemala from September 8 to 12, 1997. Formed in 1985 during the polio eradication campaign, TAG meets every 2 years and functions as the leading forum to promote regional initiatives aimed at controlling and eliminating vaccine-preventable diseases. One of its main objectives has been to strengthen the policy dialogue on immunization among governments in the Region and participating agencies. The following are some of the major conclusions and recommendations of the meeting.

Immunization in a Changing Policy Environment

All countries are moving towards delegating greater responsibility for delivery and management of health-care services to local levels. This provides an opportunity to promote community participation and commitment of local health authorities. However, with decentralization there remains a requirement at the central level to ensure that immunization program goals are met in all areas of a country. Because almost all vaccine-preventable diseases can spread widely, successful control or elimination requires coordinated national and international efforts so that no area becomes a reservoir to seed infection into other communities and countries.

Recommendations

- National governments must maintain authority to monitor the implementation of immunization programs at the state and local level and to take corrective actions should problems be detected.
- Vaccination and surveillance programs should be considered essential public goods and funded with public resources.
- Within the context of a changing environment to improve access to health services, vaccination coverage should be an indicator of the success of local and state delivery of services and a measure of the success of the health-care reform and decentralization process.

Measles Eradication

Substantial progress has been made towards achieving the goal of measles eradication in the Americas. Transmission has been interrupted in many countries of the Region. The PAHO vaccination strategy *(catch-up, keep-up and follow-up),* where fully implemented, has proven to be highly effective. However, TAG pointed out that low levels of incidence can lead to a false sense of security. In the absence of measles transmission, susceptibles accumulate in a community as a result of failure to vaccinate all children and because primary vaccination does not protect 5% to 10% of those vaccinated. These susceptibles can sustain future measles outbreaks. To maintain a measles-free state will require ongoing efforts to minimize susceptibility using the complete strategy.

The measles eradication effort is not a local or even a national campaign but a hemisphere-wide program that can only be as strong as its weakest component. This is true also on a global scale because many cases in this Region have been linked either epidemiologically or virologically to importations from outside this hemisphere. Consequently, better worldwide measles control is important for the continued success of measles eradication in the Americas.

Recommendations

General

- The occurrence of a measles epidemic in a major urban area poses, by far, the most serious threat to the overall program because of the possibility of widespread disease dissemination. Accordingly, it is important that the success of the program be monitored in all urban areas (population of $\geq$ 1,000,000) on an ongoing basis by national authorities and reported to PAHO.

Vaccination Strategies

- Routine vaccination of infants *(keep-up* vaccination) is a critical component of the PAHO measles eradication strategy.
- To maintain high immunity among the preschool population, *follow-up* measles vaccination campaigns should be conducted whenever the estimated number of susceptible children 1 to 4 years of age approaches the number of children in one birth cohort.

Surveillance and Laboratory

- Each country should periodically evaluate the quality of its surveillance system. PAHO has developed a protocol for rapid evaluation of surveillance systems that should be disseminated to all countries of the Region. A plan should be made for these evaluations to be implemented in all countries as soon as possible.

- Laboratory confirmation is an essential part of the regional measles surveillance system. A single serum specimen collected at first contact with the health care system is sufficient for confirming measles.
- Virological surveillance is important. Clinical specimens for viral isolation should be obtained from every chain of transmission. Urine, the most practical specimen to obtain, should be collected within 7 days of rash onset and forwarded to a laboratory to be properly processed.

Outbreak Response

- Countries should not implement indiscriminate campaigns to vaccinate all adults against measles. Most adults are likely to be immune, and achieving significantly higher levels of coverage among adults is extremely difficult. However, where surveillance has identified specific risk groups for measles among adults, such as university students, health care workers, or others, targeted vaccination efforts may be useful.

Management Indicators

The following indicators are essential for monitoring the performance of the program:

Notification:

- ≥ 80% of reporting sites report the presence or absence of suspected measles cases on a weekly basis.
- ≥ 80% of reporting sites report at least one suspected measles case per year.

Investigation:

- ≥ 80% of suspected measles cases are investigated within 48 hours of the report.
- ≥ 80% of suspected measles cases have a blood specimen collected if there is no epidemiological link to a laboratory-confirmed case.
- ≥ 80% of measles chains of transmission have an identified source of infection.

Laboratory:

- ≥ 80% of specimens have results available from the laboratory within 7 days of receipt of specimen by the laboratory.

Poliomyelitis

The hemisphere continues to be free of wild polio virus, and surveillance indicators for the Region show that most countries are continuing to conduct adequate surveillance for acute flaccid paralysis (AFP) cases. However, TAG noted a substantial deterioration in surveillance in some of the countries of the Region, raising concerns that future importations of wild virus could be missed.

