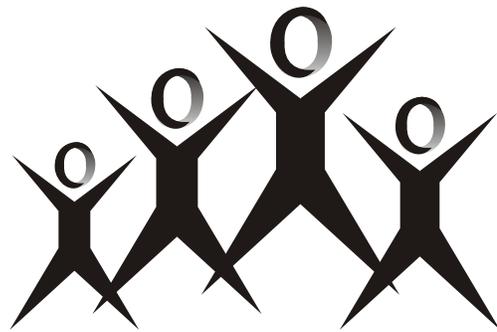


4th Canadian National Immunization Conference

*Immunization in the 21th Century:
Progress Through Education*



Halifax, December 3-6, 2000

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

Health Canada

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***Immunization in the 21th Century:
Progress Through Education***



Halifax, December 3-6, 2000

**Bureau of Infectious Diseases
Centre for Infectious Disease Prevention and Control
Population and Public Health Branch
Health Canada**

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Introductory Note

The 4th Canadian National Immunization Conference was organized by the Centre for Infectious Disease Prevention and Control, Health Canada, and the Canadian Paediatric Society, with financial support from the private sector, the provinces of Alberta, British Columbia, Ontario, Nova Scotia, and Quebec, and the Centre for Surveillance Coordination, Health Canada.

The theme of the conference — Progress through Education — was chosen to emphasize the need for education of health care providers, students, academics, policy makers, and consumers on the importance of immunization in maintaining and improving the health of Canadians. It was hoped that the sessions would serve as a forum in which to exchange information on important issues in immunization.

Topics covered during the first day included global immunization efforts and the current status of immunization programs in Canada, including the latest information on the development of immunization registries in all provinces/territories as part of the National Immunization Strategy. The day ended with a consideration of the media's role in informing the public about health issues, and an account of a successful media-public health partnership.

The second day dealt mainly with surveillance issues, including surveillance of vaccine-preventable disease, immunization coverage, and vaccine safety. As well, some of the allegations concerning immunization and chronic disease were addressed. Breakout sessions were held in the afternoon.

Information on new vaccines was presented on the third day. Other topics included the decision-making process for which immunization programs should be implemented and how public health can contribute, as well as evaluation of such programs. On the final morning,

participants heard about the status of immunization education in medical and nursing schools.

This report provides a brief account of the presentations made at the conference.

Sunday, December 3

Dr. Arlene King, Division of Immunization, Centre for Infectious Disease Prevention and Control (CIDPC), Health Canada, opened the conference and gratefully acknowledged the partnerships involved in bringing it to fruition. Dr. Sarah Shea, Canadian Paediatric Society, and the Honorable Jamie Muir, Nova Scotia Minister of Health, welcomed participants to the conference and to Halifax.

Keynote Address

Dr. Tore Godal

Executive Secretary, Global Alliance on Vaccines and Immunization

The goal of the Global Alliance on Vaccines and Immunization (GAVI), a coalition of partners from the public and private areas, is to save children's lives and protect the health of adults through the widespread use of vaccines. Of 130 million babies born worldwide each year, 30 million will not be vaccinated and, of these, 3 million will die of vaccine-preventable diseases such as measles and hepatitis B.

The current focus of international development is to reduce poverty in the less developed countries of the world. Investment in health, together with education, is the best way to achieve this. To reduce the gap between developed and developing countries, GAVI aims to

- improve access to sustainable immunization services;
- expand the use of all existing safe and cost-effective vaccines;
- accelerate the development of vaccines and technologies that can be used in the poorest countries.

GAVI is a recent initiative, whose partners include national governments and their collaborators, the WHO, UNICEF, the Bill and Melinda Gates Children's Vaccine Program, the pharmaceutical industry, and the World Bank. A 12-member Board has been established with representatives from these groups, and there are a number of task forces (e.g. on advocacy, finance, research and development) in operation. A Global Fund was established with a US\$750 million donation from the Bill and Melinda Gates Program, and this has been supplemented by significant contributions from the US Congress and the governments of Holland and Norway.

Developing countries are invited to submit proposals directed at strengthening their immunization services, with particular emphasis on hepatitis B, *Haemophilus influenzae* type b, and yellow fever. In 2000 a commitment of US\$300 million was made to fund acceptable proposals over the course of the next 5 years. Mechanisms planned for improving immunization services in ways that will not be in conflict with a country's health sector development are (i) strengthened national coordination, (ii) performance-based outputs (i.e. immunization coverage will be carefully measured), (iii) the "share" concept, by which a donation of \$20 will be made to the country for every additional child immunized, to be spent as the country decides is best for the health of its children, (iv) promotion of injection safety by pioneering the use of auto-destructible syringes, and (v) use of the immunization services for other health promotion programs, e.g. delivery of vitamin A.

Global Immunization: Towards Equity

■ Rotary Foundation of Canada

Mr. Wilf Wilkinson

President, Rotary Foundation of Canada

In 1985/86 the goal of Rotary International was to raise US\$120 million — an amount felt to be necessary to immunize all the world's children against polio. By 1998, when the fundraising campaign was over, Rotary International had raised over US\$230 million, and to date the figure is about US\$400 million. Canada's contribution has been impressive: in 1989, Canada's Rotary clubs had raised Can\$9,384,697, which was pushed over the \$11million mark with a contribution from the federal government. One ingenious example of the fundraising methods used was provided by 75-year-old John Williamson, who raised over \$13,000 in pledges by jumping from airplanes. As well as fundraising, Rotary organizations play an important role in advocacy, and their members work in the field with health care workers to ensure successful Immunization Days and "mop-up" programs.

