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Health Canada Santé Canada

Canada

Our mission is to help the people of Canada maintain and improve their health.

Health Canada

The artwork on the cover, an original drawing by Connor Mulvihill, a grade 6 student at Georges Vanier School in Belleville, Ontario, was selected as the winning design in a poster competition organized in conjunction with the second Canadian National Immunization Conference held in Toronto in December 1996.

Canadian National Report on Immunization, 1996

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Mission of the Division of Immunization

Recognizing the role of the provinces and territories in the delivery of immunization programs, and that the mission of Health Canada is to help the people of Canada maintain and improve their health, the mission of the Division of Immunization is to help reduce the incidence of vaccine-preventable diseases in Canada.

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Preface

Immunization is a cornerstone of improving the health of people worldwide. It is often referred to as the most cost-beneficial of all prevention strategies, resulting in huge savings to society and to health-care systems. Immunization was responsible for the global eradication of smallpox in 1977 and the hemispheric elimination of paralytic poliomyelitis certified by the Pan American Health Organization (PAHO) in 1994.

Many childhood and adult diseases are prevented through proper vaccination. Indeed, vaccine-preventable diseases have experienced a tremendous decrease in Canada, demonstrating the effectiveness of provincial and territorial immunization programs. For childhood vaccine-preventable diseases, the achieved rates of decrease (compared to the pre-vaccine era) have been remarkable: 95% decrease in incidence (e.g. measles, invasive infections due to *Haemophilus influenzae* type b) or total elimination (e.g. polio). However, vaccine-preventable diseases continue to occur, sometimes in epidemic proportions, as highlighted by recent measles and pertussis epidemics. In addition, cases of congenital rubella syndrome and its devastating effects continue. These have been attributed largely to inadequate immunization in certain populations. The recent increase in pertussis cases in Canada, the importation of wild polio virus during 1992, 1993, and 1996 into Canada, and the diphtheria epidemic in eastern European countries are reminders that, despite current programs, the risk for diseases still exists; it is important to keep the protection level of the population as high as possible.

A 1995 Ontario report emphasizes the importance of recognizing that "... the value of immunization has been established beyond reasonable debate and one takes its benefits for granted"[1].

The success of immunization has three major disadvantages.

- First, it leads to complacency. For example, overall immunization coverage for Canadians was believed to be relatively high for many years; however, no reliable data support this belief. Problems cannot be identified and corrected without close scrutiny of immunization programs. Levels of childhood and adult immunization are still too low; immunization rates, disease prevention, and outbreak protection need to be improved.
- Second, immunization has always had its opponents. Since younger generations have never witnessed or experienced the devastating effects of these diseases, they may tend to abandon or even oppose immunization. A recent national survey revealed that, although the public was usually well informed by health-care providers about the risks of side effects of immunization, they were less informed about the benefits[2], which are less risk of contracting diseases and suffering their negative outcomes. Knowing about the risks and benefits of vaccines is important particularly when, unlike many other countries, we do not see the devastating effects of these diseases on children. For example, the World Health Organization (WHO) 1995 Programme Report of the Global Programme for Vaccines and Immunization indicates that one million deaths and nearly 43 million measles cases still occur worldwide annually[3].
- Third, every additional advancement in coverage becomes more difficult. It is fairly easy to reach a 50% vaccination coverage. However, as higher coverages are reached, additional gains, although important, are increasingly harder to achieve. While cost-beneficial, benefits become marginal.

Impressive changes have taken place recently on the Canadian scene. National goals have been developed for vaccine-preventable diseases of infants and children. Immunization programs are undergoing greater evaluations, including areas of cold chain and vaccine wastage. Surveillance of vaccine-associated adverse events has been enhanced. Guidelines for assessing vaccine coverage and maintaining cold chain have been developed and published. Draft guidelines for childhood immunization practices are being developed. Mass immunization campaigns have been very successful. New routine programs have been implemented for hepatitis B and second-dose measles immunization. More changes will undoubtedly take place. Some will result from new vaccines becoming available, such as the acellular pertussis vaccines. Funding of immunization programs is anticipated to allow for these changes and will permit enhanced evaluation programs.

At its December 1995 meeting, the steering committee of the Division of Immunization, Laboratory Centre for Disease Control (LCDC), recommended that the Division produce an annual report on immunization achievements in Canada. The current report gives an overview and highlights important issues from a national perspective, although it does not pretend to be an exhaustive review of the immunization situation in Canada. We apologize to provinces and health units for possibly excluding information on some initiatives or omitting specific provincial and territorial data.

The report is primarily directed to health-care providers and policy makers. It also provides an opportunity to communicate with the public and increase awareness of immunization programs. It is intended as a tool to help policy makers, health-care workers, and the public measure Canada's progress in reducing the incidence of vaccine-preventable diseases, and to identify actions that can be taken to improve immunization programs. In times of fiscal restraint, it is important to take advantage of new vaccines and to make better use of current ones. This report attempts to accurately present the current immunization situation and the epidemiology of vaccine-preventable diseases in Canada. It also reviews what happens and what should, but does not, happen.

A complete report is expected to be produced every 3 to 5 years with shorter interim reports annually. Selected sections of the current report will be updated on a more regular basis as well. Each complete report will contain a feature section on a particular disease. Measles was selected for this first report because of the recent effort directed toward its elimination and the mass-vaccination campaigns that took place in 1996.

In 1996, the Division of Immunization, Bureau of Infectious Diseases, LCDC, Health Canada; the Canadian Paediatric Society; the Canadian Public Health Association; and, the Canadian Institute for Child Health, with sponsorship from Connaught Laboratories Limited, organized a national poster competition for grade 6 children. The theme was "Immunizing for Health." The winning poster is presented with pleasure on the cover page; it is a reminder that the goal of immunization is to improve the health of the population. This goal should be encouraged and all the Canadian population should be able to participate.

Comments and updated information to improve future versions of this report would be appreciated. They should be sent to:

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1. Immunization in Canada

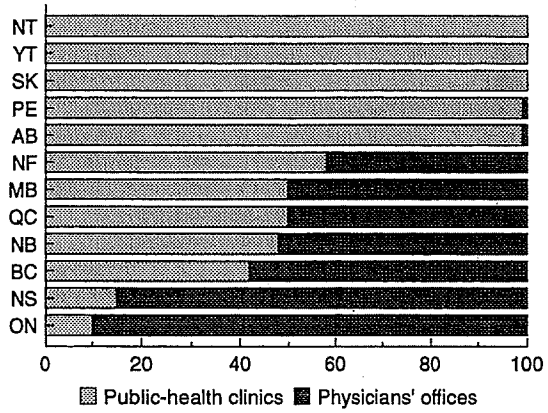
Vaccines are licensed for use in Canada by the Bureau of Biologics and Radiopharmaceuticals, Health Protection Branch, Health Canada. Licensing is conditional to an application being filed by the manufacturer and a favourable review of the supporting information submitted by the company. Provincial and territorial ministries of health then buy vaccines from available licensed products on the market, which are then provided to the public free of charge. Each province and territory is responsible for the delivery of immunization programs to its populations; vaccines and schedules are selected to suit the goals of their public-health programs. Nevertheless, general Canadian recommendations on the use of vaccines exist. They are formulated by the National Advisory Committee on Immunization (NACI) – a committee of members from across the country who are experts in areas, such as public health, infectious diseases, and pediatrics.

NACI has reported to the Assistant Deputy Minister of the Health Protection Branch since 1975. Its mandate is to provide Health Canada with ongoing and timely medical, scientific, and public-health advice relating to vaccines and certain prophylactic agents generally and, more specifically, to their use in humans, their evaluation, and the monitoring of vaccine-associated adverse events (VAAEs). In addition to updating the Canadian Immunization Guide, NACI also issues regular statements on the use of vaccines. Currently, all NACI statements are published in the Canada Communicable Disease Report (CCDR) which is available by subscription, from an automated fax delivery service at LCDC, and from the LCDC web site (http://www.hwc.ca/hpb/lcdc). Provinces and territories will adjust their recommended schedules and selection of vaccines, based on NACI recommendations as well as on local epidemiologic, program, and financial considerations.

Unlike some countries, immunization is not mandatory in Canada; it cannot be made mandatory because of the Canadian Constitution. Only three provinces have legislation or regulations under their health-protection acts to require proof of immunization for school entrance. Ontario and New Brunswick require proof for diphtheria, tetanus, polio, measles, mumps, and rubella immunization. In Manitoba, only measles vaccination is covered. It must be emphasized that, in these three provinces, exceptions are permitted for medical or religious grounds and reasons of conscience; legislation and regulations must not be interpreted to imply compulsory immunization. Requiring proof of immunization for school entrance serves two main purposes. First, parents who have forgotten to have their children properly immunized will be reminded and can rectify the situation. Second, parents who do not wish to have their children immunized must actively refuse and sign documents attesting to that fact. Also, all provinces and territories have regulations that allow for the exclusion of unvaccinated children from school during outbreaks of vaccine-preventable diseases. Currently, Quebec is the only jurisdiction in Canada to have a compensation plan for VAAEs.

In some provinces and territories, the public health-care system administers immunization programs; infants and children receive their vaccinations at public-health clinics. In other provinces and territories, vaccinations are primarily given by private physicians who order vaccines from local public-health units. Figure 1 indicates the estimated percentage of immunization provided by both ways in each jurisdiction. Generally, in provinces and territories with a dual system, the public health-care system serves rural areas while private practice predominates in urban settings. Private physicians generally administer recommended vaccines for non-institutionalized adults.

Figure 1
Proportion of Childhood Vaccines Administered at Physicians' Offices and Public-Health Clinics in Canadian Provinces and Territories, 1996



2. The Development of National Goals for Vaccine-Preventable Diseases of Infants and Children

Canada is a signatory to the *Declaration of the 1990 World Summit for Children*, which established a number of child-health goals in disease eradication and reduction, and immunization coverage. LCDC was identified as the lead agency in Canada to develop national goals for vaccine-preventable diseases of infants and children in collaboration with the Health Services and Promotion Branch. The Health Services and Promotion Branch was responsible for the Child Health Goals project.

Vaccine-preventable diseases have certain attributes that make them very suitable candidates for clearly defined national goals and targets: currently existing control programs of demonstrated effectiveness, measurable outcomes, a clear linkage of resources with strategies, and indicators for surveillance already in place. These attributes affect all population groups across Canada. A number of countries have national goals and targets for vaccine-preventable diseases; some have incorporated these into more comprehensive sets of health goals and targets.

National goals can help

- gain commitment toward improving health by further reducing major causes of preventable death or morbidity through established, cost-effective, and linked interventions, the impact of which can be easily measured and achieved within a defined period of time;
- further decrease the disease burden and permit reallocation of funds from treatment or outbreak to routine preventive strategies;
- maintain high levels of control of vaccine-preventable diseases and prevent their resurgence following an imported case;
- provide objective measures to evaluate program effectiveness; and
- identify achievable improvements in health status and reductions in health-status inequalities (e.g. hard-to-reach populations, populations with specific needs).

A coordinated national strategy is more effective than several individual programs and has the potential for being financially efficient; vaccine-preventable diseases easily cross provincial and territorial borders.

A series of four consensus conferences were used to develop national goals and targets for vaccine-preventable diseases of infants and children in Canada. The Division of Immunization, Bureau of Infectious Diseases (Childhood Immunization Division, Bureau of Communicable Disease Epidemiology at that time), LCDC, organized these conferences which were funded from December 1992 to October 1994 by the Brighter Futures Initiative. The conferences built on current achievements of provinces and territories, and involved broad consultation with a variety of stakeholders. Stakeholders included representatives from all provinces and territories, the federal government, international experts, and key non-government groups including the Canadian Paediatric Society, the College of Family Physicians, the Canadian Medical Association, the Canadian Nurses Association, the Canadian Public Health Association, the Canadian Task Force for Periodic Health Examination, the Society of Obstetricians and Gynaecologists of Canada, and the Canadian Liver Foundation. Approximately 200 people participated in these conferences, including provincial and territorial epidemiologists and chief medical officers of health.

Goals and targets were developed for poliomyelitis, measles, mumps, rubella and congenital rubella syndrome, tetanus, diphtheria, pertussis, *Haemophilus influenzae* type b (Hib), and hepatitis B. These goals involve either achieving or maintaining the elimination of disease (e.g. polio), or reducing morbidity and mortality (e.g. pertussis). The goals also identify proper handling of vaccines and good delivery programs. Targets include vaccine-coverage levels and quantifiable decreases in diseases. Proposed goals call mainly for attention to, and the strengthening of, existing immunization programs.

At the December 1995 Conference of Deputy Ministers, the goal of eliminating measles by the year 2005 was adopted. As well, the Advisory Committee on Population Health (ACPH), with the help of LCDC, expert bodies, and chief medical officers of health, was directed to pursue a process that would lead to adopting public-health goals, starting with vaccine-preventable diseases for children.

Although the goals for the remaining vaccine-preventable diseases were not formally endorsed as national goals at the Conference of Deputy Ministers, progress is being made in this area. All professional organizations which took part in their development and NACI have endorsed them. The goals were published in 1995[4] and have already had some impact in the provinces where they are being used. However, in provinces that had pre-existing and more stringent goals and targets, like Ontario, the impact has been less. The goals and targets received

overwhelming support when they were presented to nearly 600 health professionals at the December 1996 National Immunization Conference – although it was clear and agreed upon that provinces and territories might have different ways of achieving them. It was also clearly understood that these goals, with the exception of the one on eliminating measles, had not yet received formal political endorsement. It was emphasized that this endorsement was urgently needed.

The published national goals and targets are presented in the next section. Recommendations common to all diseases are presented under "General Goals and Targets." The others are listed by disease. Variation in the format for the goals and targets from one disease to another reflects different situations, achievements, priorities, and public-health impacts.

3. General National Goals and Targets

- Ensure that all vaccines to be administered have been properly transported, stored, and delivered and that there is continual surveillance for adverse reactions and monitoring of vaccine efficacy.
- Review all goals and targets in 1999.

3.1 Diphtheria

Goal

- Eliminate indigenous cases of diphtheria by the year 1997.

Targets

- Achieve and maintain up-to-date diphtheria immunization by the second birthday in 97% of children by the year 1997.
- Achieve and maintain up-to-date diphtheria immunization by the seventh birthday in 99% of children by the year 1997.

3.2 Invasive *Haemophilus influenzae* type b infections

Goal

- Achieve and maintain the absence of preventable cases of invasive *Haemophilus influenzae* type b (Hib) infections in children by the year 1997.

Target

- Achieve and maintain up-to-date Hib immunization by the second birthday in 97% of children by the year 1997, recommending that the immunization be given in accordance with the recommended schedule beginning at 2 months of age.

3.3 Hepatitis B

Goal

- Reduce the prevalence of indigenously acquired chronic hepatitis B infections in children and young adults by 90% by the year 2015.

Targets

- Screen 100% of pregnant women for evidence of hepatitis B surface antigen and immunize 100% of neonates of carrier mothers with vaccine and hepatitis B immune globulin as soon as possible after birth, by the year 1995.
- Establish routine universal hepatitis B immunization for children by the year 1997.
- Achieve and maintain 95% hepatitis B immunization of populations targeted in universal programs by the year 1997.
- Ensure that each province and territory has a policy to provide hepatitis B vaccine to all high-risk groups as outlined in the *Canadian Immunization Guide*[5] by the year 1995.

3.4 Measles

Goal

- Eliminate indigenous measles in Canada by the year 2005.

Targets

- Achieve and maintain measles immunization with the first dose of vaccine by the second birthday in 97% of children by the year 1997.
- Achieve and maintain measles immunization with a second dose by the seventh birthday in 99% of children by the year 2000.
- Achieve and maintain an incidence of less than 1 per 100,000 population in each province and territory by the year 2000.

3.5 Mumps

Goal

- Maintain an active prevention program for mumps to minimize serious sequelae.

Targets

- Achieve and maintain mumps immunization by the second birthday in 97% of children by the year 1997.
- Achieve and maintain mumps immunization by the seventh birthday in 99% of children by the year 1997.

3.6 Pertussis

Goals

- Reduce the morbidity and mortality related to pertussis infection.

- Immunize all Canadian children against pertussis according to NACI guidelines.

Targets

- Achieve and maintain up-to-date pertussis immunization by the second birthday in 95% of children by the year 1997.
- Achieve and maintain up-to-date pertussis immunization by the seventh birthday in 95% of children by the year 1997.
- Have all reported cases of pertussis managed appropriately.
- Ensure that severity of disease, as indicated by pertussis-related admissions to intensive care units, is reduced by 50% by the year 1997 (based on a moving average).
- Ensure that reporting of pertussis cases to the national level is standardized by the year 1994.

3.7 Poliomyelitis

Goals

- Maintain the elimination of wild indigenous poliomyelitis.
- Prevent future import-related cases.

Targets

- Achieve and maintain 97% immunization with three doses of polio vaccine by the second birthday by the year 1997.
- Achieve and maintain up-to-date poliomyelitis immunization by the seventh birthday in 99% of children by the year 1997.

3.8 Rubella

Goal

- Eliminate indigenous rubella infection during pregnancy and thus prevent fetal damage, congenital rubella syndrome, and other negative outcomes of infection by the year 2000.

Targets

- Achieve and maintain up-to-date rubella immunization by the second birthday in 97% of children by the year 1997.
- Achieve and maintain up-to-date rubella immunization before school entry in 99% of children by the year 1997.
- Achieve and maintain up-to-date rubella immunization in 99% of 14- to 15-year-olds by the year 1997.
- Screen serologically and/or obtain date of immunization of ALL pregnant women seen prenatally for rubella susceptibility by the year 1995.
- Achieve and maintain postpartum immunization for rubella of 99% of all susceptible women prior to hospital discharge by the year 1995.
- Ensure that all women of childbearing age have a documented history of rubella immunization and, if not, that they are offered rubella vaccine to decrease the rate of rubella-negative primigravida women to less than 4% by the year 1997.

3.9 Tetanus

Goal

- Maintain absence of neonatal and childhood tetanus.

Targets

- Achieve and maintain up-to-date tetanus immunization by the second birthday in 97% of children by the year 1997.
- Achieve and maintain up-to-date tetanus immunization by the seventh birthday in 99% of children by the year 1997.

In addition to the above goals and targets, consensus conferences have stressed the need:

- to follow the recommendations from the working group on polio eradication and from the national certification commission;
- to reinforce the importance of adult immunization for the above-mentioned diseases (tetanus in particular);
- to achieve vaccine coverage levels at the national, provincial, territorial and local health-unit levels; and
- to try to immunize at the age recommended by NACI.