Recommendations

- All countries must ensure that adequate resources are devoted to polio surveillance. AFP surveillance must continue with ascertainment of at least one case annually of AFP per 100,000 population < 15 years of age.
- For laboratory diagnosis, only one stool specimen, collected within 15 days of onset of paralysis, is needed. Such specimens should be collected from at least 80% of AFP cases.
- An inventory of all laboratories in the hemisphere with wild polio virus stocks should be completed as a first step towards the eventual destruction of all wild polio viruses as part of the global certification process.
- Oral polio vaccine remains the vaccine of choice in the Americas because it induces gut immunity, preventing the spread of wild viruses if introduced; it is easy to administer and it is relatively inexpensive.

Neonatal Tetanus

Acceleration of neonatal tetanus (NNT) elimination activities in the Region of the Americas began in 1988 and great progress has been made. The annual number of cases in the Region decreased from 1,470 in 1988 to 312 in 1996, and the number of districts with multiple cases of NNT has also decreased.

Recommendations

- To improve protection against diphtheria among women of childbearing age, other adults, and older children, tetanus and diphtheria toxoid should replace single antigen tetanus any time tetanus toxoid is indicated for vaccination.
- Surveillance and NNT case investigations should be improved in risk areas of endemic countries, particularly where information on coverage and cases is lacking.

Rubella and Congenital Rubella

Available data indicate that rubella is prevalent throughout the Americas. Cases of congenital rubella syndrome (CRS) and fetal infection have been documented in Barbados, Belize, Brazil, Cuba, Jamaica, Mexico, Panama and Trinidad. In the absence of major epidemics, it has been estimated that more than 20,000 infants are born with CRS each year in the Americas.

Recommendations

- All countries should incorporate rubella vaccine [as mumps and rubella (MR) or measles, mumps and rubella (MMR)] into childhood vaccination programs, both as part of routine childhood immunization at 12 to 15 months and as part of the *follow-up* campaigns reaching children 1 to 4 years of age every 4 years.

- Countries implementing childhood rubella programs should make efforts to reduce the accumulation of susceptible adult female groups, such as offering post-partum vaccination, and immunization in family planning clinics and other settings where females can be vaccinated. Women should be vaccinated with MR or MMR vaccine to take advantage of the opportunity to increase immunity against measles.
- Surveillance of CRS (and rubella) should be initiated throughout the Americas and should begin before, or at the same time as, implementation of a rubella vaccination program.
- Countries wishing to prevent and control CRS promptly should carry out a one time mass campaign to vaccinate all females 5 to 39 years of age with rubella or MR vaccine.
- Countries wishing to prevent and control both rubella and CRS promptly should carry out a one time mass campaign to vaccinate both males and females 5 to 39 years of age with rubella or MR vaccine.

Hepatitis B

It has been estimated that 140,000 to 400,000 new cases of acute hepatitis B occur annually in the Americas. Two thirds are believed to be in South America, primarily in areas within the Amazon Basin.

Recommendations

- Routine vaccination of all children living in the Amazon Basin is recommended as well as in other areas, if any, with high endemicity (HBsAg prevalence $\geq 7\%$).
- Routine vaccination is also recommended for those at high risk of infection, such as health care workers and hospital staff.

Yellow Fever

Between 1990 and 1996, 1,287 cases of yellow fever were reported in the Americas. As in the 1980s, 80% of these cases were from the Amazon Basin areas of Bolivia and Peru. However, important risk areas for yellow fever were also present in Brazil, Colombia, and Venezuela.

Recommendation

- Incorporate vaccination against yellow fever into national immunization programs in high-risk areas and ensure that adequate quantities of vaccines and other supplies necessary to vaccinate against this disease are available at local health services.

Haemophilus influenzae type b

Safe and effective vaccines against *Haemophilus influenzae* type b (Hib) have had an impact on the incidence of Hib disease, particularly meningitis and epiglottitis, in industrialized countries. Similar effects have also been observed in some countries in the Region (e.g., Uruguay and Chile) that have introduced Hib vaccine in their national immunization programs. It is possible that a larger impact on pneumonia will be observed in developing countries because Hib is an important pathogen in childhood pneumonias.

Recommendation

- TAG recommends the introduction of Hib vaccine in national immunization programs provided that adequate additional funds can be identified. However, implementation of Hib vaccination should not divert resources needed to sustain and enhance existing immunization efforts.

Vaccines of Quality

The quality of vaccines is assured through both quality control of the final product and Good Manufacturing Practices (GMP) during the entire manufacturing process. Both manufacturers and governments using vaccines are responsible for quality. Manufacturers must adhere to GMP that assure high quality of every lot (consistency of production). Governments must have adequate capacity to monitor manufacturers and their products.

Recommendations

- Local vaccine manufacturers should participate in the PAHO Certification Program for Vaccine Producers.
- Local manufacturers should perform feasibility and viability studies of vaccine production to demonstrate their capability to supply vaccines of quality for immunization programs in a timely and continuous manner.
- Governments in the Region must institute National Control Authorities (NCA) appropriate to their vaccine production and purchasing policies.
- Immunization program managers should only use vaccines of known quality in their immunization programs.