■ Polio Eradication

Dr. Bruce Aylward

Coordinator, Global Polio Eradication Initiative, WHO

In 1988 the World Health Organization (WHO) called for the eradication of polio globally. Since then, a partnership of WHO, Rotary International, the US Centers for Disease Control and Prevention (CDC), and UNICEF has worked towards achieving this goal by the year 2005. Through a combination of improvements in transport and communication systems, immunization program management, and surveillance the number of countries in which polio was endemic fell from 125 in 1988 to 30 by the end of 1998. Furthermore, the annual number of polio cases decreased from an estimated 350,000 in 1988 to 7,071 reported in 1999.

In 1999 the World Health Assembly called for an acceleration of the Eradication Initiative by means of increasing the number of Immunization Days. As a result of this enhanced effort, the number of polio cases has dropped, the number of polio-free areas has increased, and type 2 wild poliovirus has not been seen in over a year.

Stopping transmission in the remaining countries over the next 2 years or so requires renewed efforts in five areas:

- intensified National Immunization Days and house-to-house “mop up” campaigns;
- enhanced surveillance;
- containment of laboratory polioviruses;
- consensus on when to stop immunization;
- strengthening of routine immunization.

The countries given priority for action are India, Pakistan, Bangladesh, Ethiopia, and Nigeria. The target now is to stop the transmission of polio globally by the end of 2002.

■ Progress Towards Measles Elimination

Dr. Ciro de Quadros

Director of Vaccines and Immunization, Pan American Health Organization

Immunization prevents about 80 million cases of measles worldwide each year, but 40 million cases still occur, leading to 800,000 deaths. In 1994, PAHO set the goal of measles eradication from the Americas by the year 2000. Strategies have included high coverage of susceptible populations and active surveillance. Even with a two-dose immunization program in place there will be children who have not been vaccinated as well as cases of vaccine failure, so that periodic catch-up programs are necessary. PAHO recommended a one-time catch-up program for children 1-14 years old with follow-up campaigns targeting children aged 1-4 every 4 years. As well, surveillance has been strengthened, particularly laboratory investigation of suspected measles cases.

All countries in the region have implemented the catch-up campaign. In 1996, 2,109 confirmed measles cases, a record low number, were reported from the Americas, as compared with > 150,000 per year before the campaigns began. Although there was a resurgence in 1997 due to an outbreak in Brazil (in Sao Paulo, an area not carrying out the follow-up campaign), the figures for 2000, to date, are 1,100 cases, reported mainly from the Dominican Republic and Haiti. Other than these two countries, measles is no longer considered endemic in the Americas, most new cases being imported from Europe.

Global eradication of measles is feasible, given the careful implementation of appropriate strategies, and will have a major impact on childhood morbidity and mortality.

■ Canadian Update

Dr. John Waters

Chief Medical Officer of Health, Alberta

In 1992 a consensus conference was held to establish goals and targets for measles control. The goal of elimination of indigenous measles in Canada by 2005 was set, and later adopted by the Federal/Provincial/Territorial (F/P/T) Conference of Deputy Ministers of Health. Strategies included maintenance of routine two-dose immunization and enhanced surveillance through investigation of all measles cases and immediate response to outbreaks. A working group was set up in 1996 to develop the tools to determine the status of measles elimination, including a definition of elimination and national surveillance protocols. There were measles outbreaks in 1991, 1992 and 1995. In 1998 12 cases were reported and in 1999 there were 29, mostly cases of imported virus among non-immunized communities. In 2000, 204 cases were reported, 124 from two outbreaks in Alberta that were linked with Latin America and occurred, again, in a non-immunized community. Endemic measles, therefore, appears to have been eliminated.

With regard to polio, the last indigenous case of paralytic polio was in 1977, and the last imported case was in 1988; in 1992 there were 22 wild virus isolates picked up. With the switch from oral polio vaccine to inactivated polio vaccine in 1996 there have been no cases of vaccine-associated polio since 1995. The elimination of wild poliovirus was certified by PAHO in 1994. Surveillance of acute flaccid paralysis is carried out through networks of the Canadian Paediatric Society.

■ **Canada's Contribution to the Global Immunization Effort and How Canadians Can Get Involved**

Dr. Yves Bergevin

Principal Advisor, Canadian International Development Agency

Since the 1980s, when there was almost no child immunization in developing countries, international efforts have ensured that about two-thirds of children across the globe now receive immunization services.

One of the ways that Canada contributes to the global immunization effort is through programs funded by the Canadian International Development Agency (CIDA), in partnership with organizations such as the Canadian Public Health Association (CPHA) and the Rotary Foundation of Canada. From 1986 to 1998 the Government of Canada provided about \$14 million each year for international immunization. The three elements of this funding were CPHA's international program, collaboration with PAHO, and contributions to polio eradication.

In 1998, CIDA launched the Canadian International Immunization Initiative with a core budget of \$50 million over 5 years. The focus was those countries in greatest need, and the methods were to foster Canadian partnerships, use the most cost-effective strategies to deliver immunization services, and minimize bureaucratic involvement. UNICEF was provided with funds for vaccine purchase, WHO was given technical and programmatic support, and there was collaboration with PAHO. In 1999, Canadian-purchased vaccines helped immunize 10 million children against measles; in 2000, 5 person-years of technical expertise are being provided through CPHA. As well, Canada has contributed towards the distribution of vitamin A during National Immunization Days (a measure that reduces all-cause mortality by 20%-25% among children under 5 years). In September 2000, it was decided to double CIDA's spending on health and nutrition, from \$150 million to \$300 annually, and a health and nutrition action plan is being developed that will include support for polio eradication, a 5-year contribution to GAVI, and vitamin A supplementation.