Draft national guidelines for childhood immunization practices are being developed and will be published by LCDC. Adherence to these guidelines should help Canada achieve these goals and targets in the future. Beyond endorsement at the national, provincial, and territorial levels and by professional organizations, everyone should work toward achieving these goals and targets for a better future for our children. As can be seen in the later sections of this report, serious efforts need to be made to achieve some goals and targets, although some have been already achieved and good progress is being made for some others. Achieving the disease-reduction target for pertussis will not be possible without replacing the current whole-cell vaccine with more efficacious and acceptable (less reactogenic) new acellular vaccines. Evaluation will be the key to monitoring progress toward the achievement of the goals; then corrective action can be taken as needed. Many evaluation tools remain to be put in place at national, provincial, territorial, and local levels.

4. National Advisory Committee on Immunization – Recommended Childhood Vaccination Schedule, Canada

Immunization carried out as recommended in the following schedule (Table 1) will provide good protection for most children against the diseases shown. Modifications may be necessary because of missed appointments or concurrent illness. For details, see the *Canadian Immunization Guide*[5] or revised NACI statements published in 1997 as updates in the CCDR. The guide also contains alternate schedules for children who have not been immunized on time, as well as for adults and specifically targeted vaccinations. The NACI-recommended schedule is consistent with achieving the previously mentioned national goals and targets. Table 1 presents the recommendations at the time of publication and will be updated according to changes in the epidemiologic situation of vaccine-preventable diseases and new vaccine developments.

Table 1
NACI-Recommended Immunization Schedules for Infants and Children

Vaccine	Months					Years		
	2	4	6	12	18	4 to 6	9 to 13	14 to 16
Hepatitis B*	3 doses							
Diphtheria, Pertussis, and Tetanus (DPT)	DPT	DPT	DPT		DPT	DPT		Td**
Haemophilus influenzae type b*** (Hib)	Hib	Hib	Hib		Hib			
Polio (inactivated polio vaccine/oral polio vaccine)	Polio	Polio	Polio****		Polio	Polio		Polio****
Measles, Mumps, and Rubella (MMR)*****				MMR	MMR*****			

* Adolescents who have not received hepatitis B vaccine in infancy should receive it through school programs according to the provincial and territorial policies.
** Td (tetanus and diphtheria toxoids, adult formulation).
*** Recommended schedule for both Hib-TITER® and Act-HIB®.
**** If oral polio vaccine is used exclusively, boosters at 6 months and 14 to 16 years of age may be omitted.
***** The second dose of MMR is routinely recommended at either 18 months or at 4 to 6 years of age. It should be given any time before school entry provided that there is at least a 1-month interval between receipt of the first and second doses.

5. Measles Elimination in Canada

Measles is a severe respiratory tract infection frequently complicated by pneumonia, croup, sinusitis, otitis media, and febrile convulsions. It is the most contagious infection of humans. Every year, nearly one million children die from it worldwide. Available vaccines are safe and effective. About 90% of children vaccinated after the first birthday develop protective immunity.

The routine one-dose measles immunization program, introduced in Canada in the mid-60s, has had a very positive effect on the incidence of measles; >95% reduction from the pre-vaccine era. Before immunization, an estimated 300,000 to 400,000 cases of measles occurred annually in Canada. Several measles outbreaks have made the limitations of Canada's one-dose program apparent: one in Quebec in 1989 with 10,184 reported cases, and one in Ontario in 1991 with 5,283 reported cases. The actual number of cases was likely much higher as the reporting rate was estimated to be only 25% to 30%. Despite stable vaccination coverage levels of around 97% for 2-year-olds, these outbreaks continued to occur mostly in school-aged children even in populations with virtually 100% documented immunization. The spread of the virus was likely caused by the small proportion of children who failed to respond to primary vaccination or, less commonly, by those who lost protection over time after vaccination. It was increasingly clear that a routine one-dose program administered after 12 months of age would not achieve the goal of eliminating indigenous measles because of its extreme contagiosity. This was strongly supported by the international experience. The typical pattern of measles in highly-vaccinated populations is one of outbreaks at extended intervals involving 1% to 5% of school children, with a spillover into pre-school children. Control measures such as exclusion from school and emergency mass revaccination are extremely disruptive, costly, and of limited effectiveness. The administration of a second dose of measles-containing vaccine has been shown to diminish the proportion of susceptible children, thus decreasing the potential for outbreaks.

Despite the fact that participants of a National Conference on Measles Control in 1992 endorsed the goal of eliminating indigenous measles in Canada by 2005[6], little progress had been made. Competing developments in childhood vaccination programs pre-empted the formal introduction of a two-dose measles program in Canada. In 1995, with only 3.6% of the population in the Americas, Canada accounted for 40% of all reported cases and nearly 80% of all confirmed cases. Other countries in the Americas have recently conducted highly effective mass measles-vaccination campaigns or previously implemented routine two-dose programs for many years. The approach taken in Canada was the least effective. Compared with 1993, when the lowest level of measles activity ever recorded in Canada was 204 reported cases, the number of cases rose steadily to 512 in 1994 and 2,362 in 1995.

Analysis of the situation in Canada suggested that sufficient numbers of unprotected children existed in every province to fuel outbreaks at any time. It was estimated that, without action, an outbreak with more than 20,000 cases, 2,000 complications, and several deaths could occur as early as April 1996. Mathematical modelling and a Delphi study predicted that there were enough susceptibles in the population to have an average of 12,800 cases of measles per year. Mathematical modelling also predicted that giving a second dose only to young children would not eliminate measles for 10 to 15 years and would be inconsistent with the elimination targets. A national catch-up campaign would be the only way to avoid forecasted outbreaks as well as to prevent up to an additional 58,530 cases per year and several deaths. Cost-benefit analysis indicated that these programs would save in excess of $2.5 per dollar invested. This situation prompted the endorsement in December 1995 of a formal, politically-endorsed, national goal of eliminating measles.

In August 1995, NACI reaffirmed its commitment to the goal of eliminating measles[7]: this goal is shared by all countries of the Americas. The committee also confirmed its recommendation that a second dose of measles vaccine should be offered, at least 1 month after the first dose, on a routine basis to raise protection rates as high as possible. This dose could be conveniently linked with other routinely scheduled vaccinations. Options included giving it with next-scheduled vaccinations at 18 months of age, or with school-entry vaccinations at 4 to 6 years of age, or at any practicable intermediate age. NACI also recommended that, 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. The principal target group for a catch-up campaign is school children because they have had the highest rates of measles in recent Canadian outbreaks, and are most readily identified and served.

Following NACI's recommendation, Health Canada encouraged a massive catch-up vaccine campaign over a short period to be followed by routine two-dose immunization. All provinces (except New Brunswick) and territories, which represent 97% of the Canadian

population, have since introduced a routine second measles, mumps, and rubella (MMR) vaccination (measles and rubella [MR] in Saskatchewan to be replaced by MMR after its catch-up program is over) at either 18 months or 4 to 6 years of age, depending on the province. New Brunswick will implement such a program starting in April 1997. Six provinces and territories (Ontario, Quebec, British Columbia, Prince Edward Island, Yukon, and Northwest Territories), which represent 80% of the Canadian population, have already completed mass school catch-up programs for all school-aged children. In Quebec and British Columbia, catch-up programs have been extended for children down to 18 months of age. However, these programs have a lower priority than those for older age groups and catch-up will likely not be completed until these children enter school. A more limited catch-up program was also started in Manitoba to include all primary-school students and in Saskatchewan to include all children > 18 months of age up to the end of school age, and to be completed over a 3-year period in a staggered manner.

Public-health nurses conducted catch-up campaigns in schools, after careful planning and public awareness campaigns. Coverage levels have reached around 90% on average in targeted school-age groups in provinces that have had catch-up campaigns. Nearly 4 million children have been immunized. Although some mass immunization programs had been implemented in the past for invasive meningococcal disease, they were more limited, mostly on regional and provincial levels. This is the first national campaign of such magnitude in Canada. It has had an immediate effect; three potential outbreaks that were developing in early 1996 were stopped. Only 327 cases of measles have been reported to date for 1996; these mainly occurred before the catch-up campaigns in the largest provinces. Very few cases have occurred since May and transmission seems to have been interrupted. A total of 12 imported cases have been identified, mostly from European countries. In provinces that have not yet implemented catch-up campaigns, school-aged susceptible populations still remain in sufficient numbers to fuel outbreaks through importations.

Retrospectively, the heavy measles activity that occurred early in 1996, with 2.5 times the number of cases than that reported for the corresponding period in 1995, and the number of outbreaks indicate that the prediction of a large outbreak occurring after April 1996 was likely true; the provincial campaigns were very timely (Figures 2 and 3).

Surveillance is extremely important and must continue in a very active manner. Several evaluation and surveillance activities related to the catch-up campaigns have been implemented; these include disease surveillance, surveillance of vaccine-associated adverse events, monitoring of coverage target achievement, assessment of the process and cost (the overall estimated cost was around $8.30 per targeted child), and evaluation of promotion activities.

A survey of promotional activities in Ontario and British Columbia, conducted by the Division of Immunization, showed that the distribution of a leaflet in schools appears to have been the most common and useful source of information. The knowledge of attitudes toward, and practices of, measles immunization were strikingly similar in both provinces; notable differences were in the sources of information and those that were the most useful. Promotional materials in British Columbia were more varied because its campaign covered school-aged children and pre-schoolers; the leaflet was only 60% effective in British Columbia as compared to 80% in

Figure 2
Cumulative Number of Reported Cases of Measles, by Week, Canada, 1995-1996

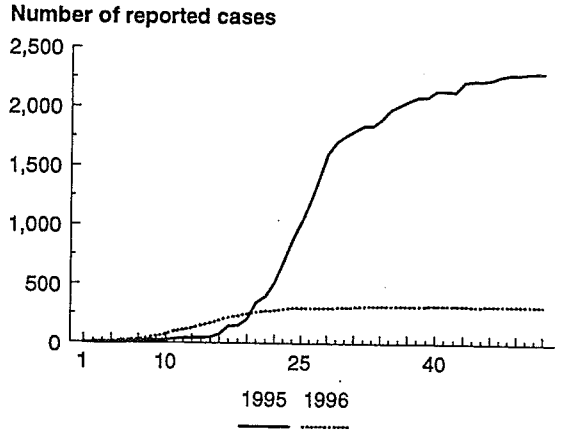
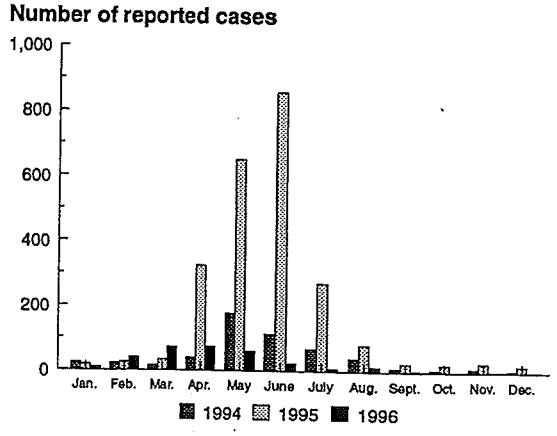


Figure 3
Monthly Distribution of Reported Cases of Measles, Canada, 1994-1996



Ontario. During the campaign, a high proportion of parents changed their opinions about immunization and recognized the importance of measles immunization, presumably as a result of the promotional materials. When parents in both provinces were asked to rank five infectious diseases (including measles) in order of decreasing severity, most replied in the following order: hepatitis B, measles, pertussis, varicella, and influenza.

Health Canada provided technical assistance, and helped to plan provincial activities and evaluate the mass catch-up campaigns. Health Canada also produced turn-key material for public awareness campaigns, and helped to reduce vaccine costs through competitive soliciting and speedy licensing of products needed for the catch-up campaigns.

6. Epidemiology of Selected Vaccine-Preventable Diseases

6.1 Diphtheria

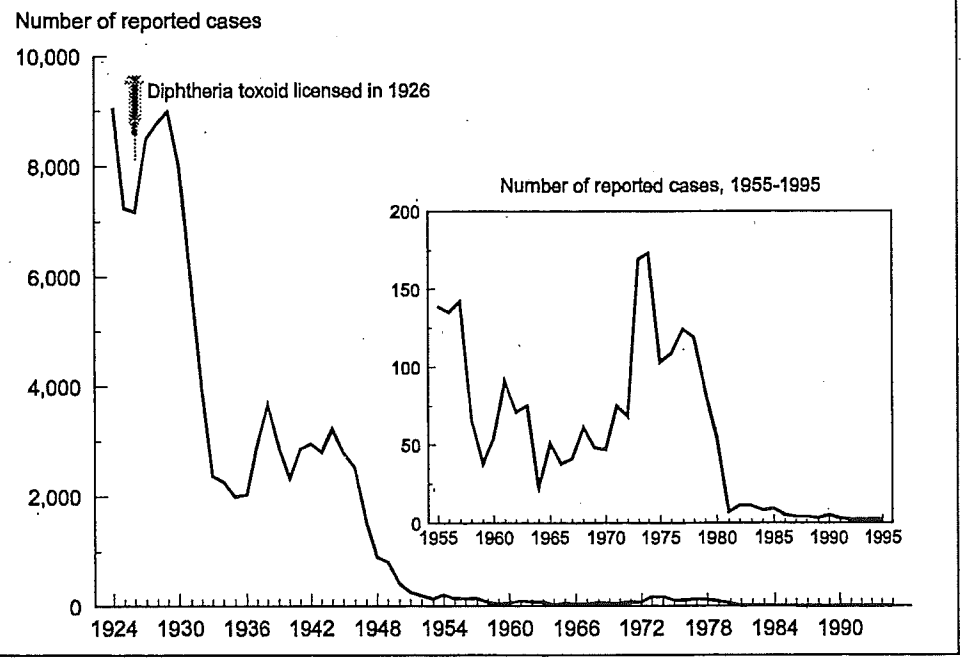
Diphtheria is an acute communicable disease primarily affecting the upper respiratory tract. It is characterized by the formation of a greyish membrane in the respiratory tract with surrounding inflammation which may lead to respiratory obstruction. Toxigenic strains of *Corynebacterium diphtheriae* cause the disease. The organism (both toxigenic and non-toxigenic strains) may be harboured in the nasopharynx, skin, and other sites of asymptomatic carriers. Diphtheria has a case-fatality rate of 5% to 10% with the highest death rates occurring among the very young and the elderly.

The highest ever-recorded annual number of diphtheria cases in Canada was 9,000 in 1924. The diphtheria toxoid was licensed for use in Canada in 1926 and introduced into routine immunization programs for infants and children in 1930. In the immediate post-immunization period, an average of 2,000 cases were reported annually. Routine immunization had led to a remarkable decline in both the morbidity and mortality of diphtheria by the mid-1950s. Diphtheria incidence has remained at a very low level since the early 1980s; only two to five cases were reported annually from 1986 to 1995. The majority of reported cases in the last 10 years have been in persons aged ≥ 20 years without adequate protection. Classic diphtheria is rare in Canada; no deaths have been reported since 1983.

National reporting of diphtheria is based on a case definition of clinical symptoms involving the upper respiratory tract (pharyngitis and/or laryngitis) with or without a membrane, and/or toxic symptoms (cardiac or neurologic involvement), and laboratory confirmation of a toxigenic strain. However, toxigenic strains of diphtheria continue to be isolated each year in carriers, mainly in northern and western Canada among Aboriginal populations; these are sometimes associated with mild clinical symptoms. Because such mild cases are not reported, the level of circulation of toxigenic strains is not entirely known. However, based on the minimal incidence of reportable cases, circulation is believed to be low. The apparent increase of diphtheria which was observed in the 1970s (Figure 4) is due to the inclusion of non-classic diphtheria cases (carriers) in the western provinces; it does not correspond to a real increase in disease incidence.

In 1996, the Division of Immunization conducted a serosurvey of a sample of healthy adult blood donors in five centres across Canada; 13% to 32% had levels of diphtheria antitoxin below the minimum considered to protect them against the disease. Overall levels of immunity also varied by age group; the proportion of susceptibility ranged from 10% in those 30 to 39 years of age to 36% in those ≥ 60 years of age. Potential susceptibility to diphtheria differed among adults in different parts of the country; however, overall conclusions about the potential for diphtheria to resurface with large epidemics are troubling. The results are even more significant given that the sample represented a relatively healthy population. The actual levels of

Figure 4
Reported Cases of Diphtheria, Canada, 1924-1995



immunity in the general adult population are likely to be lower. It is possible that a certain proportion of seronegative individuals would be protected because they may have kept their immunologic memory, although their antibody levels have fallen.

The possibility of diphtheria resurfacing in Canada is highlighted by two factors: the low levels of immunity among Canadian adults and the resurgence of diphtheria in parts of Europe during this decade. Starting from 1990, major diphtheria epidemics have been reported in the Newly Independent States (NIS) of Eastern Europe with subsequent importation to other European countries. In the Russian Federation alone, where most of the cases occurred, the number of reported cases went from about 200 to 300 annually in the mid-1970s to almost 2,000 in 1990 to 1991, and to over 15,000 by 1993. Major reasons are low immunization coverage rates among infants and children, poor quality of some vaccines, waning immunity among adults, and large movements of the population during recent years[8]. From 1990 to 1995, approximately 125,000 cases and 4,000 deaths had been reported in the NIS; this represents approximately 90% of cases reported worldwide[9]. Despite the level of serosusceptibility observed in Canada, it is reassuring to note that the epidemic in the NIS started mostly in younger age groups before spreading to older ones, and that Canadian children are very well protected against diphtheria. Despite a high volume of travel reported between Canada and affected European countries, to date no cases in Canada have been linked to the resurgence of diphtheria in Europe.

Nonetheless, travellers to those regions need to be fully informed of the current recommendations for booster immunization. Routine immunization against diphtheria is recommended in Canada for all persons. Recommendations are for primary immunization of children consisting of four doses between the ages of 2 and 18 months, and booster doses at 4 to 6 years of age and every 10 years thereafter. Although mild clinical diphtheria occasionally occurs in fully immunized persons, the antitoxin stimulated by immunization is believed to persist at protective levels for 10 years or more.

