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Immunization in Canada: Current Controversies

SUMMARY

Immunization, once used solely to control a disease, is now sufficiently widespread that elimination or even eradication of certain diseases has become possible. However, with greater control of disease, adverse reaction to immunization has taken on new prominence. Reporting of adverse reactions varies widely across Canada, and may be due to administrative differences—some provinces rely mostly on the public sector for immunizations, others on the private sector. Several controversies over immunizing agents remain, for example, live versus killed poliovirus vaccine, but generally immunization in Canada is now relatively uniform and safe. (Can Fam Physician 1985; 31:77-81).

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La pratique de l'immunisation, jadis utilisée seule pour contrôler une maladie, est maintenant répandue au point qu'il est devenu possible d'éliminer et même d'enrayer certaines maladies. Cependant, malgré un contrôle accru de la maladie, les réactions adverses aux immunisations ont pris une nouvelle envergure. Les rapports de ces réactions adverses varient considérablement au Canada, et peuvent s'expliquer par des différences administratives—certaines provinces confient davantage les immunisations au secteur public, et d'autres au secteur privé. Il persiste différentes controverses au sujet des agents d'immunisations, par exemple le vaccin au virus de la polio vivant versus tué. Mais, généralement, les immunisations au Canada sont maintenant relativement uniformes et inoffensives.

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SINCE THE 1930s, immunization has undergone many changes, in the types of immunizing agents available and who should receive them—the total population (usually in childhood), or selected high risk groups. In addition immunization has been delivered through both the public and private health care sectors. At times, community groups have given support, (e.g., during the poliomyelitis vaccination campaigns in the 1950s.

In recent years, primary immunization of Canadian infants has been shared largely between family physicians, pediatricians and public health nurses. Because provincial governments have the major responsibility for health, patterns of delivery vary between the public and private sectors from province to province. Saskatchewan and Alberta immunize most infants and children through the public sector, whereas an increasing proportion is delivered by the private sector in the other provinces.

The federal government is responsible for regulating products, providing a national disease surveillance program and giving advice. This is given through the National Advisory Committee on Immunization (NACI) and published in the 'Green Book'—"A Guide to Immunization for Canadians".[1] The first edition of these guidelines was published in 1980 and the second, which includes an extra chapter on Immunization of Health Care Workers, will be published in the very near future.[1] In recent years infant and childhood immunization schedules have become very similar across the country. The major difference is that three provinces, Ontario, Nova Scotia, and Newfoundland, prefer the use of Salk (killed) rather than Sabin (live) poliomyelitis vaccine. The schedule in Prince Edward Island includes four doses of Salk and two doses of Sabin poliomyelitis vaccine.

Purpose of Immunization

For many years, the purpose of immunization was to help control communicable diseases by reducing the number of people susceptible to infection, thereby interrupting the chain of disease transmission.

Since the vaccination program

which eradicated smallpox in the world, two new targets are now considered. These are elimination and eradication. Elimination is total control in a geographic area (e.g., the elimination of measles in North America). Elimination does not prevent the importation of new cases and contact with susceptible people from other areas. Vigilance must be maintained for such people. Eradication is the total, global extinction of a disease. The World Health Organization has established criteria for diseases which it is feasible to eradicate. These criteria include:

- that the disease is readily recognizable clinically and can be confirmed by laboratory tests.
- that the disease has a short incubation period.
- that an effective vaccine is available.
- that the disease has no reservoir other than man.

Measles meets these criteria. However, in most parts of the world control of measles is still the target.

As control of communicable diseases increases and the impact of major epidemics lessens, the small but real adverse effects associated with immunization programs take on increasing importance.[2] Provision must be made for the few people harmed by population-wide immunization programs. This has become a major issue in the U.S. and until this question is satisfactorily answered costs of vaccines will continue to increase and routine programs will be in jeopardy.

Immunizing Agents

Considerable progress has been made towards producing pure, stable immunizing agents which have a high immunogenicity but a low rate of adverse reactions. Currently, several vaccine preparations are used for active immunization. Larke[3] has described these in detail (see Table 1).

The future is probably in genetically-engineered, highly pure antigens for immunization. Until that time, the problems of adverse reactions, no matter how rare, must be faced.