Canadian Update: Towards a Better Future

■ **Canadian Accomplishments**

Dr. Victor Marchessault

Chair, National Advisory Committee on Immunization

The National Advisory Committee on Immunization (NACI) was established in 1964 with a mandate to provide Health Canada with ongoing and timely medical, scientific, and

public health advice on vaccines and certain prophylactic agents, such as immunoglobulins. Specific areas of interest were the use of vaccines in humans, their evaluation, and the monitoring of vaccine-associated adverse events (VAAEs).

NACI was responsible for developing guidelines on the use of new or existing vaccines available in Canada and for attempting to make manufacturers' product monographs consistent with NACI statements. As well, it was given the task of identifying the merits of specific licensed products that were not widely used. With regard to surveillance, NACI was asked to recommend assessment and surveillance activities for specific licensed vaccines, including surveillance of vaccine failures, adverse events, and immunization coverage. Licensed vaccines of likely interest to provincial/territorial immunization programs were to be identified, and uniformity among the different programs was to be encouraged.

There are 10 NACI members and three meetings a year, of 2.5-3 days' duration. Working groups prepare documents for approval at the meetings, and NACI recommendations are presented every 4 years in the *Immunization Guide* (next *Guide* expected to be published in 2002). Changes to NACI statements in between publication of the *Guide* are posted on the Health Canada Web site and printed in *Canada Communicable Disease Report*. Members of NACI must not be in a position that gives rise to a conflict of interest.

Challenges for the future are the continuing outbreaks of pertussis. Although there is a new vaccine for adolescents, NACI has not been able to strongly endorse it because of a lack of data on the duration of immunity, how frequently the vaccine would be needed, and whether the disease would be shifted from adolescence to adulthood. There is an effective vaccine against varicella, but so far Prince Edward Island is the only province/territory offering this program. Now that a refrigerator-stable vaccine is available there is nothing to prevent program implementation in all provinces/territories. The new pneumococcal conjugate vaccine has not yet been approved in Canada, but should be approved early in 2001. However, it is very expensive. Results from Britain of immunization with meningococcal conjugate vaccine have been encouraging in reducing meningococcal group C disease, but the possibility of another strain emerging must be borne in mind. A major problem that NACI has had to deal with in recent years is the anti-immunization lobby.

■ Current Canadian Issues

Dr. Arlene King

Chief, Division of Immunization, CIDPC

Because immunization programs have been such a successful public health story for many years, the public currently does not have experience of vaccine-preventable disease and is therefore more open to concerns about the adverse effects of immunization. Combating complacency about these diseases is vital if immunization coverage is to remain high. Other challenges are the new, complex vaccines coming onto the market at an ever-increasing rate, which will require careful implementation and optimal timing, and the difficulties in

establishing immunization registries in all provinces/territories as a result of concerns about cost, privacy, and data collection.

In terms of structural issues, although the federal regulatory role is fairly clear, its public health role is less well understood. At the provincial/territorial level there are many differences in immunization programs with respect to

- decision-making frameworks, structures and processes leading to differential funding for programs;
- access to decision-makers and funders;
- access to advocacy for immunization;
- availability of human resources.

Nevertheless, there is duplication of effort, with its associated costs. The divergence in provincial/territorial immunization schedules (timing, number of vaccines, catch-up programs) is likely to increase with the expensive and complex vaccines coming on the market.

In June 1999, the F/P/T Deputy Ministers of Health confirmed their commitment to an optimal level of immunization of Canadians and complete coverage of all children through a National Immunization Strategy.

■ **An Action Plan for Canada: What's Next?**

Dr. Joel Kettner

Chair, F/P/T Conference of Deputy Ministers of Health Advisory Committee on Population Health

The National Immunization Strategy, endorsed by the F/P/T Conference of Deputy Ministers in 1999, consists of the following components:

- ensuring that vaccines are delivered in a coordinated and cost-effective manner across Canada;
- reviewing targets recommended to date and developing national goals and objectives (coverage and prevention);
- developing a strategic approach to vaccine procurement in order to ensure price stability and security of supply;
- establishing consistent provincial/territorial immunization registries (goal: registries in all jurisdictions by the end of March 2003);
- ensuring immunization safety.

A Subcommittee on Immunization, reporting to the Public Health Working Group of the Advisory Committee on Population Health, has been charged with developing this National Strategy on behalf of the Deputy Ministers. A sum of \$130,000 has been allocated in 2000 for this purpose. With regard to the first goal (harmonization), there is a need to develop an analytic framework for improved decision making on immunization policy as one of

the steps in ensuring coordinated and cost-effective programs across the country. A survey and consultation process is under way to determine how such decisions are being made and how they *should* be made.

A national meeting is being considered to review all provincial/territorial goals and to compile a set of consistent national goals for vaccine-preventable diseases. As well, a vaccine procurement review is taking place to investigate ways of securing the best price, negotiating long-term contracts, and making bulk purchase arrangements.

As of March 2000, Manitoba and Saskatchewan were the only provinces/territories on track with regard to the goal of establishing immunization registries. The work plan is to establish a minimum data set, definitions and standards, and system compatibility standards. It is hoped to have a final report ready by March 2001 so that, together with other elements of the Strategy, it can be brought before the Conference of Deputy Ministers at their June meeting.

Education Through the Mass Media: How Can We Make it Work?