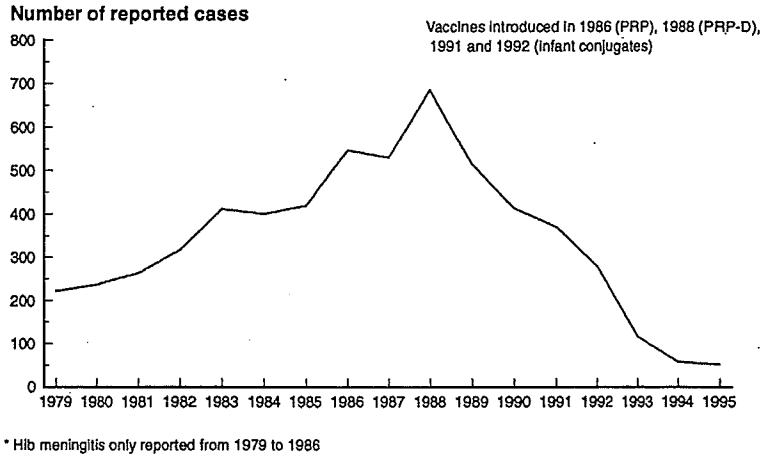
6.2 *Haemophilus influenzae* type b

Haemophilus influenzae type b (Hib) causes invasive infections mainly in young children. Other serotypes of *H. influenzae* are commonly associated with asymptomatic nasopharyngeal colonization and may cause otitis media, sinusitis, bronchitis, and other upper respiratory tract infections. Until the early 1990s, Hib was recognized as the most common cause of bacterial meningitis in Canada; Hib meningitis outnumbered all other reported bacterial causes combined. Hib infection also results in a number of clinical syndromes including epiglottitis, septicemia, cellulitis, pneumonia, septic arthritis, and pericarditis. Before immunization became routine, about two-thirds of Hib diseases occurred in children < 18 months of age and over 80% occurred in children < 5 years of age. Mortality associated with Hib disease is between 1% and 5%, and permanent neurologic sequelae occur in 20% to 30% of children who survive meningitis.

Very little was known about the frequency of Hib infections in Canada prior to 1979 when Hib meningitis became reportable nationally. Reporting improved gradually until 1988, which accounts for the change observed in Figure 5. Before the introduction of the first line of Hib vaccines in 1987, it was estimated that one in every 200 children developed invasive Hib disease by the age of 5 years[10]. This represented about an estimated 2,000 cases in Canada annually; a little more than one-half were meningitis. After the introduction of the vaccine, the incidence fell rapidly by more than 50% in Canada; similar reductions were reported in the United States. Although vaccination was limited initially to children aged 15 to 18 months or older, a decline in incidence was also reported in children < 18 months of age, suggesting either a herd-immunity effect of vaccination or a reduced transmission of the bacteria.

Since the introduction of the newer conjugate vaccines in 1992 for use in infants (starting from 2 months of age), the

Figure 5
Reported Cases of Hib Invasive Disease, Canada, 1979-1995*



* Hib meningitis only reported from 1979 to 1986

incidence of Hib disease has decreased even further. Cases admitted to pediatric centres in the Immunization Monitoring Program, Active (IMPACT) surveillance network were reported to have decreased by more than 70% from 1991 (90 cases) to 1995 (24 cases) despite the expansion of the surveillance program from five to 10 centres. A decreasing trend is also supported by the number of cases of Hib disease reported to the LCDC notifiable disease reporting system, although the numbers reported are well below the estimated incidence and indicate gross underreporting. From 1979 to 1992 more than 200 cases (and as many as 686 cases) were reported each year; however, only 117 cases were reported in 1993, the first year after introduction of the infant conjugate vaccines. In the last 5 years alone, the incidence has decreased from 1.4 per 100,000 population (370 cases) in 1991 to 0.2 per 100,000 (52 cases) in 1995; this represents an 86% reduction.

In 1994 and 1995, the percentage of reported cases < 5 years of age was approximately 41%, which is about one-half that estimated prior to infant vaccination. The majority of cases occur now in children too old to have received primary vaccination in infancy or any vaccination at all. The incidence of Hib invasive disease is expected to decrease further because more children receive immunization against Hib in infancy.

6.3 Hepatitis B

Hepatitis B virus is one of several viruses that cause hepatitis. Initial infection with the virus may be asymptomatic in up to 50% of cases. Acute illness, when it occurs, may last up to 3 months with an estimated case-fatality rate as high as 1%. An infected individual, with either symptomatic or asymptomatic acute infection, may become a chronic carrier. The risk of becoming a carrier varies inversely with the age at which infection occurs. It is highest in infants (90% to 95%) and relatively low in adults (6% to 10%). Infection with hepatitis B is usually associated with exposure to blood or infectious body fluids. Common means of transmission include heterosexual or homosexual contact, injection drug use, and perinatal transmission (mother to infant). The risk of transfusion-related hepatitis B is very low because of routine hepatitis B surface antigen (HBsAg) screening of donated blood and donor selection. Infections also occur rarely in settings of close personal contact via unrecognized contact with infective fluids. In a significant proportion of patients, no risk factor can be identified[5].

Data from the LCDC National Notifiable Diseases Registry System (NNDRS) indicate that there has been little change in the reported incidence (an average of 2,868 cases or 10.3 per 100,000 population per year from 1990 to 1994) of hepatitis B in Canada over the last several years[11]. However, there have been (and continues to be) substantial differences in types of hepatitis B infections reported from the provinces and territories to LCDC. For example, since 1990, Ontario excludes "carrier" cases and, for Quebec and British Columbia, "acute" and "indeterminate" cases are combined in the NNDRS. Further, national statistics for hepatitis B are driven by the large number of cases reported from British Columbia – 40% of all the cases in Canada from 1990 to 1994.

In the NNDRS, males have a consistently higher rate of reported hepatitis B than females (12.2 versus 8.8 per 100,000 population in 1994). The highest age-specific rates of reported hepatitis B are in those 20 to 39 years of age with low rates among those > 59 years of age, and very low rates among persons < 15 years of age.

In contradistinction to the NNDRS data, analysis of "acute cases" of hepatitis B from provinces and territories indicates that there has been a reduction in their rates in several jurisdictions (e.g. Alberta, Ontario) as well as in Canada as a whole in the last several years (close to 29% from 1992 to 1995 in Canada)[12]. A decrease in acute hepatitis B rates is consistent with that reported in the United States[13]. The only reported outbreak of hepatitis B in Canada in 1995 to 1996 involved 75 cases in Ontario that were linked to the reuse of subdermal electrodes by a technician who carried hepatitis B e antigen.

Information about risk factors for acquiring hepatitis B is not routinely provided to the NNDRS. However, some provinces recently have reported risk-factor information for hepatitis B in provincial epidemiologic documents. For example, in Ontario, the following risk factors were found for "acute" cases in 1994 (a case could have more than one risk factor): injection drug use (13%), homosexual/bisexual male (6%), heterosexual with multiple partners (9%), sexual contact of a carrier (8%), household contact of a case (4%), other risk factors (23%), and no identifiable risk factor (38%)[14].

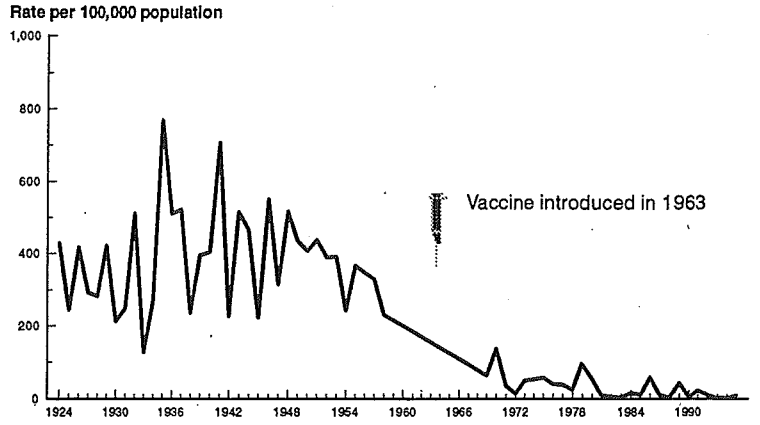
6.4 Measles

The epidemiology of measles in Canada has been discussed in the feature section "Measles Elimination in Canada." The disease has a worldwide distribution, although marked reductions in its incidence have been reported in many countries where measles vaccine has been widely used for many years. It continues to be a common disease in many parts of the world, particularly in developing countries where it is a major killer of children < 5 years of age.

Infection with the measles virus generally leads to more severe disease in infants and adults than in young children. Complications include otitis media, pneumonia, and encephalitis. In Canada, measles mortality is estimated at one per 3,000 cases for all age groups. Mortality can be as high as 5% to 10% in the very young and malnourished. Deaths occur mainly in children < 5 years of age, mostly due to pneumonia and occasionally encephalitis.

Prior to the introduction of measles vaccine, an estimated 300,000 to 400,000 cases of measles occurred annually, mostly in children. The incidence of measles in the pre-vaccine era peaked at 768 cases per 100,000 population in 1935; multiple peaks of lesser magnitude occurred at 2- to 4-year intervals (Figure 6). In the immediate post-vaccine period, measles was not reportable nationally; however, when reporting began again in 1969, the incidence had dropped significantly. More recently, from 1986 to 1995, the annual incidence of reported measles has ranged between 0.7 and 58.5 cases per 100,000 population. In 1993, 203 measles cases (0.7 per 100,000 population) were reported in Canada; this represents an almost 15-fold decrease in incidence compared to 1992. This was also the lowest total reported for any year since national notification began in 1924. However, the incidence of reported measles in 1994 increased about 2.5 times over that in 1993 and, in 1995, 4.4 times over that in 1994. Increased incidence in 1994 was mainly reported from Quebec and Ontario; however, the incidence in 1995 was largely due to widespread outbreaks in Ontario which accounted for more than 95% of the cases.

Figure 6
Reported Rate of Measles, Canada, 1924-1995*

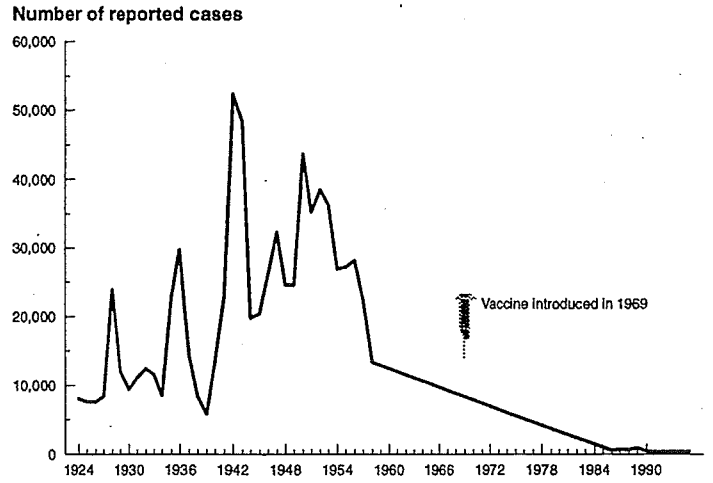


* Not reported nationally from 1959 to 1968

The median age of measles cases during the 1995 outbreak was 10 years old. The majority of cases (83%) occurred in school-aged children (aged 5 to 19 years); 33% among those aged 10 to 14 years, 30% among those aged 5 to 9 years, and 21% in those aged 15 to 19 years. Almost 90% of the cases whose immunization histories were reviewed had documented measles immunization with one vaccine, 3.9% were not eligible for immunization (born before 1957 or < 12 months of age), and immunization status was unknown for 4.5%.

The magnitude of the 1995 outbreak in Canada and its relevance to measles elimination activities in all countries of the Americas are discussed in the feature section on measles. In particular, it is important to note that mass catch-up campaigns and the implementation of routine two-dose measles immunization programs across Canada in 1996 have stopped the circulation of the measles virus. A provisional total of 315 cases was reported from January to November 1996. This puts Canada in a very good position to achieve its goal of eliminating measles by

Figure 7
Reported Cases of Mumps, Canada, 1924-1995*



* Not reported nationally from 1959 to 1985

2005, and allows for the potential elimination of measles by 2000 as per the PAHO goal.

6.5 Mumps

Mumps is an acute viral disease usually characterized by fever, swelling, and tenderness of one or more salivary glands. Prior to the widespread use of the mumps vaccine, mumps was a major cause of viral meningitis in Canada.

About one-third of exposed susceptible persons develop subclinical infections. Most infections in children < 2 years of age are subclinical. Complications are fairly frequent but permanent sequelae are rare. Deafness may occur in less than one to five cases per 100,000 population and is usually transient, but may be permanent occasionally. Mumps encephalitis has been reported to range as high as five per 1,000 cases, with a case-fatality rate of around 1.4%. Mumps infection may involve the testes in 15% to 25% of male cases occurring after puberty and the ovaries in 5% of female cases after puberty. Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion.

Through the 1940s and 1950s an average of 30,000 cases of clinical mumps were reported annually in Canada. The incidence has decreased remarkably since the introduction of vaccination in 1969 (Figure 7). From 1986 to 1995, an average of 509 cases were reported annually; incidence rates ranged from 1.2 to 3.5 per 100,000 population. More than 75% of cases occur among children aged 1 to 14 years with peak incidence in those 5 to 9 years of age.

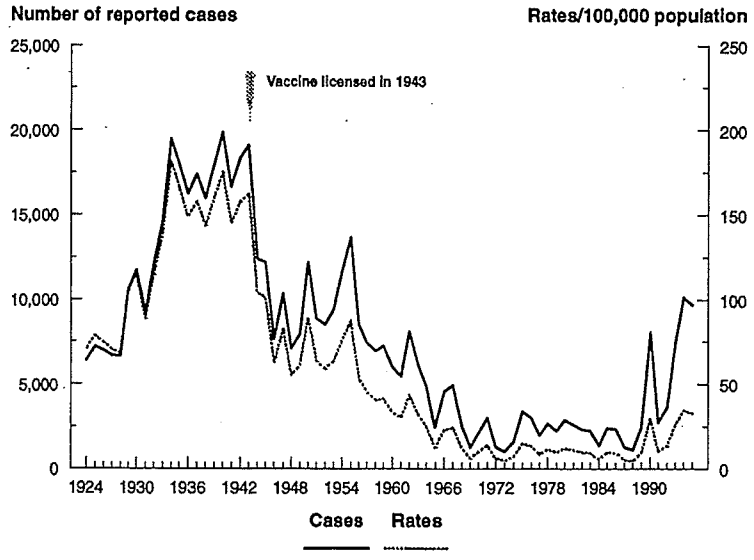
6.6 Pertussis

Pertussis (whooping cough) is a highly contagious infectious disease caused by *Bordetella pertussis*. The illness is characterized by severe coughing spasms which may or may not be associated with the classic inspiratory whoop. Pertussis is most severe and complications are most frequent in children < 1 year of age. Morbidity and mortality are generally reported to be higher in females than males. Complications include apnea, pneumonia, seizures, encephalopathy, and death. Death is estimated to occur in one in 200 cases for those < 1 year of age. Infection with *B. pertussis* produces long-term immunity from the disease but may not prevent further infection. Infection rates in immunized persons may be high, but clinical illness is infrequent and mild when it occurs.

Pertussis incidence in Canada peaked at 182 cases per 100,000 population in 1934, which was prior to the introduction of the whole-cell vaccine that was among the first to be introduced in Canada in 1943 (Figure 8). Significant reductions in incidence and mortality have been achieved since the introduction of routine vaccination. Overall, the average annual incidence has decreased by approximately 90%, from 157 cases per 100,000 population (17,463 cases) in the immediate pre-vaccine era to 17 cases per 100,000 (4,900 cases) for 1986 through 1995. The reporting of pertussis in Canada is believed to be highly underestimated; rates based on passive reporting were underestimated by as much as 14-fold in one study[15].

The highest age-specific incidence is reported in infants (mean of 168 cases per 100,000 population for the last decade). In a recent analysis of pertussis cases of children < 2 years of age who were admitted to tertiary-care pediatric centres in the IMPACT surveillance network, 75% were < 6 months of age[16]. Almost 20% of the cases had illness severe enough to warrant admission to an intensive-care unit. Overall, 10% of the cases had secondary pneumonia, and 5% had neurologic complications (mostly seizures); a case-fatality rate of 0.7% was reported. In comparison to infants and young children, the reported incidence of pertussis is relatively low among adolescents and adults (< 10 per 100,000 population in those > 15 years of age). They usually

Figure 8
Reported Cases of Pertussis, Canada, 1924-1995



develop mild disease only; however, they pose a significant problem because they are a reservoir of infection for susceptible younger children.

In recent years the incidence of pertussis has increased across Canada and epidemics have increased in size. The reported incidence in 1994 to 1995 (34.7 and 35.2 per 100,000 population, respectively) has been the highest in a decade, which makes it difficult for Canada to reach its 1997 disease-reduction target. Continuing epidemics of pertussis may be due in part to suboptimal immunization coverage which is documented in several parts of the country. Pertussis has the lowest coverage of all the vaccine-preventable diseases. This is mainly because of parental fears of serious adverse reactions to the whole-cell vaccine in addition to the practice of health-care providers who omit pertussis vaccination because of perceived "contraindications." Omitted or delayed vaccination has its greatest impact among infants because the highest incidence and greatest severity of the disease occurs in this age group. This should always be taken into consideration when a decision is being made to immunize a child according to a schedule other than the recommended routine one.

The whole-cell vaccine currently used in Canada may be another contributing factor to continuing pertussis epidemics. A number of studies have shown that it has only low to moderate effectiveness in preventing clinical illness[17]. The vaccine is still believed to be highly effective in reducing the frequency and severity of complications. Newer, safer, and possibly more efficacious acellular vaccines are currently licensed in Canada for the fourth and fifth booster doses. These vaccines are likely to become more acceptable to parents and health-care providers when they are licensed for the primary series; coverage levels will be higher and the disease will be better controlled.