Adverse Reaction

The true rate of adverse reactions to immunizing agents in Canada is unknown. Current information is based on spontaneous adverse reaction reports sent by practicing health care professionals, either directly to the Adverse Reaction Program of the Federal Health Protection Branch, or indirectly through local and provincial health authorities. Table 2 illustrates the problems with this system. The volume of reports from the four western provinces is considerably higher than in eastern Canada. The table is for the time when the western provinces were switching from fluid diphtheria, pertussis and tetanus vaccines to the adsorbed product. This change in vaccines is clearly seen in the adverse reaction reports from the western provinces. Although not all eastern provinces made the switch, because DPT-polio was not available in the adsorbed form at that time, the rate of reporting reactions to the fluid vaccine is clearly different in eastern and western Canada. Does this reflect the fact that more immunizations are given through the public sector in western Canada and therefore adverse reactions are more likely to be reported?

The utility of spontaneous adverse reaction reporting is questionable, particularly when under-reporting is evident. Some believe pertussis immunization may cause serious, acute neurological illness in children; this belief cannot be proved or disproved by a spontaneous adverse reaction reporting system. Although claims have been made from Britain of a significant association, no such association has been demonstrated in Canada. The position of NACI remains that the benefits of this vaccine far outweigh any associated risks.

Obviously, vaccination is not without a very low degree of risk. In the U.S., court action following non-negligent, vaccine associated disability has become relatively commonplace.[13, 14] This has led many manufacturers to discontinue vaccine

TABLE 1
Vaccines Used for Active Immunization[3]

Vaccine	Examples
Whole microorganisms inactivated by heat or chemicals	Pertussis, typhoid, killed poliovirus
Fractions of extracted microorganisms	Pneumococcal and meningococcal polysaccharide vaccines
Toxoids made by formalin inactivation of purified bacterial toxins	Tetanus and diphtheria toxoids
Live, attenuated virus vaccines	Measles, rubella, mumps and Sabin poliovirus
Vaccines which afford 'cross protection'	Vaccinia virus gives protection against smallpox

TABLE 2
Reported Adverse Reactions to Adsorbed and Fluid DPT and DT, Canada, Jan 1980-Jun 1981[13] (Source: Adverse Reaction Program, HPB, Ottawa)

	Jan-Jun 1981		Jan-Dec 1980	
Area	Adsorbed	Fluid	Adsorbed	Fluid
Newfoundland	0	0	0	0
Prince Edward Island	0	0	0	0
Nova Scotia	0	0	0	0
New Brunswick	0	0	0	2
Quebec	0	1	0	4
Ontario	0	0	0	2
Manitoba	8	0	3	3
Saskatchewan	20	5	2	15
Alberta	47	3	18	16
British Columbia	13	3	0	19
Canada (except Yukon and Northwest Territories)	**88**	**12**	**23**	**61**

production. To date, this has not been a problem in Canada.

However, Canadian governments should be discussing full, no-fault compensation for patients who suffer from one of the rare, but unpredictable, disabilities resulting from a recommended immunization program.

Immunization Schedules

Due to the efforts of the NACI, Canada is the closest it has ever been to having common, recommended vaccination schedules in all provinces.

However, small differences still occur. I have already mentioned the choice of Salk virus or Sabin poliovirus vaccine. The exact timing of the routine immunization schedule for infants and children may vary slightly, but not greatly from that recommended by NACI (see Table 3). Also, if Sabin (oral) poliovirus vaccine is used, the need for six doses of poliovirus vaccine during childhood is debatable. NACI currently states that the doses of poliovirus vaccine at six months and 14-16 years may be omitted if live (oral) poliovirus vaccine is used. However, at this time, most Canadian jurisidictions continue to recommend that these doses be given.

The immunization of adults requires special attention. Guidelines for adult immunization are given in the 'Green Book'.[1] Such immunization may be primary series in those not immunized in childhood; other immunizations may be for those who have received an incomplete schedule, who received vaccines which are now considered inadequate (e.g., killed measles vaccine), were given incorrect procedures (e.g., concurrent administration of immune globulin with live virus vaccine).