■ How the Media Portray Immunization

Dr. Bruce Gellin

Director, National Network for Immunization Information

People who are making their own decisions about health care rely on many sources of information, and reports in the media are a very important factor influencing opinion and behaviour about health. Yet health professionals often wonder why information is not presented in the way they would wish, or not even presented at all.

The media have been criticized for their coverage of health risk because of the dominance of controversy, implications of danger, and focus on human interest rather than science. There is superficial reporting of risk, with information only on the events that have occurred and little in the way of explanation for readers to understand the risks involved. One recent example is a story in *Red Book* magazine (8 million subscribers) that attributes the cause of shaken baby syndrome to DPT immunization. Part of the reason for the discrepancy between what the media portray and what the medical profession would like them to portray is that both sides are approaching the issue from a different culture and a different way of looking at the facts, not least of which is the influence of commercial profit on the part of the media. The media's interest in controversial claims about the adverse effects of immunization has now shifted from the scientific aspects to the story of the controversy itself.

If the media structure reality rather than merely recording it, as has been claimed, what is their responsibility in ensuring that their interpretations and presentations reflect reality? In Britain, the alleged link between MMR immunization and autism has resulted in a decline in MMR immunization coverage (92% to 88%), and it has been predicted that 70,000 cases of measles will result together with the expected number of deaths, possibly about 150. A survey of newspaper coverage of MMR and autism showed that the rate of MMR immunization was lower among readers of a particular newspaper that carried many scare stories of the controversy than among those of newspapers with less coverage.

The medical profession should be prepared for potentially newsworthy events in their field so that they are not left in the position of having to react to scare stories that are without foundation and yet are reported in the media. It needs to be ready and able to work with reporters to ensure that they have the best information communicated in the clearest possible way.

■ What Journalists Need (Principles, Ethics, and Practice)

Mr. Bruce Wark

School of Journalism, University of King's College, Halifax

A problem for journalists is that everyone wants to use the media to get their message across, and always because it is “in the public interest”. Yet journalists are looking for stories that surprise as well as inform. In their search for information that is newsworthy they have to remember their responsibility to be critical of what their source is telling them; on the other side, scientists must be sure that what they are promoting *is* in the public interest. Journalists try to give both sides of a story until one or the other side has been convincingly shown to represent the truth.

The media's function is to make a profit, and this is what drives the selection of items that make the news. However, journalists do have a professional standard to tell the truth and to provide information that is credible and factual. Conveying information is not the primary role of the media. They must provide interest, or they will not attract readers. To do this they tell stories that have the following characteristics:

- impact
- conflict/controversy
- emotional appeal
- timeliness
- proximity
- the unusual
- interesting visual elements.

Journalists will tend to focus on the personalities involved in the news stories and the elements that carry the most drama. Thus, their stories usually consist of the background

facts and figures to give a context for what follows; a description of the people involved together with direct quotations; the event itself presented in a way that appeals to the emotions; and whatever anecdotes, preferably humorous or intriguing, that are necessary to increase the appeal of the story. The bias of the media tends to be the focus on personalities, drama, and fragmentation — i.e. the preponderance of short stories that do not provide sufficient context or explanation to allow readers to understand the issues involved. With regard to immunization and its promotion, an immunization success story is not one that will be in the news, since it is nothing out of the ordinary; the latest confrontation between those in favour of immunization and those questioning its benefits are more likely to be of interest. It is necessary for the medical profession to take this as an opportunity to work with journalists in producing good stories that will educate the public and restore confidence in their public health programs.

■ Successful Local Partnerships with the Media

Ms. Naideen Bailey

Manager, Communicable Disease Control Programs, Waterloo Region

Three years ago, an outbreak of type C meningococcal meningitis in Waterloo provided an example of the valuable role the media can play in communicating to the public the information it needs to know. Usually, 3-8 cases of meningococcal disease occur annually, but in the first half of 1997 there had already been 7 cases, aged 2 months to 20 years. An eighth case (group C) reported in December of that year died, and follow-up of her contacts was extensive. After a further 3 cases, a report of a case in the Guelph area, and subsequent laboratory confirmation of group C meningococcal meningitis, it was decided to immunize the population aged between 2 and 22 years living in the region (an estimated 100,000 people).

The media were invited to a news conference before and after the decision to conduct a mass immunization campaign had been taken, and they had many questions about the disease, the vaccine, and the logistics of mass immunization. The Health Department appointed a communications coordinator, who was responsible for answering the media requests for information from two television stations, four radio stations, two daily newspapers, seven weekly newspapers, and student newspapers and radio stations. Briefings from the Associate Medical Officer of Health focused on the signs and symptoms to look for, modes of transmission of the infection, and reduction of high-risk behaviour, even after immunization.

The media followed progress at the immunization clinics and encouraged attendance. A further case of meningitis before the new year prompted a decision to bring forward the second half of the immunization campaign, aimed at those aged 2 to 11. Once again, the local media alerted parents to the change of plans and provided details of the forthcoming immunization clinics; as well, they warned young adults of the risks associated with large

gatherings on New Year's Eve. One newspaper published an editorial supporting the benefits of immunization in the face of opposition from a local chiropractor.

Involving the local media at an early stage allowed them to become not only a valuable source of information for the public throughout the outbreak but also a critical part of the public health response to it. Many media outlets ended up answering queries from people who could not reach the health department. Having one communications coordinator in place to deal with the media and prioritize their requests helped everyone meet their deadlines. The relationship between public health and the media was a successful one in this outbreak.