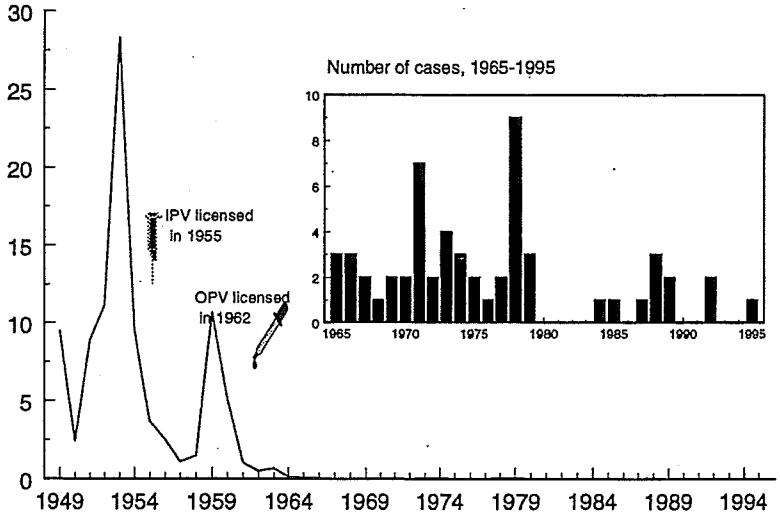
6.7 Poliomyelitis

Poliomyelitis is caused by one of three serotypes of the polio virus. Depending on the serotype, it is estimated that < one in 100 or one in 1,000 infections results in paralysis and a similar proportion may result in aseptic meningitis. More than 90% of infections are asymptomatic or result in non-specific fever only.

In the pre-vaccine era, paralytic poliomyelitis was a common childhood disease in Canada and other industrialized countries. Around 11,000 people in Canada were estimated to be left paralyzed by the disease between 1949 and 1954 (paralytic and non-paralytic polio cases were reported prior to 1949). Polio incidence peaked at approximately 28 cases per 100,000 population in 1953 (Figure 9). The inactivated poliovaccine (IPV) or Salk vaccine was introduced into Canada in 1955 and the oral poliovaccine (OPV) or Sabin vaccine in 1962. By the early 1970s, poliomyelitis was controlled in Canada mainly through immunization. The last case of paralytic poliomyelitis due to indigenous wild virus infection occurred in 1977. Wild virus imported from the Netherlands in 1978 and 1979 led to outbreaks in Alberta, British Columbia, and Ontario among closed communities that do not accept immunization for religious reasons (similar to communities affected by the outbreaks in the Netherlands)[18]. Another significant importation from the Netherlands occurred in 1993 and involved the same communities. Imported wild virus was also detected in Alberta but no clinical cases occurred[19]. Paralytic poliomyelitis occurred almost exclusively in those < 19 years of age during the pre-vaccine period. In contrast, more than 50% of the cases reported since 1965 were aged ≥ 20 years; only 35% were < 15 years of age.

While the circulation of wild polio virus had been arrested in Canada for almost two decades, a polio-free status was not certified officially until 1994 when the elimination of the disease in the American Region was announced. The announcement followed a decade of intense surveillance and immunization, and came 3 years after the last indigenous wild case was reported in the region (from Peru in August 1991). Paralytic poliomyelitis has also been eliminated in several other countries,

Figure 9
Reported Cases of Paralytic Poliomyelitis, Canada, 1949-1995



particularly in Europe. WHO continues to report progress toward achieving its target of global eradication by the year 2000[3]. The estimated number of worldwide cases was reported to have fallen from 400,000 in 1980 to just over 100,000 in 1993, and to close to 5,000 in 1995. Global eradication will be a major achievement because it will mark the second time that a human disease has been eradicated from the world through immunization; smallpox was eradicated in 1977.

In addition to disease caused by the wild virus, paralytic disease can be caused in rare instances by OPV. The risk of OPV-associated paralysis has been estimated as one case per 11.7 million doses distributed among vaccine recipients and one case per 3.1 million doses among unimmunized contacts of vaccine recipients in Canada. Between 1965 and 1995, approximately 63% of the 56 reported cases of paralytic poliomyelitis were due to wild virus infection and the remaining to vaccine virus. The last case of wild paralytic poliomyelitis in Canada occurred in 1988 as a result of importation. Since 1988, all cases of paralytic poliomyelitis have been associated with OPV. The extremely low but very real risk of vaccine-associated paralysis has been magnified by the elimination of wild polio virus: this has led to changes in the use of OPV in routine immunization programs across Canada. Seven Canadian provinces and the two territories had switched from the exclusive use of OPV to IPV in their immunization programs by 1995. Quebec switched to an IPV-based program in early 1996. Manitoba continues to use OPV exclusively, and Prince Edward Island uses a mixed schedule of OPV and IPV. OPV continues to be used in most of the developing world for the control of poliomyelitis because it provides better immunity from secondary spread of the vaccine virus to unimmunized contacts. Also, unlike IPV, it produces intestinal immunity that prevents infection of the gut by wild virus and thus its spread to susceptible individuals.

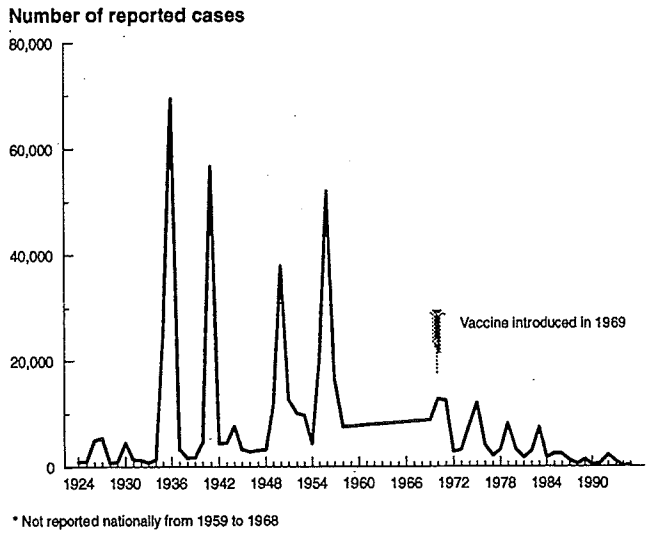
Routine immunization of children against poliomyelitis is still recommended because of the risk of imported wild virus from countries with endemic polio. This risk was highlighted most recently in Canada in March 1996; a 15-month-old boy, who had travelled to India, was found to be infected with an imported wild virus even though there were no associated clinical symptoms[20]. Travellers to endemic regions may still be at risk and should have their immunization checked and updated when needed. Only global eradication of poliomyelitis will eliminate the need for immunization against this disease in Canada.

6.8 Rubella

Rubella is a mild febrile viral disease which mainly affects children; approximately one-half of rubella infections are subclinical. By far the most important clinical problem associated with rubella is the occurrence of congenital rubella syndrome (CRS) following infection of pregnant women. CRS can result in miscarriages, stillbirths, and fetal malformations, including congenital heart diseases, cataracts, deafness, and mental retardation. The risk of fetal damage is highest when maternal infection occurs just prior to conception or in the earliest months of pregnancy – 85% of CRS cases occur with infection in the first trimester – and is very rare after the twentieth week of pregnancy. Infected infants may appear normal at birth and fetal malformations may not become apparent for several years. Congenital infection can become chronic, and may result in diabetes and panencephalitis later in life. The costs associated with long-term care for cases of CRS represent a huge economic burden for affected families and for society at large ($514,000 per case on average).

Vaccination against rubella was introduced in Canada in 1969. Since the mid-1970s, rubella incidence in Canada has remained relatively low (Figure 10). An average of approximately 1,000 cases (ranging from 237 to 2,450) were reported annually from 1986 to 1995; this represents a mean rate of 4.0 per 100,000 population. A number of college and university outbreaks have been reported in recent years. About one-third of the rubella cases reported in the last 5 years have been among adolescents 10 to 19 years of age. Overall, 50% to 60% of reported cases in Canada occur in persons between the ages of 10

Figure 10
Reported Cases of Rubella, Canada, 1924-1995*

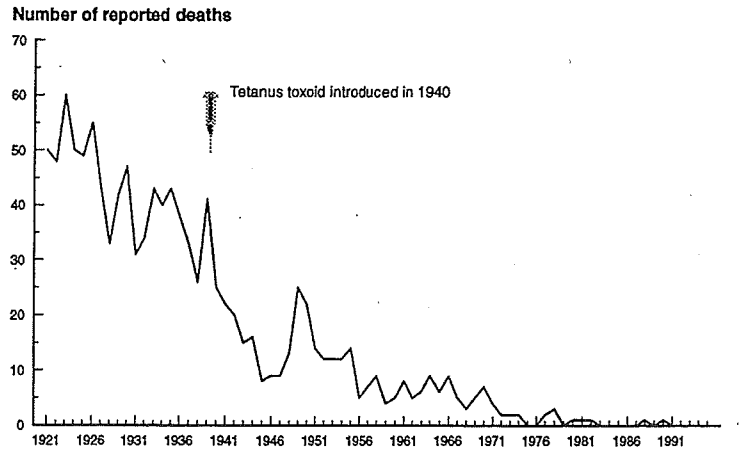


* Not reported nationally from 1959 to 1968

and 39 years. Thirty-two cases of CRS were reported in Canada from 1986 to 1995; however, CRS is believed to be grossly underreported.

The primary objective of vaccination against rubella is to prevent infection during pregnancy. In addition to routine vaccination of children, vaccination is also recommended for all females of childbearing age unless they have documented prior immunization, or laboratory evidence of detectable antibodies from natural infection or previous immunization. Protection of pregnant women and women of childbearing age can be further ensured by vaccination of males, particularly those likely to come into contact with women at risk (such as males in secondary, post-secondary, and health-care institutions).

Figure 11
Reported Tetanus Deaths, Canada, 1924-1995



6.9 Tetanus

Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *Clostridium tetani*, which is found in soil. Tetanus occurs sporadically worldwide but it is uncommon in Canada and other developed countries, mainly because of immunization and hygienic precautions taken in the management of wounds and surgical procedures. Neonatal tetanus is a particular risk for infants born to unimmunized mothers under unhygienic conditions; it is associated with a high mortality rate and is a significant cause of neonatal deaths in some developing countries. The case-fatality rate for tetanus ranges from 20% to 90%, and is highest in infants and the elderly.

Canadian data for tetanus indicate that the disease has decreased significantly with immunization. During the 1920s and 1930s, 40 to 50 deaths from tetanus were reported annually. With the introduction of tetanus toxoid in Canada in 1940, mortality rapidly declined; only five deaths from tetanus have been reported since 1980 (Figure 11).

Immunization against tetanus is highly effective and provides long-lasting immunity. Primary immunization against tetanus is recommended for all children in Canada and booster doses are recommended for adults at 10-year intervals. Unless previous immunization (i.e. primary and booster within appropriate intervals) can be documented, tetanus toxoid and/or tetanus immune globulin should be used in the management of wounds likely to be contaminated with *C. tetani*.

7. Canadian Paediatric Surveillance Program

Special active surveillance systems have been implemented to complement routine surveillance activities. They include the pediatric hospital-based surveillance system, i.e. IMPACT, described in the section on surveillance of VAAEs, some laboratory-based active surveillance of abortions due to rubella infections, and the Canadian Paediatric Surveillance Program (CPSP) described below.

The CPSP was established as a joint venture between the Canadian Paediatric Society (CPS) and LCDC to carry out active surveillance of rare pediatric conditions. The specific objectives are as follows:

- to develop, establish, and maintain a surveillance system to monitor health in Canadian children and youth;
- to involve pediatricians and professionals in related disciplines in the surveillance of rare childhood conditions important to public health, and to facilitate research into uncommon childhood disorders for the advancement of knowledge and the improvement of treatment, prevention, and health-care planning;
- to encourage awareness and education within the medical profession of less common disorders; and,
- to respond rapidly to public-health emergencies where these relate to Canadian children and youth by adapting surveillance activities.

A one-year pilot phase began in January 1996 and presently consists of surveillance for three conditions: acute flaccid paralysis (AFP), CRS, and Group B streptococcal syndrome in the newborn. Reporting is based on monthly voluntary reporting of the diseases under surveillance by pediatricians. A reporting card is mailed monthly to pediatricians and returned to the CPS indicating the number of cases of each condition seen in the preceding month; participants are also instructed to return the card indicating if no cases have been seen. For each case reported, the reporting pediatrician is sent a detailed case-report form for further information in accordance with the study protocol for that condition; follow-up is conducted as necessary.

Surveillance data are disseminated through quarterly summary progress reports, and annual disease-specific analyses and reports. As well, a survey is planned at the end of the pilot phase to evaluate the attitudes of reporting pediatricians and other aspects of the reporting system. A steering committee established in mid-1996 to oversee the development of the program will assist in identifying conditions to be included for future surveillance. For 1997, other conditions to be targeted will include: AFP, CRS, Creutzfeldt-Jakob disease, neural tube defects such as spina bifida, subacute sclerosing panencephalitis, hemorrhagic disease of the newborn, and Reye's syndrome.

8. Vaccine Coverage

Regular assessment of vaccine coverage is important in evaluating progress toward the achievement of goals and targets for vaccine-preventable diseases, and to maximize the benefits and efficiency of the immunization programs. In order to obtain the maximum benefits offered by vaccines, coverage should be as complete as possible and based on the appropriate recommended ages for vaccination. Even in areas with good overall coverage, pockets of poor coverage may exist. It is only by regular and detailed assessments of coverage at the local level that such underimmunized groups can be identified and targeted for enhanced programs as needed. In 1993, the Division of Immunization, LCDC, published a set of guidelines for the assessment of vaccine coverage in children[21].

In recent surveys conducted by the Division of Immunization, LCDC, on the assessment of immunization coverage in the provinces and territories, most jurisdictions reported collecting vaccine coverage data; however, methods of data collection and the ages at which coverage is assessed vary by jurisdiction. Of the five provinces and two territories which reported specific information on these ages, Ontario is the only province that evaluates coverage for all children enrolled in school, including day care and kindergarten. Other jurisdictions (Nova Scotia, New Brunswick, British Columbia, Yukon, and the Northwest Territories) have reported assessment for preschoolers (aged 12 to 24 months), or at school entry (4 to 6 years of age), or both depending on the vaccine. Nova Scotia and Quebec report assessment of hepatitis B coverage for grade 4 students. British Columbia reports assessment of hepatitis B coverage for grade 6 students, and coverage for tetanus and diphtheria toxoid for grade 9 students.

Because the jurisdictions which assess coverage do so at different ages, a direct comparison of coverage levels is not possible. Reported coverage levels range from 81.0% for four doses at 24 months of age to 97.9% for three or more doses by school entry (4 to 6 years of age) for diptheria toxoid, tetanus toxoid, and pertussis (DPT) vaccine; 80.4% to 93.6% for three or more doses of polio by school entry; 93.5% to 97.9% for one dose of MMR vaccine by school entry; and 67.0% for four doses of Hib to 93.4% for three or more doses at school entry.

National estimates of childhood vaccination coverage were not collected in a standardized manner or on a regular basis prior to 1994. From 1994 to 1996, annual surveys were conducted by the Division of Immunization, LCDC, to obtain population-based estimates of vaccination coverage of 2-year-olds in Canada (i.e. children who had turned 2 but not 3 years of age). Data were collected by mailed questionnaires for four cohorts of children born between February 1990 and January 1994. Information was collected on coverage for eight vaccines recommended for routine childhood immunization as well as other incidental vaccinations. National surveys were conducted to provide reliable population-based national estimates of vaccination coverage; these are useful for the evaluation of national goals and targets for vaccine-preventable diseases. The surveys were not aimed at provincial and territorial specific assessments and, therefore, do not provide reliable provincial or territorial coverage estimates. Data obtained on parental attitudes toward vaccination and other aspects of vaccination services should also be useful for reviewing and planning the delivery of immunization programs.

The vaccine-specific coverage rates (Table 2) have increased by 1% to 3% for most vaccines across the four cohorts surveyed. Current coverage rates are 85%, 86%, and 87% for four doses of pertussis, tetanus, and diphtheria vaccine, respectively, and 90% for three to four doses of polio vaccine. Pertussis vaccine coverage has been slightly lower in comparison to diphtheria and tetanus toxoids (which are given as a combined vaccine with pertussis in the majority of cases). This reflects, to a degree, the omission of pertussis vaccination from one or more doses in most cases because parents are unduly fearful of possible severe adverse reactions; cases where a child has a true contraindication to pertussis vaccination are rare. However, the discrepancy may also be explained, in part, by inaccurate recording of specific vaccines administered to a child.

An increase of 5% was recorded in pertussis coverage between the first and fourth cohorts, which likely reflects the recommendation by NACI in 1993 that certain conditions be no longer considered as contraindications to pertussis vaccination[5]. Overall, no statistically significant differences were documented between the coverage levels for children in families with different income levels.

One-dose measles vaccine coverage has remained fairly constant and was estimated in the last cohort as 97%, as was coverage for mumps and rubella. Slight discrepancies in coverage for the three antigens (particularly in the first two cohorts) may be due to the use of monovalent measles vaccine in a small proportion of children or inaccurate recording of immunization data. Among the last two cohorts surveyed, 91.4% and 93.3%, respectively, had received at least one dose of measles

vaccine on or after their first birthday, indicating that a small proportion of children do receive their measles immunization prior to their first birthday contrary to recommendations.

For Hib, coverage for the conjugate vaccines used in infants (based on the current recommendation of four doses) increased from 55% to 69% in the last two cohorts. However, because of the relatively recent introduction (1992) of these vaccines to routine immunization programs, some of the surveyed children would not have been eligible to receive four doses. Eighty-four percent of children born between February 1993 and January 1994, and 72.0% of those born between February 1992 and January 1993, had received at least three doses. Coverage for Hib is much lower than for other childhood vaccines for the reason outlined above and is expected to continue increasing in the short term.

The national estimates of coverage for four-dose DPT and one-dose MMR in Canada are higher than the rates reported in the United States 1995 National Immunization Survey for children aged 19 to 35 months: 78% and 89%, respectively[22]. Estimated Hib coverage is higher in the United States (91% for three doses) while coverage against the polio virus is comparable between the two countries (86% for three doses in the United States). When compared with global vaccine coverage estimates provided by the WHO Expanded Programme on Immunization, Canada appears to be one of the leading countries in childhood immunization, even when the comparison is limited to industrialized countries. The overall coverage reported for industrialized countries is 83% for three doses of DPT, 86% for three doses of OPV, and 81% for one dose of measles[3].