Specific Vaccines

Immunization is changing. Questions are raised about many immunization agents, the dose and route by which they are delivered, and the correct age or time for delivering the vaccine.

Poliovirus vaccine

The debate about live virus vs. killed poliovirus vaccines is longstanding. Melnick[4] has comprehensively addressed the advantages and disadvantages of these two products. Both products have been successful in controlling paralytic poliomyelitis in Canada. Both are equally recommended by the NACI. However, the cost of producing the killed vaccine is higher, as a greater virus dosage is required to elicit a satisfactory immune response.

The other current issue concerns the number of doses of vaccine required during childhood to produce and maintain an adequate response. It is now felt that six doses of oral vaccine during childhood are not necessary and some authorities[1] suggest that this may be cut to four. It is still recommended that six doses of the killed product be given.

Diphtheria, pertussis and tetanus vaccine

No vaccine has created more controversy in recent times than the pertussis component of diphtheria, pertussis and tetanus vaccine. In April 1982, NBC television aired an hour-long show emphasizing the dangers of pertussis vaccine. The show was based on the reported neurological problems associated with the vaccine in Britain.[5,6] The vaccine was introduced in England in 1942. By 1974, it was estimated that 75% of British children were vaccinated against pertussis. Following allegations of adverse reactions after pertussis immunization, the estimated coverage of pre-school children dropped to 30% by 1978. British notifications of pertussis began to increase in 1977 and in 1978-1979 a major epidemic resulted in more than 100,000 cases of pertussis and 36 deaths.[15] This British experience clearly shows that the continued, routine vaccination of infants is necessary to prevent a resurgence of pertussis. This policy is supported in Canada, which has continued to have low rates of whooping cough over the last ten years.

In 1980, diphtheria and tetanus toxoids became available in Canada in the adsorbed form, compared with the previously available fluid product. In the adsorbed preparation, the toxoid is combined with aluminum phosphate, which produces an agent which gives a higher immune response than that provided by the fluid product. These products are available alone, in combination with each other and combined with pertussis vaccine. This last product is the one most commonly used for primary immunization of children under seven.

Adsorbed vaccines must be given intramuscularly, compared with fluid preparations' subcutaneous route of injection. When the adsorbed products were introduced, higher rates of local adverse reactions, including sterile abscesses, were reported.[7] A case has been made that this increased rate may be due partly to the amount of aluminum phosphate in the product. In addition, the intramuscular route of injection may have contributed to the problem.

Not all provinces switched to the DTP adsorbed product, as it was not initially available in a combined form with killed poliomyelitis vaccine. This combined quadruple antigen became available in Canada in 1984.

Historically, local or systemic reactions after DPT have been attributed to the pertussis component. The reaction rates from the combined vaccines are the same as from pertussis vaccine alone.

Because of an increased risk of adverse outcomes, pertussis vaccine is

TABLE 3
Routine Immunization Schedule for Infants and Children[1]

Age	Immunization Against			
2 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
6 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis*
12 mos.	Measles	Mumps	Rubella**	
18 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4-6 yrs.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
14-16 yrs.	Diphtheria***		Tetanus***	Poliomyelitis*

* This dose may be omitted if live (oral) poliovirus vaccine is used.

** Rubella vaccine is also indicated for all girls and women of childbearing age who lack proof of immunity.

*** Diphtheria and tetanus toxoid (Td), a combined absorbed 'adult type' preparation for patients age seven and older, contains less diphtheria toxoid than preparations given to younger children, and is less likely to cause reactions.

not recommended in those aged seven or older. An adult preparation of diphtheria and tetanus toxoids is available, with a reduced dosage of diphtheria toxoid (Td, adult-type preparation). If the adsorbed adult preparation is used, a Schick test or sensitivity test is not considered necessary.

Measles, mumps and rubella vaccine (MMR)

These three live-virus vaccines are available as single antigens or combined. All provinces now recommend immunizing infants with the triple vaccine. Most provinces advise immunization at or just after one-year of age. However, Nova Scotia, New Brunswick, and Prince Edward Island promote its use after 15 months. Evidence to date indicates that such vaccination will result in long lasting immunity.[8]

Rubella vaccine should be offered to all women of child-bearing age who do not have either documented evidence of vaccination or laboratory evidence of previous infection.[1,8] However, live measles, mumps or rubella vaccines should not be given to women who are already pregnant or suspected to be pregnant.