Monday, December 4

Keynote Address

■ Raising Awareness of Immunization

Ms. Karen Chudzik

Niagara Regional Health Unit

Ms. Chudzik described how, through her nursing experience, she was able to contribute to the local Polio Plus Committee of the Rotary Foundation. At first, funds were raised and sent to Rotary International for general polio eradication. Then, more specific projects were targeted, and when an immunization program was planned for Togo, Ms. Chudzik volunteered her services to help the international organizations that would be running the National Immunization Days in that country.

Immunization awareness was raised by means of banners, hats and t-shirts with the logo “Kick Polio Out of Africa!”. A 9-mile parade (the Hashrun) led by hundreds of polio victims on hand-powered tricycles or supported by crutches and canes was another promotional activity that Ms. Chudzik witnessed in the capital of Togo. Hundreds of clinics were held over 3 days throughout the country, music and dance being used to attract people to the clinic locations. Despite the challenges posed by maintaining the vaccine at the correct temperature, it was estimated that about 1 million vaccines were successfully administered. “Mop-up” campaigns continued for a further 3 days.

Myths, Truth and Logic About Immunization

Ms. Catherine Noton

Public Health Nurse, Winnipeg Regional Health Authority

The Association for Vaccine Damaged Children and the Eagle Foundation are two groups in Manitoba whose mission is to inform parents of immunization risk and to support them in any resulting clashes with the public health authorities. The first of these organizations believes that if immunization is mandatory then there should be no element of risk at all; it also supports a no-fault compensation program.

In 1998 the groups worked hard to sabotage the hepatitis B immunization program taking place in Winnipeg. Their strategy was to focus on what they believed was a lack of informed consent and on the use of schools for a medical procedure, namely mass immunization. They also began a court action that challenged whether parents had been truly informed of all the risks and benefits of hepatitis B immunization, specifically the alleged link with multiple sclerosis. The challenge was not successful, but considerable media coverage resulted, not all of it unbiased. The Winnipeg public health department had not had time to prepare for this onslaught, and workers in the field were faced with the difficult task of answering questions and countering arguments on topics about which they knew little.

Additional factors that reinforced the anti-immunization efforts were the cancellation in France of a school-based hepatitis B immunization program as well as the publication in the United States of *Hepatitis B: the untold story*, produced by the National Vaccine Information Centre (formerly known as DPT: dissatisfied parents together). The overall result of the lobby group's campaign was that participation rates in the immunization program fell from 80% to 62%.

The Winnipeg Regional Health Authority revised its approach during the following year's campaign, by providing nurses with the information they needed to respond to the misapprehensions of parents, revising fact sheets to include more information about the risks of hepatitis B and to state that immunization was voluntary, establishing a Web site with further information, and carrying out presentations in schools. The immunization rate has increased, and is currently at about 79%.

Dr. Donna Mitchell

Health Promotion Consultant, Ontario Ministry of Health and Long-Term Care

In a survey of the 37 health units in Ontario it was found that 81% reported local initiatives (individual or groups) actively opposing immunization. The main messages, promoted in newspapers, chiropractors' offices, and by personal contact, were that immunization was not necessary, vaccines caused serious adverse effects, government and public health were

covering up the risks, and vaccines weaken the immune system. Investigation of some of the claims of the anti-immunization lobby has revealed the following.

For example, Dr. Viera Scheibner from Australia continues to maintain that DPT vaccine is associated with Sudden Infant Death Syndrome (SIDS). This concern has long been investigated, but no well-controlled study has found a difference in the incidence of SIDS between vaccinated and unvaccinated groups. Dr. Bart Classen, an investigator from the United States, is the main proponent of a theory that vaccines can cause type I diabetes, depending on the timing of the immunization. A panel of experts from the Institute for Vaccine Safety Diabetes Working Panel looked into the claims and concluded that Dr. Classen's analytic methods were incorrect. Although somewhat biologically plausible, the claim was far from proven, and epidemiologic studies did not support it. A supposed link between autism and the MMR vaccine has been made by Dr. Andrew Wakefield, whose theory is that the vaccine causes inflammation of the intestines and that this precedes autism. However, in 1999, a large, epidemiologic study by Taylor et al. found no increased autism incidence after the MMR was introduced and no difference in the age of autism diagnosis in vaccinated and non-vaccinated groups. Autism *has* been increasing, partly due to a change in the diagnostic classification system. The CDC is supporting further research to explore this issue. A claim that the aluminum and mercury in influenza vaccine is linked with Alzheimer's disease has surfaced in long-term care facilities in the province. However, the vaccine does not contain aluminum, and the amount of mercury in the vaccine does not increase overall mercury levels to above those of any safety guidelines.

In common to these conditions is the fact that the causes are not well established and the vaccine is given at around the age when the condition emerges — for instance, people over 70 are the most likely to be receiving yearly influenza immunization, and this is the age at which Alzheimer's disease tends to become evident. It is necessary to determine what are the most credible sources of information about immunization for parents and how to feed into them, as well as to recognize the emotional component of parents' reactions and how that will affect their decision making.

Dr. Robert Pless

Team Leader, Vaccine Adverse Event Reporting System (VAERS) section, National Immunization Program, CDC

Although vaccines have been effective in reducing disease, they do carry side effects, though usually minor. However, they have been instrumental in controlling disease. For example, there were many hundreds of thousands of cases of now vaccine-preventable diseases in the United States, as compared with only many thousands of cases today, although there were no cases of adverse events before vaccination came along. Interruptions in immunization coverage, however, have led to outbreaks of disease throughout the world. Individual decisions not to be immunized, therefore, have repercussions for the community ("tragedy of the commons"), and reliance on community protection is flawed, since no vaccine is 100% effective and imported cases of infection remain a possibility.