The above data indicate acceptable coverage levels for the primary series of the routine vaccines. However, with time, the lag between the recommended age to receive the vaccination and the actual age of immunization increases. These figures also clearly indicate that much effort is still needed to increase coverage levels to reach national vaccination coverage targets. Also, despite overall high coverage, there are still small pockets of population with very low coverage. Coverage is virtually zero particularly in some religious groups or sects which oppose immunization. It is fortunate that individuals in these groups are partly protected by the high level of protection in the surrounding populations, which prevents direct transmission. However, recent measles outbreaks and, in

Table 2
Vaccine Coverage of Children at 2 Years of Age, Canada

Antigen	Percent coverage (95% CI) by year of birth							
	1990-1991		1991-1992		1992-1993		1993-1994	
Diphtheria	84.7	(81.7 to 87.4)	84.0	(80.5 to 87.0)	84.4	(81.5 to 86.8)	87.1	(84.3 to 89.3)
Pertussis	80.1	(76.8 to 83.1)	81.6	(78.1 to 84.8)	82.9	(80.0 to 85.5)	84.8	(82.0 to 87.3)
Tetanus	82.0	(78.8 to 84.8)	82.5	(78.9 to 85.6)	83.9	(81.1 to 86.5)	85.9	(83.2 to 88.3)
Polio*	89.7	(87.1 to 91.9)	89.0	(86.0 to 91.5)	87.4	(84.8 to 89.7)	89.9	(87,4 to 92.0)
Measles**	96.1	(94.3 to 97.4)	97.2	(95.3 to 98.4)	96.2	(94.6 to 97.5)	97.0	(95.4 to 98.1)
Mumps**	92.8	(90.4 to 94.6)	93.6	(91.1 to 95.5)	96.0	(94.3 to 97.2)	96.8	(95.3 to 98.0)
Rubella**	93.0	(90.8 to 94.9)	94.4	(91.9 to 96.1)	96.0	(94.3 to 97.2)	96.7	(95.1 to 97.8)
Haemophilus influenzae type b***					54.6	(50.9 to 58.1)	69.3	(65.8 to 72.6)

* Three to four doses (three for exclusive use of OPV, four for IPV or a mixed schedule).
** Estimates for 1995 and 1996 were 91.4% and 93.3%, respectively, for children who received at least one dose of measles vaccine **on or after their 1st birthday.**
*** Coverage for the last two cohorts is based on the current recommendation of four doses for the conjugate infant vaccines; however, because of the relatively recent introduction of these vaccines to routine immunization programs, some of the children in the surveys would not have been eligible to receive four doses; 72.0% (95% CI - 68.6 to 75.2) of those born in February 1992 to January 1993 and, 84.4% (95% CI - 81.6 to 87.0) of those born in February 1993 to January 1994 had received at least three doses.

particular, outbreaks of wild polio virus are reminders that these populations remain vulnerable. As well, less positive data have been obtained for vaccines recommended for adults. NACI recommendations for adult immunization are published in the *Canadian Immunization Guide*[5].

A national survey of vaccine coverage in the Canadian adult population aged ≥ 18 years showed the following selected coverage rates: 11% for influenza (ranging from 3% in those aged 18 to 44 years to 43% in those aged ≥ 65 years); 0.25% for pneumococcal infections (1% in those aged ≥ 65 years); and 6% for tetanus and diphtheria (3% in those aged ≥ 65 years to 9% in those aged 18 to 24 years)[23]. These low rates have been supported by a recent survey conducted in Quebec[24] with the following results: 11% for influenza (18.4% in those aged 18 to 64 years with risk factors and 39.7% in those aged ≥ 65 years); 32.5% for tetanus and 1.2% for pneumococcal vaccine (1.9% in those aged 18 to 64 years with risk factors and 1.8% in those aged ≥ 65 years). In the latter survey, only 2.3% coverage was reported for vaccination against diphtheria, despite evidence that most tetanus vaccination in adults is given as combined tetanus and diphtheria toxoids. This suggests inaccurate recording of vaccinations as well as inadequate information given to vaccinees about the products they receive. Immunization programs, including education about recommendations for immunization and evaluation of coverage, have been directed mainly toward children. Special efforts are still needed to improve knowledge about recommendations for adult immunizations and to ensure the delivery of vaccines to the right target groups.

Despite strengthened awareness and activities for assessing immunization coverage, provinces, territories, and local health units have encountered program and financial difficulties in trying to meet the vaccine coverage guidelines. After nearly 20 years of discussion and literature on the issue, the time is long overdue for the provinces, territories, and the federal government to become serious and more proactive about monitoring immunization. They should be committed to the feasibility of connected province-wide immunization programs to constitute a national registry. Such a registry would allow for proper, easy assessment of vaccine coverage as well as proper, individual tracking of immunization status; major savings and improved coverage in the midterm to long term would likely result.

9. Surveillance of Adverse Events Temporally Associated with Vaccine Administration

9.1 Background

As indicated in the section, "Immunization in Canada," all vaccines undergo extensive testing for safety and efficacy before being licensed. Quite often, large-scale clinical trials have already taken place, and sometimes the product is already in use in other countries as well. However, pre-market assessments may not be able to detect all the potential side effects of a vaccine, nor can they detect the rare conditions that occasionally arise once a product is in use on a larger scale and in the general population. This does not suggest that unsafe products are being licensed, only that rare adverse events which do not affect the overall benefit/risk of the vaccine **may** still occur. For this reason, most countries have systems in place for the post-marketing surveillance of drugs. Vaccines are biologic products that require lot-by-lot testing before being released. This potential lot-by-lot variation further strengthens the need for post-marketing surveillance.

The VAAE surveillance system was developed to monitor vaccine safety and maintain public confidence in vaccines and immunization programs. The specific objectives of the system are as follows:

- to identify illnesses of infrequent occurrence that may be caused by a vaccine;
- to develop estimates of rates of occurrence of more serious illnesses following immunization by type of vaccine;
- to monitor for any unusually high rates of adverse events, both with individual vaccines and individual lots of vaccine;
- to provide timely information that can be made available to potential recipients as well as to health-care providers so that they can weigh the risks and benefits of immunization; and
- to identify areas that require further epidemiologic investigation and research, or problems that require immediate investigation and intervention.

9.2 Surveillance systems

The cornerstone of surveillance activities is a voluntary system in which health-care providers (mainly public-health nurses and physicians) report events that they feel are temporally associated with an immunization to local, provincial, and territorial public-health authorities. These authorities, as well as a small proportion of vaccine manufacturers, forward all such reports to the Division of Immunization, LCDC, for compilation on a national level. Particular VAAEs that have been cited in the literature are included on a special reporting form (with modifications) used by all provinces and territories. Other severe or unusual events are also solicited and reported if the health-care provider feels that they may have been due to the administration of a vaccine.

The *Canadian Immunization Guide* provides more information on the nature of adverse events occurring with specific immunizing agents[5]. A copy of the special reporting form can be found in current issues of *Compendium of Pharmaceuticals and Specialties* published by the Canadian Pharmaceutical Association. Reports which are received by LCDC are computerized after immediate scrutiny. The database includes epidemiologic and medical information on the reported events. To calculate VAAE reporting rates, the Division of Immunization obtains lot-specific data from vaccine manufacturers on the number of doses of their products which are distributed across the country. These "vaccine distribution" data are used as an approximation of the actual number of doses of aministered vaccine. However, because of varying reporting practices, differences in lot-specific VAAE rates require cautious interpretation. Although these denominator data are limited in reliability, they are very useful in generating signals that should be investigated. Further estimates of denominator data are obtained from studies of vaccine coverage.

The reporting of VAAEs by health-care providers is voluntary, except in Ontario which has specific mandatory reporting requirements. However, there is no evidence of a higher reporting rate with this approach. This is partly explained by the fact that immunization in this province is usually provided by physicians who have lower reporting rates than public-health nurses.

In addition to this spontaneous voluntary reporting system, Canada also has an active surveillance system, IMPACT, for serious VAAEs, vaccination failures, and selected infectious diseases. The system is operated through a contract with CPS. It involves a network of 11 pediatric centres across Canada which comprise over 2,000 pediatric beds with over 85,000 children admitted annually. This represents over 80% of all pediatric tertiary-care admissions in the country.

At each centre, a nurse monitor and clinical investigator actively look for cases based on a daily review of

admission records; they search for diagnoses of illnesses that are potentially linked to immunization. They are helped by an informal network, which includes admitting-department staff, infection-control nurses, neurology-ward staff and physicians, infectious-diseases staff, and medical-records technicians.

Since IMPACT monitors are so visible in institutions, they have become a focal point for vaccination-related questions from other medical staff and therefore learn of any concerns about vaccine safety that may arise. The IMPACT monitoring program was designed to actively and more systematically detect the most serious VAAEs that are temporally linked to the administration of vaccines, such as cases of neurologic illness. In addition, any hospitalization that is discovered to have followed an immunization is also recorded. Under the more recent CPSP, practising pediatricians actively report selected disease conditions and may also contribute to VAAE monitoring. The first related target disease is AFP, but other more specific VAAEs may be added in the future (see the section on the "Canadian Paediatric Surveillance Program" for more details).

Several aspects of the post-marketing surveillance program also serve to enhance signal-generating capabilities. In 1994, an external and multidisciplinary advisory group, the Advisory Committee on Causality Assessment (ACCA), was formed to help evaluate all cases involving serious events and identify signals for in-depth investigation. The specific mandate of this group is to review, in a systematic fashion, all serious cases of VAAEs temporally associated with immunization that are reported either through IMPACT or through the spontaneous reporting system[25]. In addition, provincial public-health authorities can refer selected cases for special review by ACCA, although most often such reports would automatically meet the selection criteria for ACCA review.

An assessment that a particular report was possibly due to the administration of a vaccine is not an indication that there should be a concern about immunization, but more often represents a rare but expected event that is known to occur with the vaccine. By reviewing a large number of cases in a careful manner, a potential signal (indicating a suspicion that a vaccine may be causing a particular event that previously has not been well described) can be identified.

ACCA meets twice a year. Approximately 50 cases are reviewed during each meeting. A specially designed causality assessment form, developed according to the principles of adverse drug reaction causality assessment, is used. The outcome of the assessment is described using WHO International Drug Monitoring Program criteria.

A number of signals have been generated and evaluated by the committee during these reviews. None has led to the need for immediate action but, in one case, an initial concern was later refuted when further cases were evaluated. Should an urgent issue arise, ACCA would be immediately involved through a conference call. The issues generated or reviewed by ACCA are outlined in the section below on trends in vaccine safety. ACCA actively collaborates with many other national and international agencies, as well as public-health authorities in the provinces and territories.

9.3 Trends in vaccine safety

The VAAE system receives between 4,000 and 5,000 case reports per year through the reporting network. The trend is increasing as provinces begin to promote VAAE reporting more heavily. This has been most noticeable in Alberta where VAAE reporting has been actively solicited from all public-health immunization clinics since 1980. As a result, the number of case reports involving vaccine products contained in the Canadian Drug Adverse Reaction Reporting Program database rose from an average of 50 to 60 per year, from 1965 until 1980, to an average approaching 2,000 by 1987. Although the upward trend levelled off, other provinces began to report more frequently when the program was implemented in 1987 as a separate reporting system apart from that reporting other drug products. By examining the distribution of case reports by reaction category, it can be seen that the majority are, in fact, minor reactions. The VAAE program solicits such events in order to monitor lots on the market. As expected, the number of local, minor reactions is a more sensitive indicator of some problems than is the number of rare, serious reactions. This was highlighted by discovering, retrospectively, a dramatic increase in parotitis with the Urabe strain of mumps virus in the late 1980s, which heralded an increase in the risk of viral meningitis from that product. Although meningitis rates were clearly higher with the Urabe strain than with the Jeryl-Lynn strain, the absolute numbers were not so high; however, the number of cases of parotitis were much more readily detected. The vaccine was quickly withdrawn from use in Canada following identification of the problem. Canada was the first country in the world at that time to detect such a problem with this specific vaccine and most other countries later followed Canada's action. Still, at the time, the Canadian reporting system was far from being as effective as it is today.

Table 3 shows the distribution of reported VAAEs by reaction category. Table 4 shows the distribution of case reports by vaccine. As expected, the majority of reports pertain to VAAEs which occur in temporal coincidence with vaccines that are given most frequently, according to the immunization schedule.

Since 1991, IMPACT has reported a total of 274 cases to the VAAE system. These represent the results of systematic case finding; therefore, it is not surprising that just under 20% involved seizures; neurologic events are a major focus of surveillance. Table 5 shows the distribution of reports by year and Table 6 shows their distribution by nature of the VAAEs reported.

Table 3
Distribution of Overall Reported VAAEs, by Reaction Category

VAAE	COUNT
Fever	12,619
Severe pain and swelling	6,685
Screaming episode/persistent crying	5,687
Other severe or unusual events	3,589
Severe vomiting and diarrhea	2,579
Hypotonic-hyporesponsive episode	2,158
Allergic reactions	2,119
Convulsion/seizure	1,424
Rashes	1,372
Sterile abcess	672
Arthralgia/arthritis	573
Adenopathy	380
Infective abcess	152
Anaphylaxis	148
Anesthesia/paresthesia	97
Parotitis	85
Meningitis and/or encephalitis	32
Paralysis	28
Guillain-Barré syndrome	27
Thrombocytopenia	25
Encephalopathy	22
Orchitis	11

Table 4
Distribution of Overall Reported VAAEs, by Vaccine Administered

VACCINE ADMINISTERED	COUNT
DPT	13,727
DPT-Polio	5,314
Hib	2,096
MMR	1,692
Hepatitis B	1,304
Influenza	1,030
Td	973
Meningococcal	680
DT	327
Typhoid	277
Polio, inactivated*	149
Td-Polio	126
Rabies	90
BCG	70
Rubella	57
Yellow fever	57
Pneumococcal	34
Measles**	15

* OPVs are not included in this table because they are given in combination with other antigens and are unlikely to be responsible for the adverse event reported to the combination, with the exception of a very limited number of cases of vaccine-associated paralytic poliomyelitis.

** There are very few reports for single antigen measles vaccine; the product used in Canada is MMR. Analysis of reports from the mass measles catch-up campaigns (involving measles or measles-rubella vaccines) had not been compiled when this report was prepared.

Table 5
Cases Reported by IMPACT, by Year of Vaccine Administration, 1991-1995

YEAR OF VACCINE ADMINISTRATION	COUNT
1991	18
1992	30
1993	17
1994	36
1995	96
TOTAL	197

Table 6
VAAEs Reported by IMPACT, by Nature of the Event

ADVERSE EVENTS	COUNT
Fever	92
Convulsion/seizure	92
Other severe or unusual events	77
Severe vomiting and diarrhea	30
Rashes	19
Hypotonic-hyporesponsive episode	14
Meningitis and/or encephalitis	12
Screaming episode/persistent crying	7
Severe pain and swelling	6
Adenopathy	5
Encephalopathy	5
Thrombocytopenia	4
Infective abcess	3
Paralysis	2
Anaphylaxis	1
Sterile abcess	1
TOTAL	370

9.4 Discussion

The safety of vaccines marketed in Canada is monitored on a continuous basis. Each lot of vaccine is tested and released on an individual basis and, once in use, spontaneous reporting, active surveillance, and the systematic review and evaluation of serious concerns are all undertaken. Despite the usual limitations shared by all spontaneous reporting systems, namely that of underreporting and poor documentation of case reports, Canada's post-marketing surveillance system for vaccines has been a model for other countries. This is due to two major factors:

1. cooperation and collaboration with provincial public-health networks, leading to very high reporting rates; and

2. multiple active and passive components of surveillance systems, along with an expert advisory committee as mentioned above.

The improvement of surveillance activities has also been made possible by extraordinary VAAE funding allocated by Treasury Board specifically for post-marketing surveillance. This money is scheduled to sunset in 1998. It is hoped that funding will be continued (although there is no indication that it will) so that Canadians will continue to benefit from one of the best vaccine-surveillance systems in the world.

Reports of adverse events are solicited for any event that is felt to be temporally related to the administration of an immunization, but not necessarily absolutely causally related. In addition, reports are encouraged for "minor" events in order to monitor lot-by-lot performance. These two factors account for the fact that the 4,000 to 5,000 case reports received every year represent a higher reporting rate than that in most other countries that have well-developed post-marketing surveillance programs. This rate is a credit to the reporting system and not a marker for poor vaccines. Over 12 million doses of vaccine are distributed every year and very few concerns arise despite intense searching. Until diseases are eradicated, immunization remains our best defence.

10. Current Immunization Programs in Canada

The roles and responsibilities of federal, provincial, and territorial health authorities in the planning and delivery of immunization programs are described in a previous section, "Immunization in Canada." A summary of the routine childhood immunization programs across Canada, as well as special immunization programs offered to selected high-risk groups, is presented below. Information is also provided on cold-chain monitoring of vaccines and screening programs for hepatitis B carriage and rubella protection.

10.1 Routine childhood immunization programs

Surveys conducted by the Division of Immunization (and the Division of Blood-borne Pathogens for hepatitis B immunization), LCDC, to review provincial and territorial immunization programs show that most jurisdictions have a recommended schedule (Table 7) very similar to that recommended by NACI (Table 1). Differences among jurisdictions are mostly due to the specific products that are used. All provinces and territories have revised their recommended schedules to accommodate the second dose of measles vaccine at 18 months of age or between 4 to 6 years of age.

Manitoba is the only province currently using OPV exclusively. Quebec switched to IPV in early 1996. Prince Edward Island did use a sequential schedule consisting of IPV for the first three doses and the booster for those 14 to 16 years of age, and OPV for the dose at 18 months of age and the booster between 4 to 6 years of age and has just switched to using IPV only. With the exception of Manitoba, all provinces and territories currently have a universal childhood hepatitis B immunization program; grade levels targeted for immunization are indicated in Table 7. Ontario currently has a one-time catch-up program for students in grades 9 to 13, after which a program for grade 7 will be maintained. Prince Edward Island, New Brunswick, and the Northwest Territories also have immunization programs for infants.

10.2 Special immunization programs

Table 8 summarizes information regarding special immunization programs. In most cases, these programs are based on NACI recommendations; however, the specific target groups for some vaccines differ among jurisdictions. The target groups for influenza and pneumococcal vaccines are very consistent among jurisdictions and with NACI recommendations. They include persons with chronic cardiac, pulmonary, and renal diseases; institutionalized children and adults; people ≥ 65 years of age; children and adolescents with long-term histories of treatment with acetylsalicylic acid; and persons with specific chronic diseases (such as cancer, immunodeficiency, anemia, and hemoglobinopathies).

Prince Edward Island does not have a program to immunize against pneumococcal infection or influenza. Reported recommendations for meningococcal vaccine vary more widely among jurisdictions that have programs for this vaccine. One or more of the four specific NACI recommendations are included in each jurisdiction; Prince Edward Island does not offer the vaccine to any group. Seven jurisdictions report special Bacille Calmette-Guérin vaccination programs, mainly for Aboriginal populations. In addition to the vaccines listed in Table 8, most provinces and territories provide hepatitis B vaccination to some of the recognized high risk groups, e.g. household or sexual contacts of cases and chronic carriers, hemophiliacs, and persons on hemodialysis. No specific information is available for coverage under any of the special programs.