Influenza vaccines

Traditionally, influenza vaccines have been recommended for people of any age who have specific conditions which place them at high risk[1] and for older people, particularly those over age 65. Consideration may also be given to people who provide essential community service (e.g., hospital workers).

The efficacy of influenza vaccine in the face of an epidemic has never been truly demonstrated. In fact, the only attempt at mass influenza immunization was against the perceived threat of swine-flu in 1976. This resulted in a considerable threat to the credibility of influenza immunization specifically, and immunization programs generally.

During the 1960s and early 1970s some virologists believed that an understanding of the 'shifts' and 'drifts' of the antigens in the influenza A virus was being achieved.[16] However, events since 1976 have led to the proposed cyclical pattern, with similar strains of virus returning every 50-80 years and a major epidemic or pandemic every ten to 15 years, being drawn into question.

Only minor shifts in the two current strains of influenza A virus (H3 N2) and (HINI) have occurred in the last seven to eight years, and so the usefulness of annually vaccinating the well elderly must be reexamined. The most recent recommendations for prevention and control of influenza, issued by the U.S. Immunization Practices Advisory Committee (ACIP), have decreased the emphasis on vaccinating healthy people over age 65.[9]

Rabies vaccine

The advent of rabies virus vaccine grown in human diploid cells (HDCV) was a major advance. The HDCV is now the vaccine of choice for both pre- and post-exposure immunization. The HDCV is a highly efficacious product which has reduced the chance of adverse reactions and at the same time improved the immune response and thereby reduced the number of doses required for post-exposure prophylaxis. A comprehensive set of recommendations for use is included in the 'Green Book' guide.[1]

Currently, the advantages, disadvantages, and cost of small (0.1 ml) doses given intradermally compared with larger (1.0 ml) doses given by the deep subcutaneous or intramuscular route are under discussion.[10] Considerable work is being done in this area, and the use of the intradermal route is slowly being introduced for pre-exposure vaccination in high risk groups. The intradermal route is not recommended at this time for the post-exposure treatment, although several trials are being undertaken in this area.[11,12]

Other vaccines

In recent years, hepatitis B vaccine, meningococcal polysaccharide vaccine and pneumococcal vaccines have been introduced. Each of these products is marketed for use in specific, high-risk individuals rather than for universal immunization programs. Specific details on the recommended use of these may be found elsewhere.[1,17]

Vaccination for travellers

The number of Canadians travelling outside North America has greatly increased. Thus, the risk of exposure to diseases not normally encountered in this country, but for which vaccines are available, is increased. These include polio, typhoid, cholera, and yellow fever. In certain parts of the world exposure to hepatitis (both A and B) should be considered.

Vaccination requirements will vary depending on the individual's destination, length of stay and activities. In general, people going on vacation for a short time are over-vaccinated against typhoid and perhaps under-vaccinated against polio.

The World Health Organization produces regular updates for countries in which yellow fever and cholera vaccination is required. These are distributed through provincial health authorities.

Passive immunization

Standard immune serum globulin (or gamma globulin) is available for treatment of those exposed to measles, rubella and hepatitis A.

Specific immune globulins available are hepatitis B, rabies, pertussis, tetanus, and varicella-zoster as well as botulism, diphtheria and gas gangrene antitoxins.

The recommended use of all these products is described in the 'Green Book'.[1]

Conclusion

Immunization schedules across Canada are more consistent than they have ever been. However, provincial differences do occur, particularly in the use of Salk and Sabin poliomyelitis vaccine. There are also differences in the provincial provision of vaccines, such as influenza and hepatitis B vaccine, and vaccines for travellers.

In general, Canadian immunization programs are safe and effective and have greatly reduced the occurrence of infectious diseases. For example, from 1953-1983 the disease rates per

100,000 population have been reduced from 28.3 to zero for paralytic poliomyelitis, from 0.9 to <0.1 for diphtheria, and from 380 to 3.8 for measles.[18,-20]

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