Deciding whether vaccines are truly safe depends on the definition of “safe”. Nothing is completely without risk, so we continually demand greater benefits from vaccines than risks. For example, the case of polio illustrates how refinements in vaccines over the years have altered this concept. The polio vaccine was first tested in 1954, when three doses of the inactivated vaccine were given to 400,000 children, a placebo was given to 200,000 children, and 1.2 million were unvaccinated. The efficacy was determined to be 83% in preventing paralysis. In its widespread use, however, cases of paralytic disease occurred, which were found to be the result of an inadequate inactivation process. The vaccine in that situation was not safe, because it caused more disease than it prevented. Extra filtration steps in the production process corrected the problem, although the resulting vaccine was less efficacious. With widespread use of the vaccine, the number of polio cases began to diminish, but not optimally. In 1962 the oral polio vaccine was developed, offering almost 100% efficacy and some protection for contacts of immunized individuals. However, there was a risk of vaccine-associated paralytic polio of 1 in 700,000 vaccine recipients after the first dose. This vaccine was safe, because polio was still endemic and there was not a more effective alternative. In the 1990s, when immunization rates were higher and the enhanced inactivated vaccine, with greater efficacy, became available, the oral polio was no longer considered safe. The inactivated product now provided greater benefits. The switch was therefore made to the new vaccine.

The current questioning of the value of immunization is healthy, and there are issues that must be addressed. However, parents need to understand that they cannot be offered a guarantee of no risk for any medical product. In a recent U.S. survey, 19%-25% of parents had important misconceptions about immunization that undermined their confidence in the procedure. Messages are being developed through parent focus groups to reinforce the benefits of immunization, while better vaccines are also being developed.

Surveillance: Why Bother Looking

■ Surveillance of Vaccine-Preventable Diseases

Dr. Monique Douville-Fradet

Bureau de surveillance épidémiologique, ministère de la Santé et des Services sociaux, Québec

Surveillance is a unique tool for the implementation and follow-up of our immunization strategy. Surveillance data often represent the tip of the iceberg, but they are sometimes the only readily available data to use as the basis for action. Surveillance is about valid indicators that detect trends and lead to hypotheses that can be tested. Since immunization is administered to healthy people, there is a need and a duty to follow up and monitor the vaccine product, its adverse events, and its impact on disease epidemiology over time.

There have been some outstanding immunization successes, but challenges remain. Rates of pertussis have been increasing and decreasing over time across the country, and this has led to investigation of coverage rates and vaccine efficacy. Better results are expected with the new acellular vaccine. Mild reactions have been associated with the current year's influenza vaccine, and these are being studied further.

A comprehensive, post-marketing surveillance program must examine four types of data: epidemiologic, laboratory, product data (including impact on different populations over time, cost-benefit/cost-effectiveness), and data on attitudes towards immunization of medical professionals and the public. Methods to obtain data include sentinel surveillance, surveys, disease notification, laboratory surveillance, and special projects. Research has to be an integral part of post-marketing programs.

Epidemiologic data will include information about the disease (trends, burden of disease, risk factors, outbreaks, progress toward elimination), immunization (coverage rates, characteristics of susceptible individuals, vaccine failures), and adverse events (basic descriptive data, investigation of severe or unusual events, attributable risk estimates). Laboratory surveillance is needed for strain characterization, detection of emerging strains, and outbreak investigation. Product data include cold chain monitoring, vaccine quality, evaluation of vaccine loss and efficacy, follow-up of immunogenicity data, and economic analysis. Repeat studies over time will be needed to follow changes in the public and professionals' attitudes towards immunization. Information systems are one tool that will be used more and more to pull together the data from these various sources.

■ Surveillance of Vaccine Coverage

Dr. David Mowat

Acting Director General, Centre for Surveillance Coordination, Health Canada

Although there are separate databases for disease epidemiology, immunization, and adverse events, the value of the data lies in the possibility of linking the three. Information technology (IT) and infostructure are being developed to support the activities that health surveillance data are used for: to monitor trends in disease as evidence for decision making (managing immunization programs, identifying under-immunized groups, evaluating the efficacy of vaccines or delivery methods), and as input for research.

In a model of health surveillance — including collection, analysis, and dissemination of information — developed by the Health Surveillance Group of the Advisory Committee on Health Infostructure, the system Health Surveillance Tracking and Alerts has the responsibility for rapid provision of alerts and the information needed to make decisions, for instance, about vaccine-preventable diseases and adverse effects. This depends on its “feeder system”, Service Delivery Information System, which receives information from the field workers (physicians, public health nurses). The model allows two issues to be

addressed together: surveillance and IT support for service delivery. The model is part of a plan to move toward a system of electronic health records (longitudinal, person-oriented).

The immunization registries to be developed by 2003 as part of the National Immunization Strategy are envisaged as information systems or “records networks” in each province/territory that are nationally compatible and thus facilitate inter-provincial exchange of records, rather than as a national, centralized database. To this end, national standards must be developed, to include a minimum data set, common data elements and definitions, and functional standards (e.g. registry record established within 7 days after birth for each newborn). Work is already under way. One of the greatest challenges will be to capture all the relevant data.

■ Global Vaccine Safety

Dr. Yves Bergevin

Principal Advisor, CIDA

Although immunization programs have been very successful over the years, the delivery of vaccines is often not carried out under optimal infection control conditions, particularly in developing countries. It is estimated that of the 20 billion injections given annually (for curative and immunization purposes), up to 50% are unsafe. Achieving a goal of safe vaccine delivery and immunization services worldwide will necessitate a number of international efforts.