10.3 Vaccine cold-chain monitoring

An important goal of effective vaccine delivery programs is ensuring that administered vaccines have a maximum potency. Not adhering to the vaccine cold chain (maintaining appropriate temperatures from the time vaccines leave the manufacturer to their administration) can result in reduced potency and vaccine effectiveness, as well as increased rates of local reactions after administration of the vaccine.

Exposure to either excess heat or freezing, depending on the vaccine, can damage vaccine products. A number of local, provincial, and territorial studies across Canada have demonstrated breaks in maintaining the cold chain during transportation and storage. It is important for all persons involved in immunization programs (including vaccine handling and storage) to recognize cold-chain monitoring as an integral part of these programs and not as a limited activity. Sources of information on vaccine storage and transportation include national guidelines published by the Division of Immunization, LCDC[26], provincial and territorial guidelines, WHO cold-chain documents, and various product monographs produced by vaccine manufacturers; some of these are listed in the selected reading list at the end of this report.

Table 7
Routine Immunization Schedule for Infants and Children
Provincial and Territorial Practices, Canada

Province or Territory	DPT	Polio	Hib	Td-Polio	Hepatitis B (3 doses) Grade/Age	MMR (first dose)	MMR/MR (second dose)
NF	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV	2,4,6,18 months	14 to 16 years: Td-IPV	Grade 4	12 months	18 months: MMR
PE	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV	2,4,6,18 months	14 to 16 years: Td-IPV	Grade 3 & Infants: 2,4,15 months	15 months	18 months: MMR*
NS	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV	2,4,6,18 months	14 to 16 years: Td-IPV	Grade 4	12 months	4 to 6 years: MMR
NB	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV	2,4,6,18 months	14 to 16 years: Td-IPV*	Grade 4 & Infants: 0,2,12 months	12 months	18 months: MMR
QC	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV*	2,4,6,18 months	14 to 16 years: Td-IPV	Grade 4	12 months	18 months: MMR
ON	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV*	2,4,6,18 months	14 to 16 years: Td-IPV**	Grade 7	12 months	4 to 6 years: MMR
MB	2,4,6,18 months & 4 to 6 years	2,4,18 months & 4 to 6 years: OPV	2,4,6,18 months	14 to 16 years: Td-OPV	Not planned	12 months	5 years: MMR
SK	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV*	2,4,6,18 months	14 to 16 years: Td**	Grade 6	12 months	18 months: MR
AB	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4-6 years: IPV	2,4,6,18 months	14 to 16 years: Td	Grade 5	12 months	4 to 6 years: MMR
BC	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV*	2,4,6,18 months	14 to 16 years: Td	Grade 6	12 months	18 months: MMR
YT	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV	2,4,6,18 months	14 to 16 years: Td-IPV	Grade 4	12 months	18 months: MMR
NT	2,4,6,18 months & 4 to 6 years	2,4,6,18 months & 4 to 6 years: IPV*	2,4,6,18 months	14 to 16 years: Td-IPV**	Grade 4 & Infants: 0,1,6 months	12 months	18 months: MMR

Notes:

PE* Currently a second MMR dose is also given to children 4 to 6 years of age who would not have received their second dose at 18 months.

NB* Polio booster is recommended for adolescents 14 to 16 years of age who received every previous dose (IPV) by injection.

QC* Polio vaccine at 4 to 6 years and 14 to 16 years of age are omitted if OPV was used for earlier doses.

ON* DPT-Polio 5th dose at 4 to 6 years of age not necessary if the 4th dose was given after the 4th birthday.

ON** Polio vaccine at 14 to 16 years of age is not required if the child has completed primary series and received one or more doses of OPV in the past. OPV was used routinely in Ontario from January 1990 through March 1993.

SK* DPT-Polio 5th dose at 4 to 6 years of age not necessary if the 4th dose was after the 4th birthday.

SK** Polio vaccine at 14 to 16 years of age given only if one dose of OPV not received.

BC* DPT-Polio 5th dose is not necessary if the 4th dose was given after the 1st birthday.

NT* DPT-Polio 5th dose at 4 to 6 years of age not necessary if the 4th dose was given after the 4th birthday.

NT** Polio vaccine at 14 to 16 years of age is not required if the child has completed primary series and received one or more doses of OPV in the past.

Manufacturers, provinces, and territories have devoted a lot of effort in recent years to improve the cold chain through better transport conditions and the use of cold-chain indicators. Two provinces and the two territories have established a cold-chain monitoring system, including a process to evaluate the system in two jurisdictions. One other province is in the process of developing a formal system and three others report varying levels of monitoring despite the lack of formal systems. Reported methods of cold-chain monitoring include the use of chemical (cold and warm) temperature monitors for shipping vaccines; the distribution of maximum and minimum refrigerator thermometers to public-health units, and/or physicians' offices; distribution of guidelines on cold-chain maintenance; regular recording and/or monitoring of refrigerator temperatures for temperature deviations by 24-hour alarm systems or by frequent (e.g. twice daily) manual checks on refrigerator temperatures at central storage points; and the use of special containers for transporting

Table 8
Special Immunization Programs by Target Groups, Canadian Provinces and Territories

	Influenza	Pneumococcal	Meningococcal	BCG
≥ 65 years of age	All except NB, PE, NT	ON, NT, YT		
Immunodeficiencies	All except PE	NF, NB, ON, MB, AB, NT, YT	MB, SK, BC	
Chronic cardiac diseases	All except PE	NB, ON, MB, SK, AB, NT, YT,		
Chronic pulmonary diseases	All except PE	NB, ON, MB, SK, AB, NT, YT,		
Diabetes mellitus and other metabolic diseases	All except PE	NB, ON, MB, AB, NT, YT		
Chronic renal diseases	All except PE	NB, ON, MB, AB, NT, YT		
Cancer	All except PE	NF, ON, MB, NT, YT		
Hemoglobinopathies	All except PE, NT	NB, YT		
Long-term acetylsalicylic-acid therapy	All except PE, NT			
Institutionalized children or adults	All except PE	ON, NT, YT		
Sickle-cell syndrome	NF, NS, MB, BC	ON, MB, AB, YT	MB	
Asplenia (hereditary/post splenectomy)	NS, MB, BC	All except PE, QC	QC, MB, SK, AB, BC	
Cirrhosis	NS, QC, BC, YT	NB, ON, MB, SK, AB, YT		
Nephrotic syndrome	NS, QC, MB, BC, YT	ON, MB, AB, YT		
Chronic cerebrospinal fluid leak	BC	NS, NB, ON, MB, AB, NT, YT	NT	
Travellers to endemic areas	NS		NB, MB	
Contacts of cases in an outbreak			NF, QC, ON, SK, NT, YT	
Family, sexual or other close contacts	MB, AB		NF, QC, YT	
Aboriginal populations				QC, ON, MB, SK, AB, NT, YT

vaccines by health units. In addition to some of the methods mentioned above, Ontario requires manufacturers to provide evidence of maintaining cold chain during transportation to the central government pharmacy. Still the cold chain is far from optimal and more efforts will have to be made to try to comply with the published guidelines.

10.4 Hepatitis B screening in pregnancy

The Division of Blood-borne Pathogens, LCDC, conducted a survey of all provincial and territorial epidemiologists in the summer of 1996; the survey was on policies and data related to the national goal and targets for hepatitis B infection and immunization[27]. Information was obtained on the specific national target, "to screen 100% of pregnant women for evidence of HBsAg, and to immunize 100% of neonates of carrier mothers with vaccine and hepatitis B immune globulin (HBIG) as soon as possible after birth, by the year 1995." The information is summarized below.

- Prenatal screening for hepatitis B is the stated policy of the health departments in eight provinces and the territories; screening of prenatal blood is routine in nine. No province or territory was able to provide data to directly address the specified target (i.e. in a recent period, the number who should be screened prenatally and the number actually screened). Some available information for 1995 indicates that 47,532 prenatal women in Alberta were screened (Statistics Canada lists 40,063 livebirths and stillbirths in Alberta for 1994); all prenatal women are screened in Prince Edward Island with 1,746 screened (1,729 livebirths and stillbirths for 1994); 56,133 prenatal women were tested in British Columbia, (47,304 livebirths and stillbirths for 1994); and 166,818 prenatal women were tested in Ontario (148,013 livebirths and stillbirths for 1994).
- Eleven provinces and the territories have programs to identify and immunize neonates of infected mothers. Again, few provinces or territories were able to provide data to directly address the specified target (i.e. in a recent period, the number of neonates of carrier mothers and the number of those immunized). Two neonates of HBsAg-positive mothers were completely immunized in Prince Edward Island in 1995. From 1986 to 1994 in Calgary and 1991 to 1994 in Edmonton, 95% completed immunization.

The impact of the 1989 NACI guidelines for universal hepatitis B screening was evaluated in a study of pregnant women in the Ottawa-Carleton region[28]. The study also surveyed the proportion of women who had their HBsAg results available when their infants were delivered, and it examined characteristics of patients, physicians, and hospitals to determine if the characteristics were related to the lack of available HBsAg results. The availability of the antenatal HBsAg-screening results increased from 5% between 1988 and 1989 to 81% between 1993 and 1994. There was, however, little change over time in the proportion of women admitted to hospital without HBsAg results and who were tested in hospital. In fact, in-hospital testing for HBsAg only increased the overall screening rate in 1993 to 1994 by 2%, up to 83%. At a hospital with a written policy on the HbsAg screening, HbsAg results were available for 96% of women. At a hospital with no policy, HBsAg results were available for only 74% of women. Other hospitals had unwritten policies, which involved calling physicians' offices for results if antenatal HBsAg results were not available. These hospitals tended to be less firm than the hospital with a written policy about screening women who were admitted without HBsAg results.

Another survey, conducted and presented at the 1996 National Immunization Conference, evaluated prenatal screening for hepatitis B infections in Quebec hospitals[29]. The random sample consisted of 2,551 women who delivered liveborn infants between 1 April 1993 and 31 March 1994 in eight randomly selected large (≥ 500 births/year) hospitals and in eight randomly selected small (< 500 births/year) hospitals. The sample included 212 women from each large hospital and 114 from each small hospital. The adjusted overall screening rate for hepatitis B, as assessed by a review of hospital and physicians' office records, was 91.2% (95% CI - 88.3 to 94.2). Large hospitals had a significantly higher rate (93.0%) than small hospitals (67.1%).

An Ontario survey presented at the 1996 Canadian Immunization Conference indicated that, according to physicians' replies, of 250 infants of positive mothers who were followed, 218 (87%) had received HBIG at birth and 216 (86%) had received a complete hepatitis B vaccine series[30].

10.5 Rubella screening

The survey to evaluate prenatal screening for hepatitis B infections in Quebec hospitals also examined prenatal screening for rubella[31]. The adjusted overall screening rate for rubella was 94.0% (95% CI - 91.7 to 96.4). A total of 200 (8.4%) women tested seronegative; 121 were considered at risk of future infection because, either they were known to be not vaccinated or their vaccination status was unknown. The results are being used to recommend in-hospital postpartum vaccination of seronegative women.

10.6 The acceptability of multiple injections and perceptions of parental preferences

In a study of parental and health-care provider vaccine preferences, mothers of newborn infants were asked about their vaccine preferences (Dr. S. Halperin, Clinical Trials Research Center, Halifax, Nova Scotia: personal communication, 1996). Mothers were asked if they would prefer a new acellular pertussis vaccine associated with

fewer adverse reactions but requiring separate injections of the poliovirus and conjugate Hib vaccines, or the currently licensed, whole-cell pertussis vaccine which could be given in a single injection but is associated with more adverse reactions in the 48 hours after immunization. Of the 400 mothers surveyed, 57.3% preferred the new acellular pertussis vaccine compared to 29.5% who preferred the whole-cell vaccine. In contrast, of 200 health-care providers (100 nurses and 100 physicians), 29.3% preferred the new acellular vaccine and 61.1% the whole-cell vaccine. When asked to predict parental preferences, health-care professionals predicted that 19.1% of parents would choose the new acellular pertussis vaccine and 71.4% the whole-cell vaccine. The study demonstrated a clear difference in vaccine preferences of parents and health-care professionals. It also demonstrated an even larger gap in the understanding of parental preferences by health-care providers.

11. Activities Related to the Elimination of Polio and the Report of the Working Group on Polio Elimination

11.1 Activities leading to polio elimination

The historical and recent epidemiology of poliomyelitis in Canada is described in the preceding section, "Epidemiology of Selected Vaccine-Preventable Diseases." Poliomyelitis was under control in Canada by the early 1970s, mainly through extensive immunization, improved sanitation, and surveillance. A total of 56 cases of poliomyelitis were reported from 1965 to 1995; 35 (63%) were due to wild virus infection and the remaining were associated with the use of OPV.

Starting in 1975, wild virus cases were identified as indigenous or imported. Of the 15 wild virus cases reported since 1975, only one (in 1977) was the result of indigenous wild virus infection. The last case of wild paralytic poliomyelitis in Canada occurred in 1988 as a result of virus importation. Wild polio virus was imported from the Netherlands to Canada in 1978-1979[18] and in 1993[19]. Both these importations were linked to outbreaks in religious communities in the Netherlands; outbreaks in Canada were limited to similar closed communities (i.e those that do not accept routine immunizations for religious reasons). In the earlier importation, 11 paralytic cases occurred in British Columbia, Ontario, and Alberta. No clinical cases resulted from the 1993 importation to southern Alberta.

In 1989, NACI established a committee to review potential cases of paralytic polio for classification as wild or vaccine-related and to monitor the importation of wild polio virus[32]. With increasing efforts in the American Region to meet the PAHO goal of regional elimination by 1995, it was imperative that Canada formally evaluate poliomyelitis surveillance and gather evidence for a certification of polio elimination.

In October 1993, the Advisory Committee on Epidemiology (ACE) convened a meeting to discuss the importation of wild polio virus from the Netherlands. Based on ACE recommendations, the Working Group on Polio Elimination was established in 1994. The Working Group reviewed all reported cases of suspected paralytic poliomyelitis and monitored continuing evidence for the elimination of polio in Canada. The Working Group on Polio Elimination and the Division of Immunization, LCDC, prepared documentation on the elimination of polio for a National Certification Commission. Upon the Commission's favourable review of the situation and its report to the International Certification Commission, Canada and the rest of the American Region was certified as polio-free in September 1994. This was three years after the last indigenous wild case of poliomyelitis was reported in the Region.

Routine childhood immunization against poliomyelitis is still recommended because of the risk of importation of wild virus from other countries. Relatively high coverage rates have been maintained (approximately 90% for three or more doses of polio vaccine by 2 years of age). Paralytic poliomyelitis remains as a nationally notifiable disease in Canada; however, no cases due to wild virus have been reported since the imported case in 1988. In March 1996, wild virus importation from India was detected in an asymptomatic 15-month-old boy following a trip to that country[20]. Although no paralytic disease occurred, the incident emphasizes the importance of continuing routine immunizations and surveillance activities until the global eradication of polio is achieved.

11.2 Report of the Working Group on Polio Elimination

In its first year, the Working Group on Polio Elimination collaborated with the National Certification Commission (established according to PAHO recommendations) in preparing a report on the evidence for the elimination of indigenous poliomyelitis in Canada. Polio surveillance had been enhanced in 1992 through the inclusion of active surveillance for AFP; admissions to pediatric hospitals in the IMPACT network were monitored. As well, all provincial laboratories were asked to refer polio virus isolates (whether or not they were obtained from symptomatic patients) to the National Reference Centre for Enteroviruses in Halifax for typing. In addition, LCDC conducted surveys to obtain information about levels of polio immunization in 2-year-olds in Canada.

To ensure that Canada continues to be polio-free, the Working Group currently monitors surveillance activities for potential cases of poliomyelitis. The Working Group meets at a formal annual meeting and additional teleconference meetings are held as required throughout the year to evaluate reported cases of suspected paralytic poliomyelitis.

AFP surveillance has been further enhanced through the CPSP established in January 1996, which has been described previously in the section, " Canadian Paediatric Surveillance Program." The National Reference Centre for Enteroviruses continues laboratory surveillance to detect Sabin strains of polio although this has declined since

most provinces and territories no longer use OPV. The coincidental finding of an imported wild type polio virus in 1996 supports the effectiveness of the laboratory surveillance program. Age-appropriate coverage levels for polio vaccination at 2 years of age remain at approximately 90%. The Working Group recently developed a protocol for the investigation and reporting of suspected paralytic poliomyelitis, including AFP cases for those < 15 years of age. This protocol should serve as a standard guide to health units and further enhance the surveillance of poliomyelitis in Canada.

12. Working Group on Measles Elimination

A major national initiative toward measles elimination was made in 1996 with the adoption of the two-dose measles vaccine schedule across most of the country and the completion of a number of mass catch-up campaigns. In moving toward measles elimination in Canada, it is important to ensure that high levels of measles immunity across the country are maintained, and that any outbreak is rapidly detected and controlled with enhanced surveillance. At that time, Canada will be able to anticipate when it can claim to have eliminated measles.

To this end, the Working Group on Measles Elimination in Canada (WGMEC) has been established. The mission of the working group is as follows:

- to develop the tools to determine where Canada stands with respect to measles elimination;
- to develop a national surveillance protocol; and
- to propose its implementation across the country.

The first meeting of WGMEC was held in Ottawa on 25 October 1996. The scope of the task was outlined, and discussion focused on documenting measles coverage and enhancing surveillance with particular emphasis on laboratory issues, outbreak control, and research priorities. WGMEC recommended that vaccine coverage be assessed through national survey data with the 2-year-old age group being a priority, and that efforts should also be made to collect data on a two-dose coverage for school-entry children. With respect to laboratory issues, it was recommended that a representative of the Technical Advisory Committee, which is the federal/provincial body supporting public-health laboratories across the country, should join the working group. In addition, it was recommended that LCDC put mechanisms in place for standard serologic confirmation of cases of measles and "rash" illnesses from across Canada as a high priority. Increased efforts should be made to obtain as many measles virus isolates as possible in order to better assess the origin of importations and potential circulation of wild measles virus.

13. New Vaccines on the Horizon

Many more vaccines, such as conjugate pneumococcal and meningococcal vaccines, will appear in the coming years. Some will likely be available in a few years, thanks to the development of new technologies. Three products deserve special mention because of their recent or possible short-term availability and/or their availability in other countries, as well as their potential impact on child health: acellular pertussis vaccines, varicella vaccine, and rotavirus vaccines. The use and availability of the hepatitis A vaccine will not be elaborated upon. Although it is an extremely safe and efficacious vaccine, its use is more limited to high-risk groups; it is not, nor is it likely to be, recommended for routine use.