Research and Development: the Regional Vaccine Initiative

Although governments recognize that vaccines and immunization are key to the control, elimination and eradication of vaccine-preventable diseases, this recognition has not been translated into concrete actions to promote and support research and development for vaccine production. Research and development teams in the Region are few and not coordinated among themselves or with vaccine producers. The introduction of new vaccines into national immunization programs in the Region may be facilitated if some existing public laboratories participate in the process.

Results obtained by the Pneumococcal Surveillance Network demonstrate the importance of inter-country collaboration and coordination to standardize laboratory and epidemiologic methodologies for monitoring a specific pathogen, to determine the regional burden of disease, and to define particular characteristics

of the burden such as serotype distribution or antimicrobial resistance. This system can be established and developed as the basis for a more comprehensive surveillance network for vaccine-preventable diseases.

Recommendations

- Formal programs for vaccine research and development must be established with appropriate financial resources, together with strong coordination at the country and regional level in order to enhance existing research, development and production capabilities.
- This initiative should give priority to the development of polysaccharide and polysaccharide conjugated vaccines because this methodology will provide vaccines against several important childhood pathogens such as *H. influenzae, Neisseria meningitidis, Streptococcus pneumoniae, Salmonella typhi,* and *Shigella* spp., responsible for significant mortality and morbidity in the Region.
- The Network should collect information on cases and correlate those data with laboratory information to answer questions such as whether the increasing trend of antibiotic resistance has been associated with increased disease severity, complications, and cost. These data will be important in guiding clinical management and future policies for pneumococcal vaccination.

Technical Advisory Group Members

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For a complete version of the TAG conclusions and recommendations, please contact the PAHO Special Program for Vaccines and Immunization in Washington, D.C.

Vaccine-Preventable Diseases Summary

Cumulative number of cases reported* for selected vaccine-preventable diseases, Canada, January 1995 - October 1997

Divisions of Immunization and Disease Surveillance, Bureau of Infectious Diseases, LCDC, Ottawa

Disease	1995		1996		1997
	Jan-Oct	Jan-Dec	Jan-Oct	Jan-Dec	Jan-Oct
Diphtheria	2	2	0	0	1
Haemophilus influenzae type b	53	55	38	56	44
Measles§	2,313	2,361	310	327	606
Mumps	328	402	244	280	244
Rubella¶	277	300	189	237	3,448
Congenital rubella syndrome	2	2	0	1	0
Pertussis	8,211	9,799	3,542	4,809	2,914
Paralytic poliomyelitis	1‡	1‡	0	0	0
Tetanus	5	6	2	2	3

* Based on cases reported to the *Notifiable Disease Reporting System*, Division of Disease Surveillance, LCDC; 1996 and 1997 data are provisional. Also cumulative totals for the current year to date may not represent national totals due to incomplete reports from the provinces/territories.

§ Measles data are based on cases reported to the *Enhanced Measles Surveillance System,* Division of Immunization, LCDC. Cases reported in 1997 comprise 380 (63%) confirmed cases, 197 (32%) clinical cases and 29 (5%) suspected cases (or cases with unknown status). The majority of cases in 1997 have been reported from British Columbia (50%) and Alberta (40%).

¶ Approximately 98% of rubella cases reported in 1997 have been reported from Manitoba where an outbreak of rubella occurred, starting October 1996 through October 1997.

‡ The single report was a case of vaccine-associated paralytic poliomyelitis in a male adult (30-39 years old).

Announcement

3rd Canadian National Immunization Conference

Partnerships for Health Through Immunization

The Calgary Convention Centre, Calgary, Alberta, Canada
December 6 - 9, 1998

Organized By

The Laboratory Centre for Disease Control, Health Canada, and the Canadian Paediatric Society

Objectives

To present a forum for discussion and information exchange related to the practical aspects of immunization programs in Canada, and means of improving them. This will cover issues such as vaccine supply and delivery, education, assessment of vaccine programs, regulations and legislations, and global immunization efforts. The conference will look at both programmatic and disease-related issues, with primary focus being on programmatic issues. The main focus will be on childhood immunization. There will also be an examination of progress towards the achievement of established Canadian national goals for the reduction of vaccine-preventable diseases of infants and children.

To access information as it becomes available, or to be put on the conference mailing list, visit the Conference Website at:

http://www.hc-sc.gc.ca/hpb/lcdc/events/cnic/index.html

Or fax your request to:
Chuck E. Schouwerwou, BA, CMP
Conference and Committee Coordinator
Division of Immunization
Fax: (613) 952-7948

Note that the proceedings of the previous Canadian National Immunization Conferences can also be accessed at that site.

Dear Reader,
For your information, last year's volume (Volume 5, 1997) will only have three issues and not four. You are now reading the first issue in Volume 6, 1998.

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Health Canada

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