The Immunization Safety Priority Project, a collaborative project between CIDA and WHO, among others, is a partnership whose goal is to support countries in their delivery of immunization services with the highest levels of safety. There has to be a shift from immunizing as many children as possible to immunizing as many as possible in a way that ensures quality; this will involve prevention, early detection, and rapid response to VAAEs. The four areas of work are (i) research and delivery of safer delivery technologies (e.g. Uniject), (ii) access to safe delivery and disposal technologies, (iii) quality control and assessment tools to ensure vaccine safety to the point of use, and (iv) identifying and managing risks. The Safe Injection Global Network has been initiated for immunization and injection safety.

Progress in vaccine administration to date includes a standard assessment tool and data collection, technology transfer to allow a shift to autodisable syringes, use of Uniject (pre-filled syringes), and development of safe disposal policies. GAVI has stated that all vaccines purchased through its partnership should be delivered with autodisposable syringes. It has also been agreed that the vaccines that UNICEF buys for GAVI should meet WHO standards of quality. With regard to risk identification and management, the focus is on establishing national regulatory agencies in developing countries. The Global Public Health Intelligence Network is a system that will provide a warning of unexpected

VAAEs, and the Global Vaccine Safety Advisory Committee provides independent assessments to the Department of Vaccines and Biologicals.

■ Canadian Surveillance of Vaccine-Associated Adverse Events

Dr. Wikke Walop

Acting Head, Vaccine-Associated Adverse Event Surveillance Section, CIDPC

A national survey carried out early in 2000 found that of 1,012 households with children under 18 years at home, 5% had children who had not been vaccinated. This rate was higher among children of young versus older parents. The reasons given for non-immunization were that the survey participant was not the parent (32%) and that the child was too young (20%); 21% gave no reason.

Mechanisms in place to ensure immunization safety in Canada include the Vaccine-Associated Adverse Event Surveillance System (a passive reporting system); IMPACT (an active surveillance system); an Advisory Committee on Causality Assessment, which meets twice a year to review reports of serious adverse events and to determine whether the temporal relation is likely to be causal and in need of further investigation; the Canadian Paediatric Sentinel Surveillance Network of about 2,500 pediatricians across Canada, who report on a monthly basis about various conditions, e.g. acute flaccid paralysis, anaphylaxis; and NACI.

In the Vaccine-Associated Adverse Event Surveillance System (VAAESS), the report of an event originates with the health care provider and proceeds to the health unit, the provincial health department, and then on to Health Canada. Manufacturers also report to HC. The VAAESS database is being switched from a tree-structure to an Oracle database, which has become the HC standard. There are 25 adverse events listed in the system's reporting form that are considered to be of public health importance together with space for further descriptions and other adverse events. The responses are coded using WHO-ART (WHO adverse reaction thesaurus), which provides a basis for rational coding of text and consists of synonyms and preferred terms for data input, plus high level terms and system organ classes for summarization. IMPACT covers 12 pediatric hospitals, where nurses monitor admission charts for pre-determined adverse events, vaccine-preventable diseases, and other signs or symptoms of interest.

It is hoped that within a comprehensive immunization program, all children will be entered into the immunization registry at birth, and core data elements will be entered at each immunization, probably using a bar code. Information about an adverse events would be added to the vaccine adverse event module (signal generation). Evaluation of such events and implementation of any necessary response will be part of HC's risk-benefit assessment model for its post-marketing surveillance.

■ Allegations Regarding Immunization and Chronic Disease

Dr. Robert Pless

Team Leader, Vaccine Adverse Event Reporting System (VAERS) section, National Immunization Program, CDC

The allegations that vaccines cause chronic illness (e.g. multiple sclerosis, autism) have been difficult to refute because in many cases the triggers responsible for these illnesses have not been identified; moreover, incidence rates of some of these diseases *have* been increasing without obvious explanation. In the gap that exists while evidence against such claims of a link is being gathered, the public is vulnerable to unfounded claims.

Applying causality assessment to some of the allegations can be useful. Some of the criteria include biologic plausibility (a physiologic reason why the vaccine should cause the event in question), the strength of the association between vaccine and disease, the consistency and specificity of the association, and the temporal sequence of events. It has been suggested, for example, that there is a link between hepatitis B immunization and multiple sclerosis such that the vaccine triggers the onset of the disease in someone already predisposed, but so far the epidemiologic evidence is against this. In France, where the alleged link was first reported, a concerted effort to immunize the adult population has led to vaccination in an age group in which the incidence of multiple sclerosis peaks – prime conditions for confusing temporal association with causation.

Another example is of association between immunization and type 1 diabetes. A matched case-control study using a large linked database in the United States analyzed data on hepatitis B and *Haemophilus influenzae* type b immunization in children born between 1988 and 1997 together with data on cases of diabetes. The risk for type 1 diabetes associated with hepatitis B and Hib immunization was not found to be significant, nor did the timing of the immunization alter the risk. Further, with respect to autism, an observed increase in incidence in the 1990s is felt to have been due to many factors, including changes in case definitions, improved services for autistic children that result in more identification of cases for treatment, and population increases. The claim of a link between autism and the MMR vaccine was originally based on what were essentially self-reports of only 12 cases, with no controls. A recent epidemiologic study in the U.K. found no increase in autism that could be related to the introduction of the MMR vaccine into immunization programs.

No substantiated link has been demonstrated between immunization and these chronic diseases. Unfortunately, when allegations arise that have little or no valid supporting evidence, it becomes the responsibility of immunization programs to do the work of properly investigating the claims and gathering the data that do exist in order to confirm or refute them, so that health professionals are equipped to address the issues with their patients.