13.1 Acellular pertussis vaccines

Acellular pertussis vaccines (APVs) contain purified inactivated components of *Bordetella pertussis*. Several APVs have been developed with different components in varying concentrations, but all contain pertussis toxin (PT) and usually filamentous hemagglutonin. Some have been in widespread use in Japan for primary immunization of children > 2 years of age for over 15 years and for infants > 3 months of age since 1988. In the United States, APVs were first licensed in 1992 for the fourth and fifth booster doses in children 15 months to 6 years of age.

In Canada, between March and July 1996, three APVs were licensed to be used as booster doses in children from 15 months to 6 years of age. They include: Acel-P™ (Wyeth-Ayerst Canada Inc.), a monovalent APV; ACEL-IMUNE™ (Wyeth-Ayerst Canada Inc.), an APV combined with diphtheria and tetanus toxoids; and TRIPACEL™ (Connaught Laboratories Ltd.), an APV combined with diphtheria and tetanus toxoids. In December 1996, two APVs combined with diphtheria and tetanus toxoids (Connaught Laboratories Ltd. and SmithKline Beecham Pharma Inc.) were licensed for primary series in infants. At the recent National Immunization Conference, Connaught Laboratories Ltd., SmithKline Beecham Pharma Inc., Wyeth-Ayerst Canada Inc., and North American Vaccine Inc. indicated that they have applied for licensing of other combination products or intend to do so. Licensing of more combination products is expected in the foreseeable future.

Generally, reactogenicity is less than that reported following the use of the whole-cell pertussis vaccine. Immunogenicity compares favourably with whole-cell vaccines tested. Efficacy of these products as fourth and fifth doses, especially in regard to the whole-cell vaccines used for the primary series in Canada, is not known.

From 1990 to 1995, seven independent field trials of APVs were conducted in Germany (three trials), Italy (one trial), Senegal (one trial), and Sweden (two trials) for primary immunization in infants. Estimated vaccine efficacies were generally greater or more favourable than the whole-cell vaccines, depending on the whole-cell vaccine product compared. Licences were subsequently granted in several European countries for primary immunizations. In the United States, the Food and Drug Administration (FDA) licensed Tripedia® (Connaught Laboratories Inc.) in 1996 for use in infants and children ≥ 2 months of age for the primary series. As new data become available and additional licenses are granted in Canada, NACI will be recommending expanded indications. The present use of these products requires multiple injections for simultaneous administration of IPV, Hib, and hepatitis B vaccines. Data on the safety and immunogenicity of combined injections are not available as yet. Products combined with inactivated polio and Hib vaccine may become available in the near future.

It is likely that acellular vaccines will be more efficacious than the whole-cell vaccine currently used in Canada. Although the pertussis disease-reduction target will not be achieved on time, the general use of these new products will likely allow Canada to quickly correct the situation. In preparation for the incorporation of APVs for routine administration, a cost-benefit study was contracted out by the Division of Immunization, LCDC. Its results are favourable to the use of the new APVs.

13.2 Varicella vaccines

Varicella (chickenpox) is usually a benign disease, generally experienced by 90% of people; however, it can be severe in immunocompromised individuals. Herpes zoster is also a local manifestation of reactivated, latent varicella infection in the dorsal root ganglia; it occurs in 35% of individuals.

Currently no varicella vaccines are licensed in Canada and it is unlikely that a vaccine will be available for routine use within the next 2 years. A safe, effective, live, attenuated varicella vaccine against varicella zoster was licensed in 1995 in the United States. The American Academy of Pediatrics recommended varicella vaccine for universal use in early childhood and immunization in older adolescents. The recommendation was based on the frequency of serious complications and deaths after mild varicella, the excess cost to the family and society incurred by varicella infection, and the safety and efficacy of the vaccine. Routine use of the vaccine was reported to

result in savings of $384 million per year in the United States[33].

However, the Canadian public and health-care providers do not perceive varicella as a severe disease. It does not present a burden to the public-health community. Health-care providers are not completely convinced by the cost-benefit analysis, although savings are great from a societal perspective. Seroconversion in healthy children is 90% versus 87% in leukemic children and 94% in healthy adults. The immunity conferred by the vaccine is considered to be probably long-term. This vaccine may also reduce the risk of herpes zoster, at least in the short term. Reported adverse events include rash, usually maculopapular rather than vesicular, with < 50 spots in 4% to 10% of recipients; injection-site lesions, swelling, pain, and systemic reactions are rare. The vaccine currently used in the United States is difficult to handle because it has to be frozen at all times (below –15° C). A similar vaccine has been licensed in Japan, Korea, and several European countries. A new more heat-stable vaccine has been developed. In Canada, varicella vaccine can be obtained from manufacturers for compassionate use in emergency situations. Varicella has been monitored through IMPACT and a Canadian cost-benefit study of the potential use of the vaccine will likely be implemented in 1997.

When a vaccine becomes available for routine use in Canada, it will be important to have a common approach across the various jurisdictions. Significant but partial coverage of children may result in older persons (who are at higher risk for complications) being exposed and a shift in the epidemiology of the disease.

13.3 Rotavirus vaccines

Rotavirus infections are an important cause of gastroenteritis in children < 5 years of age. In the United States, where data are available, these infections are an important cause of dehydration and hospitalization. They result in an estimated 55,000 hospitalizations per year due to dehydration; however the number of related deaths is very limited (300 in 1985). No vaccines are licensed in Canada or the United States. Advances toward development of a successful rotavirus vaccine have been slow. A variety of live attenuated vaccines have been developed including animal rotavirus reassortment strains and temperature-sensitive human rotavirus mutants. Efficacy of candidate vaccines is still under evaluation.

It is likely that the first vaccines adopted for widespread clinical trials will be the multivalent, live, attenuated reassortant vaccines that seem to confer around 50% protection against any diarrhea. They are significantly more effective (around 80%) against severe gastroenteritis and virtually 100% efficacious against dehydration. Vaccines are unlikely to become available on the market before a few years.

Currently, epidemiologic data on rotavirus infections in Canada are almost totally lacking. To prepare for the potential introduction of this vaccine, IMPACT is assessing the burden of the disease through specific surveillance of rotavirus infections. A Canadian cost-benefit analysis will hopefully be conducted in the near future.

14. Report from the 1996 Canadian National Immunization Conference: "Immunizing for Health – Achieving Our National Goals"

The 1996 Canadian National Immunization Conference, held in Toronto from December 8 to 11, was attended by nearly 600 participants. It was a forum for discussion and information exchange related to the practical aspects of immunization programs in Canada, and covered disease-related and programmatic issues. Progress toward the achievement of recently established Canadian national goals for the reduction of vaccine-preventable diseases of infants and children was examined. The following summarizes the important points raised by the participants.

Carol Bellamy, executive director of UNICEF International, stated in her keynote address, that immunization is "...not only the right thing to do but an obligation for society. It is unacceptable to have the capacity to save lives and not to use it." Ms. Bellamy said the past two decades have witnessed a "quiet revolution" in public health. Basic immunization services now reach four out of five of the world's children. She stressed that only strong political will and determined efforts at collaboration between the public and private sectors can translate today's scientific breakthroughs into real help for children.

The Honourable David Dingwall, the federal Minister of Health, emphasized in his opening address that, "Immunization is not simply a worthy but isolated activity. It is part of the evolution of our health system." He congratulated the participants "...on their efforts to build an effective system that has helped relieve financial pressure on the health-care system while improving health and saving lives." He made special mention of the success in halting an outbreak of measles and gave credit to the public-health professionals in the field.

A number of issues raised during the conference generated consensus among the participants and are worthy of mentioning because some of them call for action. First and foremost, participants agreed that there is an important need to raise the profile of immunization as a useful population-health strategy. Calculation of deaths prevented, diseases avoided, and costs saved by the prevention of diseases for which immunization is available, as well as the cost-effectiveness of immunization for the new or expanded programs provide useful background data to support this effort. Such an initiative could be led by the Council of Chief Medical Officers of Health for Canada. The second part of this strategy indicates opportunities for disease reduction and cost savings by the promotion and placement of certain vaccine initiatives. These may include providing a uniform schedule of childhood immunizations across the country, promoting the utility of increasing the uptake of influenza and pneumococcal vaccine, and possibly introducing a broader pneumococcal vaccine use. The Council could also lead these initiatives.

A series of national conferences and extensive consultation with stakeholders has resulted in broad consensus on goals for vaccine-preventable diseases of infants and children. These goals are invaluable as an expression of Canada's commitment toward improved health and the reduction of inequalities; they also provide an opportunity for program evaluation and more effective targeting of resources. Early political approval has not been forthcoming, except for measles; the goal of eliminating indigenous disease by the year 2005 was endorsed at the December 1995 Conference of Deputy Ministers. However, it is hoped that the full set of goals will become a political reality soon. Only a regular evaluation mechanism built into the core budget can ensure the development of standard methods and allow the full benefits of the goals to be realized. Although some goals and targets are already achieved and good progress is being made, much effort is needed to achieve others (e.g. the need to replace the current whole-cell vaccine for pertussis with less reactogenic and more efficacious, new generation, acellular pertussis vaccines). Many evaluation tools remain to be put in place at all levels.

Participants clearly supported the development of goals for other diseases for which effective vaccines currently exist and those diseases for which vaccines are likely to be licensed in the next several years. These diseases include varicella, rotavirus infections, hepatitis A, influenza, and meningococcal and pneumococcal diseases. The importance of the goals and an informed use of vaccines was emphasized. For instance with varicella, scattered vaccine use may result in the eventual shift of cases to older children and adults, possibly resulting in more complications and more serious disease.

The growing anti-immunization lobby was also discussed. Research suggests that likely only 1% of the overall population is firmly opposed to immunization but that up to 6% or 7% are ambivalent. Parents want to be informed and involved. For them, the issue is safety. More education of health-care providers and consumers,

and social marketing is needed. The conference coincided with the official launch of the National Immunization Awareness Program, which involves public-service announcements on the radio, posters, and printed public-service announcements. Current campaign partners are the Canadian Public Health Association, the Canadian Medical Association, the Canadian Paediatric Society, and Health Canada.

Conference participants acknowledged that a strong Canadian post-marketing surveillance system must be maintained. This system must have an active component to ensure detection of rare but serious adverse events.

An immunization tracking system is urgently needed in Canada to identify children due or overdue for immunization, to notify parents, to make appointments, to provide a database for health-care providers to monitor the immunization of patients at each encounter regardless of where the vaccine was administered, to assist in planning and identifying populations at risk for delayed immunization, to target interventions appropriately, and to evaluate the success of the program. In provinces where physicians deliver the bulk of the immunizations, tracking systems adapted for practice, as well as for public-health needs, must be developed. The positive exchange of ideas between conference participants suggests that the time has arrived for a national program to be administered provincially, thus ensuring compatibility between provinces so that this health-care information can be accessed when needed. A clearing-house of current provincial, territorial, and local projects related to the issue and a consensus conference is needed to decide on standards and core information to be collected, and to ensure further compatibility of systems.

The task of providing immunization is growing rapidly in complexity and accordingly must focus on provider preparedness and performance expectations. Following extensive consultation between the NACI and professional societies, provincial epidemiologists, public-health workers, hospital associations, advocacy groups, and federal agencies, draft guidelines for childhood immunization practices are being developed. They contain several recommendations for greater accessibility, including clinic hours convenient for drop-ins and semiannual audits of coverage. These guidelines were discussed at a break-out session. Seventy-six percent of participants said the guidelines were very much needed in Canada. From the provincial and territorial perspective, the consultative process is appreciated.

The guidelines could serve as a trigger for change and a tool for program evaluation. From the public-health provider's perspective, implementation strategies are essential to facilitate achieving the guidelines in all settings. From the private-practice provider's perspective, the provision of immunization is undervalued as a medical service; better education and resources are needed if the guidelines are to be achieved. Around 70% of participants indicated their willingness and ability to use routine clinical encounters to screen for immunization and provide updates as needed. A majority also found the idea of a comprehensive, audited tracking system feasible. However, about one-half indicated that they would be unable to accommodate drop-in immunization at unscheduled hours. Serious concern was expressed about frequent discrepancies between expert opinion statements and product monographs regarding contraindications to particular vaccines; these discrepancies need to be addressed. In disseminating the guidelines to providers, it is essential to "prepare the way." It should be emphasized that the guidelines are goals and, as such, should serve to express the ideal, as well as stimulate dialogue on what is needed to achieve them.

As many vaccine-preventable diseases approach eradication in Canada, the immunization status of new Canadians becomes increasingly important. At a break-out session, participants discussed the barriers to reaching new Canadians with information about the benefits of immunization. Every year, about 60,000 newcomers < 18 years of age arrive in Canada. Inadequate or non-existent immunization records, partial immunizations, and cultural or linguistic misunderstandings are common problems. Before coming to this country, immigrants are screened only for physical status and general medical history. Once they arrive, there is little or no systematic effort to upgrade immunization status. When newcomers come into contact with the health-care system, health-care providers are often not well-informed about the pertinent issues; moreover, in some provinces, even this contact is discouraged by a policy of withholding health cards until a residency requirement has been met. There was strong consensus among participants that this situation demands urgent attention. A multi-faceted approach is essential with federal leadership, special consideration for areas with high immigrant populations, and an outreach program designed to address cultural and linguistic needs. It was felt that there was a need to change the medical immigration screening process to include immunization update and other documentation.

First Nations children are at much higher risk for vaccine-preventable diseases than others because of lower rates of immunization. There is evidence that the foundation of this problem is socioeconomic. Participants identified a widespread "knowledge deficit" about the effects and appropriateness of immunization, especially common among older community members. The need for a solution is urgent. A solution will take a sensitive and a multi-faceted approach, as well as a commitment for change which is backed by real resources.

15. Cost-Benefit Analyses of Immunization Programs for Vaccine-Preventable Diseases

The World Bank has stated that immunization should be among the first public-health initiatives in which governments around the world invest[34]. Indeed, vaccines are considered to be the most cost-beneficial health intervention and one of the few that systematically demonstrates more benefits than costs by far. A review of 587 life-saving interventions and their cost-effectiveness indicated that routine immunization programs for children were among the ones with better cost-effectiveness[35]. They were also one of the very few programs with a cost of < $0 per year of life saved. The 587 interventions ranged from those that save more resources than they cost, i.e. a cost of < $0 per year of life saved, to those that cost > $10 billion per year of life saved. Overall, median intervention costs were US $42,000 per year of life saved. Many cost-benefit studies of immunization programs almost invariably demonstrate a very positive cost-benefit ratio, often in the range of 7 to 80 per 1. However, very few studies of immunization programs have been or are being conducted in the Canadian context; findings on *Haemophilus influenzae* type b, hepatitis B, measles, mumps, rubella, pertussis and invasive pneumococcal diseases are presented below.

15.1 *Haemophilus influenzae* type b

A study was undertaken in 1986 by Connaught Laboratories Ltd. to assess the effects of various vaccination programs on Hib systemic diseases in Canada. The morbidity, mortality, and cost impact of the disease in Ontario was examined extensively, and a model was developed to predict the morbidity, mortality, and cost impact of the disease under different circumstances. These included different hypothetical vaccination programs, including a routine single-dose program with a polysaccharide-conjugate PRP vaccine used at 24 months of age, a routine single-dose program at 18 months of age with a conjugate vaccine, and a routine three-dose primary series with a single booster at 18 months of age using a conjugate vaccine. The study indicated that all programs would be cost beneficial but that the most effective program would be the latter one, which would result in a net saving of $37,000,000 annually. This program is the one currently applied across Canada. More information on this study can be obtained from Dr. Van Exan, Connaught Laboratories Ltd.

15.2 Hepatitis B

A cost-effectiveness analysis of universal vaccination of infants against hepatitis B in Canada was conducted in 1993[36]. If the cost of a dose of vaccine was approximately $7, the analysis concluded that universal vaccination would result in a net cost saving to society. Universal vaccination against hepatitis B in infancy was concluded to be economically attractive and comparable in cost-effectiveness to existing health-care interventions. Lower vaccine prices (in 1993, the cost was approximately $30 per dose) would also greatly improve the attractiveness of universal immunization. Today the cost of vaccine is substantially lower, and provinces have started universal immunization, mostly of adolescents.

15.3 Measles, mumps, and rubella

Health Canada commissioned a cost-benefit study of a routine two-dose MMR immunization program together with a mass campaign using MR vaccine, compared to the current one-dose immunization strategy. The use of MR and MMR vaccines (instead of monovalent measles vaccine) was based on the recommendation of a federal/provincial working group on measles elimination.

The benefits included all direct health-care costs which would be averted by a two-dose program and a mass campaign. Also included were all indirect costs incurred by patients or their families, such as loss of productivity. The estimated direct and indirect costs added up to $929 on average for each measles case. The averted costs related to outbreak-control activities by using a two-dose program and a mass campaign were also taken in consideration; they averaged $520 for each outbreak-related case of measles. Costs of the program included the price of the vaccine, its administration, the direct and indirect costs of VAAEs, and other mass-campaign costs such as planning, management, promotional activities, and evaluation.

The study presented cost-benefit analyses for two scenarios. The calculations covered a prospective 20 years. The first scenario was a routine two-dose schedule of MMR vaccine at 18 months of age **plus** a mass-campaign with MR vaccine for all people from 18 months of age to 18 years of age. The cost-benefit ratio for this scenario was that for each $1.00 spent, benefits were $2.61. The second scenario was a routine two-dose schedule of MMR vaccine at 5 years of age **plus** a mass-campaign with MR vaccine for all people from 5 to

18 years of age. The cost-benefit ratio for this scenario was slightly higher, i.e. for each $1.00 spent, benefits were worth $2.92. A sensitivity analysis, using measles monovalent vaccine for the mass campaign instead of MR vaccine, found a similar ratio, i.e. for each $1.00 spent, benefits were worth $2.92. A further sensitivity analysis, using the MMR vaccine instead of MR vaccine for the mass campaign, found a lower ratio, i.e. for each $1.00 spent, benefits were worth $2.56. The costs of purchasing these vaccines may vary in a ratio of up to 8:1 with costs for MMR vaccine potentially being prohibitive for a mass campaign.

A study of the economic benefits of a routine second dose of MMR vaccine in Canada was also sponsored by Merck-Frosst Canada Inc. and conducted by the Montreal-based health economics company, Benefit Canada Inc. Findings also indicate that a routine second-dose immunization with MMR would result in considerable cost savings in Canada. More information can be obtained by contacting Dr. Marc Rivière of Benefit Canada Inc.

15.4 Pertussis

Acellular pertussis vaccines are currently licensed in Canada for use as the fourth and fifth booster doses at 18 months of age and 4 to 6 years of age, respectively. Licensing of acellular vaccines for primary series in infants is expected in the near future. The relative safety, protection provided from disease, and cost-benefit ratios of the acellular vaccines in comparison with currently available whole-cell vaccines are critical issues related to the introduction of acellular vaccines into routine immunization programs of infants.

A selective license for the use of acellular vaccines as fourth and fifth booster doses was given in 1993 in the United States. An overall direct cost-benefit ratio for the DTP vaccine was estimated as $6.21 saved for each $1.00 spent on immunization; the cost-benefit ratio of the pertussis component alone is $8.39 saved for each $1.00 spent. Recently a cost-benefit study was conducted on the use of DTaP vaccines for all doses. Assuming no additional visits and that the prices of new acellular vaccines would be similar to those already licensed, a direct cost-benefit ratio for immunization with DTaP vaccines was estimated for each $1.00 spent, benefits were worth $5.35; for the acellular pertussis component alone, benefits were worth $5.98 for each $1.00 spent.

The analyses were based on assumed savings of $20.5 million averted from the treatment of common and moderately serious adverse events. However, additional savings (not included in the modelling for the above estimates) could be anticipated: $12 million from lower rates of more serious adverse events; $40 million from reduction of pertussis cases; $15 million from reduction of compensation costs; and potentially $30 to $80 million if more DTaP vaccines were allowed, thus eliminating the one-dose pertussis vaccine.

The Division of Immunization sponsored a study under contract to the Ottawa-based firm of Pran-Manga and Associates regarding the new acellular pertussis vaccines. The purpose was to provide quantitative estimates of the economic benefits and costs of introducing new acellular pertussis vaccine combinations to replace previous whole-cell pertussis vaccine combinations in routine immunization schedules in Canada. The intent was to present estimates in a manner suitable for purposes of provincial and territorial policy and program planning. The analysis assumed that the five-dose schedule for pertussis would continue to be used. Analysis of multiple versus single injections (assuming no additional visits were included) was done based on trivalent or quadravalent products because, at the time, a penta product (i.e. with diphtheria, pertussis, tetanus, Hib and polio) was not licensed. Extra time spent for multiple injections was envisioned as well as the potential negative impact on public acceptance. The results indicated a very favourable cost-benefit ratio for introducing the new products and overall cumulated potential savings of up to $370 million by the year 2007.

15.5 Invasive pneumococcal diseases

The utility and costs of an immunization program against invasive pneumococcal infections is currently being studied. The effectiveness of an immunization program using the pneumococcal polysaccharide vaccine to reduce mortality and morbidity is being evaluated in four categories of high-risk patients: residents in long-term care facilities, patients with chronic illnesses, persons ≥ 65 years of age, and HIV-infected persons. Quality-adjusted years of life gained will be used to assess the program's utility. Costs for the program promotion, and supply and administration of vaccines will be estimated from a societal perspective. The principal investigator in this study is Dr. Philippe De Wals, University of Sherbrooke; the work is being conducted under a grant from the *Conseil d'évaluation des technologies de la santé du Québec.* A report is expected in the near future.

16. Addressing Concerns Regarding Immunization and Vaccines

The text that follows is directed to health professionals who counsel patients about the benefits and risks of vaccination, and to patients who may have read some disturbing allegations about the risks that raise doubts about the value of vaccination in preventing disease. The text is adapted from a booklet by the Centers for Disease Control and Prevention[37]. The text will be expanded over time, although it is not meant to be an exhaustive commentary containing responses to all the allegations questioning the safety and effectiveness of vaccines. It is hoped instead that the reader will use it to learn about some of the ways that these allegations are misleading, and thus develop a healthy skepticism when confronted by the views of special interest groups that attempt to discredit vaccines in favour of alternatives, which rarely, if ever, have stood the test of true scientific examination. No drug products, vaccines included, are perfectly safe. But when the risks and benefits of vaccination are compared, a clear choice emerges.

16.1 Preamble

It was more than 200 years ago that Jenner was able to protect a man from the dreaded disease, smallpox, through vaccination. Since then, smallpox has been eradicated from the planet through mass immunization. Other miracles have taken place, such as the elimination of polio from the Americas – a disease that 40 years ago caused paralytic illness in almost 2,000 Canadians in 1 year – and controlling diseases that once maimed or killed in large numbers.

Nevertheless, there are individuals who are hesitant about or refuse immunization for themselves or their children. There may be several reasons.

- Some have religious or philosophic objections.
- Some see mandatory vaccination as government interference in an area which they believe should be open to personal choice.
- Some are concerned about the safety and/or efficacy of vaccines.
- Some believe that vaccine-preventable diseases do not pose a serious health risk.
- Some believe that immunization is not "natural."

Health-care providers should take these fears and beliefs into consideration when counselling patients about immunization. Parents and patients should be aware that immunization is considered by international health experts as one of the most important interventions to prevent disease that have ever been discovered. To have a tool as valuable as vaccines and not use it is considered unconscionable. The information below addresses common misconceptions which are often expressed by concerned parents who are reluctant to have their children immunized.

16.2 Misconceptions

16.2.1 Diseases had already begun to disappear before vaccines were introduced, because of better hygiene and sanitation.

Statements like this (variations include assertions that vaccines had absolutely no effect on disease rates) are very common in anti-vaccine literature, suggesting that vaccines are not needed. Improved socioeconomic conditions have undoubtedly had indirect effects on disease. Better nutrition, not to mention the development of antibiotics and other treatments, have increased survival rates among the sick; less crowded living conditions have reduced disease transmission; and lower birth rates have decreased the number of susceptible household contacts. But looking at the actual incidence of disease over the years can leave little doubt of the significant **direct** effects vaccines have had, even in modern times. Are we expected to believe that better sanitation caused the incidence of each disease to drop, coincidentally, just at the time a vaccine for that disease was introduced? Some examples follow to illustrate this.

1. Invasive disease due to *Haemophilus influenzae* type b, such as meningitis, was prevalent until just a few years ago when conjugate vaccines that can be used in infants (in whom most of the disease was occurring) were finally developed. Since sanitation is no better now than it was in 1990, it is hard to attribute the virtual disappearance of Hib disease in children in recent years to anything but the introduction of routine immunization. Data from reportable disease surveillance systems show that, from an estimated 2,000 cases a year prior to the availability of vaccine, there are now < 52 cases per year being reported; the majority are in infants and children who have not been immunized.

2. Varicella (chicken pox) can also be used to illustrate the point, since modern sanitation has obviously not prevented cases from occurring each year; almost all children get the disease sometime in their childhood, just as they did 20 or 80 years ago. If diseases were

disappearing, we should expect varicella to be disappearing along with the rest of them.

3. We can also look at the experiences of several developed countries that let their immunization levels drop. Three countries – Great Britain, Sweden, and Japan – cut back on the use of pertussis vaccine because of fear about the vaccine. The effect was dramatic and immediate. In Great Britain, a drop in pertussis vaccination in 1974 was followed by an epidemic of more than 100,000 cases of pertussis and 36 deaths by 1978. In Japan, around the same time, a drop in vaccination rates, from 70% to between 20% and 40%, led to a jump in pertussis from 393 cases and no deaths in 1974 to 13,000 cases and 41 deaths in 1979. In Sweden, the annual incidence rate of pertussis per 100,000 children, 0 to 6 years of age, increased from 700 cases in 1981 to 3,200 in 1985.

It seems clear from these experiences that not only would diseases not be disappearing without vaccines, but if we were to stop vaccinating, they would come back.

Of more immediate interest is the major epidemic of diphtheria now taking place in the former Soviet Union, where low primary immunization rates in children and lack of booster immunizations in adults have resulted in an increase from 839 cases in 1989 to nearly 50,000 cases and 1,700 deaths in 1994, with the number of cases increasing by two- to 10-fold each year. There have already been at least 20 imported cases in Europe and two cases in American citizens working in the former Soviet Union.

16.2.2 The majority of people getting disease have been fully immunized.

This is another argument frequently found in anti-vaccine literature – the implication is that vaccines are not effective. In fact, it is true that, in outbreaks occurring in highly vaccinated populations, cases who were immunized often outnumber those who were not – even with vaccines such as measles, which we know to be about 90% to 95% effective in one dose.

This apparent paradox is explained by two factors. First, no vaccine is 100% effective. To make vaccines safer than the disease, the bacteria or virus is killed or weakened (attenuated). For reasons related to the individual, not all persons vaccinated will develop immunity. Most routine childhood vaccines have efficacy in the 85% to 90% range. Therefore, over the years there is a buildup of susceptible individuals (each year contributing 10% to 15% of its cohort). Second, in a country like Canada with high immunization coverage, people who have been vaccinated vastly outnumber those who have not. How these two factors work together to result in outbreaks where the majority of cases have been vaccinated can be more easily understood by looking at a hypothetical example.

In a high school of 1,000 students, none has ever had measles. All but 30 of the students have had their dose of measles vaccine and so are considered vaccinated. However, among these 970, there would be about 97 who are not protected by the vaccine. When the student body is exposed to measles, every susceptible student becomes infected because measles is highly contagious. The 30 unvaccinated students will be infected, of course. But of the 970 who **have** been vaccinated, we would expect the 97 who are not protected to fall ill. Therefore 97/127, or about 76% of the cases are fully vaccinated.

As you can see, this doesn't prove the vaccine didn't work – only that most of the children in the school had been vaccinated, so the vaccine failures outnumbered the unvaccinated susceptibles. Looking at it another way, 100% of the children who were not vaccinated got measles, compared with only 10% of those who were. Measles vaccine protected most of the school; if nobody in the school had been vaccinated, there would have been 1,000 cases of measles. In this example, the vaccine was in fact 90% effective in preventing measles.

16.2.3 There are many case reports of harmful side effects from vaccines, including deaths. This proves that vaccines are not safe.

The above statement implies that the number of side effects reported is related to the safety of the product, and that the more adverse event reports received, the more dangerous the vaccine. Moreover, since not all adverse events are reported, this implies that vaccines are even more dangerous than the number of cases reported leads us to believe.

This is misleading because reports of adverse events are only suspicions that are **temporally associated** with receipt of vaccine; reports should not be interpreted to imply that the vaccine caused the event. Statistically, a certain number of serious illnesses, even deaths, can be expected to occur by chance alone among children recently vaccinated. While vaccines are known to cause minor, temporary side effects like soreness or fever, there is little, if any, evidence linking vaccination with permanent health problems or death. The point is that just because an adverse event has been reported, it does not mean it was caused by a vaccine. This fact is often, if not always, overlooked by the media when adverse events are mentioned.

In the United States, some anti-immunization groups also focus on so-called "hot lots" of vaccine. They counsel parents to avoid certain lots of vaccine because more adverse events had been reported involving those lots than others. This is misleading because vaccine lots may vary in size from several thousand doses to several hundred thousand, and some are in distribution longer than others. Naturally a larger lot or one that is in distribution longer will be associated with more adverse

events, simply by chance. Also, more coincidental deaths are associated with vaccines given in infancy than later in childhood since the background death rates in children are highest during the first year of life. So knowing that lot A has been associated with x number of adverse events while lot B has been associated with y number would not necessarily tell you anything about the relative safety of the two lots, even if the vaccine **did** cause the events.

If the number and type of reports for a particular vaccine lot suggested that it was associated with more serious adverse events or deaths than are expected by chance, the federal government has the responsibility and will, as well as the legal authority, to immediately recall that lot.

Every vaccine manufacturing facility and vaccine product is licensed. In addition, every vaccine lot is safety-tested by the manufacturer and by the federal Bureau of Biologics and Radiopharmaceuticals of the Therapeutic Products Directorate. A vaccine lot would be recalled at the first sign of problems. There is no benefit to anyone in allowing unsafe vaccine to remain on the market – since vaccines are given to otherwise healthy children, the public would not tolerate them if they did not have to conform to the most rigorous safety standards.

Further, there will always be articles in the press or medical journals that report possible bad outcomes as a result of vaccination. Reports in medical journals are sometimes just preliminary findings to stimulate further work and provide an opportunity for exchange of information. It is necessary to assess many sources before drawing final conclusions. As well, articles in some newspapers and magazines are written from a very biased standpoint. Their manner of presenting the data can be misleading, and must be interpreted with caution. Assertions about the link between vaccines and bad outcomes are rarely corroborated.

16.2.4 Vaccines cause many harmful side effects, illnesses, and even death – not to mention possible long-term effects we don't even know about.

Vaccines are actually very safe, despite implications to the contrary in much anti-vaccine literature. The vast majority of vaccine adverse events are minor and temporary, like a sore arm or mild fever. These can often be controlled by taking acetaminophen before or after vaccination. More serious adverse events occur rarely (on the order of one per thousand to one per million doses), and some are so rare that the risk cannot be accurately assessed. This is the case for severe neurologic illness (including encephalopathy). Most often, the illness attributed to a vaccine occurs much more frequently in individuals with no recent vaccination. As to vaccines causing death, again there are so few deaths that could plausibly be attributed to vaccines that it is hard to assess the risk statistically. Each death reported to the Canadian VAAEs surveillance system is thoroughly examined to ensure that it is not related to a new vaccine-related problem.

As to long-term effects, many vaccines have been in use for decades with no evidence of any long-term adverse effects. The requirements for licensing vaccines in Canada are stringent and ensure that excellent research into potential adverse effects has been conducted prior to widespread use. No long-term effects have been associated with any vaccine currently in use. Any such claims have not been substantiated.

But looking at risk alone is not enough – you must always look at both risks and benefits. Even one serious adverse effect in a million doses of vaccine cannot be justified if there is no benefit from the vaccination. If there were no vaccines, there would be many more cases of disease, and along with them, more serious side effects, including death. The examples from those countries who have stopped or decreased their immunization programs has illustrated this time and again. In fact, to have a medical intervention as effective in preventing disease as vaccination and not use it would be unconscionable.

DTP Vaccine and Sudden Infant Death Syndrome

One myth that persists is that DTP vaccine causes Sudden Infant Death Syndrome (SIDS). This belief came about because a moderate proportion of SIDS deaths occur in children who have recently been vaccinated with DTP; and, on the surface, this seems to point toward a causal connection. But a temporal association does not imply a causal one. For example, you might as well say that eating bread causes car crashes, since most drivers who crash their cars could probably be shown to have eaten bread within the past 24 hours.

If you consider that most SIDS deaths occur during the same range of ages when three doses of DTP are given, you would expect DTP doses to precede a fair number of SIDS deaths simply by chance. In fact, when a number of well-controlled studies were conducted during the 1980s, they found, nearly unanimously, that the number of SIDS deaths temporally associated with DTP vaccination was within the range expected to occur by chance. In other words, the SIDS deaths would have occurred even if no vaccinations had been given. In fact, in several of the studies children who had recently had a DTP shot were less likely to get SIDS. The Institute of Medicine in the United States reviewed the evidence regarding SIDS and vaccination, and reported, "All controlled studies that have compared immunized versus non-immunized children have found either no association...or a decrease risk...of SIDS among immunized children." It concluded, "The evidence does not indicate a causal relation between DTP vaccine and SIDS."

16.2.5 Vaccine-preventable diseases have been virtually eliminated from Canada, so there is no need for my child to be vaccinated.

It's true that vaccination has enabled us to reduce most vaccine-preventable diseases to very low levels. However, some of them are still quite prevalent – even epidemic – in other parts of the world. Travelers can unknowingly bring these diseases into the country, and if we were not protected by vaccinations these diseases could quickly spread throughout the population, causing epidemics here. At the same time, the relatively few cases we currently have could very quickly become tens of thousands of cases without the protection we get from vaccines.

We should still be vaccinated, then, for two reasons. The first is to protect ourselves. Even if we think our chances of getting any of these diseases is small, the diseases still exist and can still infect anyone who is not protected.

The second reason is to protect those around us. There is a small number of people who cannot be vaccinated (because of severe allergies to vaccine components, for example), and a small percentage of vaccine failures. These people are susceptible to disease, and their **only** hope of protection is that people around them are immune and cannot pass disease along to them. A successful vaccination program, like a successful society, depends on the cooperation of every individual to ensure the good of all. We would think it irresponsible of a driver to ignore all traffic regulations on the presumption that other drivers will watch out for him. In the same way we shouldn't rely on people around us to stop the spread of disease without doing what we can as well. One important example is vaccination against rubella. A woman who contracts rubella during pregnancy is at high risk of having a baby with congenital rubella syndrome, a devastating illness. Children who are not immunized against rubella can infect those around them.

16.2.6 Giving a child multiple vaccinations for different diseases at the same time increases the risk of harmful side effects and can overload the immune system.

Children are exposed to many foreign antigens every day. Routine consumption of food introduces new bacteria into the body, and numerous bacteria live in the mouth and nose, exposing the immune system to still more antigens. An upper respiratory viral infection exposes a child to between 4 and 10 antigens, and a case of "strep throat" to between 25 and 50. According to a 1994 report, "In the face of these normal events, it seems unlikely that the number of separate antigens contained in childhood vaccines...would represent an appreciable added burden on the immune system that would be immunosuppressive[38]." And, indeed, available scientific data show no adverse effects of simultaneous vaccination with multiple vaccines on the normal childhood immune system.

A number of studies have been conducted to examine the effects of giving various combinations of vaccines simultaneously. In fact, simultaneous administration of any vaccine would not be recommended by Health Canada or its national expert advisory committee until such studies showed the combinations to be both safe and effective. These studies have shown that the recommended vaccines are as effective in combination as they are individually, and that such combinations cause no greater risk for adverse side effects. Research is currently under way to find ways to combine more antigens in a single vaccine injection. This will assure all the advantages of the individual vaccines, but require fewer shots.

There are two practical factors in favour of giving a child several vaccinations during the same visit. First, we want to immunize children as early as possible to give them protection during the vulnerable early months of their lives. This generally means giving inactivated vaccines beginning at 2 months of age and live vaccines at 12 months of age. Therefore, doses of the various vaccines tend to fall due at the same time. Second, if we can give several vaccines at the same time it will mean fewer office visits for vaccinations; this saves parents both time and money and may be less traumatic for the child.

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