Breakout Sessions

Communicating with the media: In this session, video clips were shown for comment and discussion. Panel members from public health, communications, and the media made presentations on effective communication skills and the need for guidance from professionals in that area. Some tips were to

- prepare key messages by using facts, statistics and examples;
- understand your most vulnerable points and be ready to respond when asked about them;
- never lie or guess; say that you will find out;
- keep your personal opinion out of any communication;
- target your audience (to reach the undecided and the “don’t knows”);
- stick to your area of responsibility.

Cold chain successes and challenges: Different strategies were reviewed for improving cold chain practice by vaccine providers. Representatives from Alberta, Ontario, Quebec, and Newfoundland described the ways in which those provinces are monitoring cold chain programs. It was felt that a cooperative and educational approach would be the most successful.

Facilitating informed consent: After presentation of several real-life scenarios, participants were asked for comment on the issues surrounding informed consent that emerged: what constitutes informed consent, how it can be obtained, how much information is needed for consent to be fully informed, and who are the appropriate people to provide it. Topics included disclosure of *alleged* associations between immunization and adverse events, divorced parents’ disagreement about immunization for their children, and proxy decision-makers.

Sources of immunization information: Participants learned more about electronic and written sources of immunization material developed in Canada and internationally. Web sites that are linked with established sources, such as the Centers for Disease Control and Prevention and WHO, are particularly useful. The Web site of the Canadian Immunization Awareness Program (<http://www.immunize.cpha.ca>) has many relevant references.

Tuesday, December 5

Keynote Address

Dr. Bruce Gellin

Director, National Network for Immunization Information

Although great progress has been made in preventing disease through immunization, whether the momentum can be maintained has become less certain with the complexities of the present day: not only are there hundreds of new vaccines on the market or in development, but also attitudes toward medicine and science have changed, such that new products are less likely to be accepted unquestioningly. The public is more concerned about risk, has better access to current information, takes more responsibility for health, is more inclined to be sceptical of medical “advances”, and more likely to take legal action. Characteristics of medical practices, including immunization, that magnify risk perception (over and above their true risk) are

- uncontrollability
- involuntary nature
- involvement of children
- delayed effects
- lack of trust in responsible institutions
- media attention
- irreversible effects
- unclear benefits
- risk caused by human (rather than divine) action.

In parent focus groups, the National Network for Immunization Information has found that participants had a limited knowledge of vaccine-preventable diseases, trusted the older vaccines more than the new ones, and considered immunization against life-threatening diseases to be the most important. Their most valued source of information was health care providers. Interpersonal and written communications were considered useful. Other sources were parenting books and magazines, the Internet, and friends in health care related fields. Many parents said that they already had information on immunization, although a lot of what they “know” may be inaccurate and new material may not be acceptable: people judge science by how well it agrees with the way they want the world to be.

In another survey, 25% of respondents believed that immunization weakened the immune system, and 23% felt that people receive more vaccines than are good for them. On a scale of 1 to 10 (10 = extremely worried), concern about vaccines side effects for most childhood vaccines was in the 3-5 range.

The audience for educational campaigns about immunization are not those who oppose it but those who do not know — parents who have heard partial information from various sources and have been unable to find answers from one reliable one. Periodic assessments of parental attitudes and beliefs are necessary in order to maximize trust and cooperation in consumers. The paradigm of “vaccines good, diseases bad” may need to be reviewed in light of the many developments in immunization currently taking place.

New Vaccines

■ Efficacy of Heptavalent Conjugate Pneumococcal Vaccine

Dr. Steve Black

Co-Director, Kaiser Permanente Vaccine Study Center

Streptococcus pneumoniae has 90 serotypes, which fall into 45 groups; a small number of these account for most of the pneumococcal disease in children. *S. pneumoniae* results in pneumonia, invasive disease, and otitis media. In developing countries it causes 4 million deaths globally per year.

A randomized, double-blind controlled trial was conducted to assess the efficacy of a heptavalent pneumococcal conjugate vaccine in 37,000 children, randomly assigned to receive either PCV (pneumococcal conjugate vaccine) or meningococcus type C CRM₁₉₇ (control group). The outcomes measured included invasive disease, clinical otitis media, and pneumonia. As of August 2000, no cases of disease had occurred in the PCV group, as compared with 17 cases in the control group. Up to the end of 2000, the figures are 1 case in the PCV group versus 39 cases in the control group (94% efficacy). There has

been no evidence of increased disease due to non-vaccine serotypes. Among low birth weight and small for gestational age infants all cases of disease occurred in the control group.

With regard to otitis media, there was a reduction in medical visits of 8.2% (confidence intervals 5.6-10.6) and in tube placement (the most frequent surgical procedure carried out on children in the United States) a reduction of 20.1%. It was also found that the number of antibiotic prescriptions for otitis media dropped by 5%.

This conjugate vaccine appears to be safe, highly effective in preventing pneumonia, and helpful in the prevention of otitis media.

■ Conjugate Meningococcal Vaccine – Public Health Applications

Dr. Philippe De Wals

Head, Department of Community and Health Sciences, University of Sherbrooke

Between 1995 and 1998 the average annual incidence rate of meningococcal disease was 0.8 per 100,000. The rate of disease is highest among children < 5 years of age and in the group aged 15 to 24 years (3.3 and 1.3/100,000 respectively). The overall case fatality rate is > 10%. Forty-nine percent of cases are caused by serogroup B strains, 37% by serogroup C, and 11% by serogroup Y.

The currently available meningococcal polysaccharide vaccines (MPVs) induce a T cell-independent immune response without memory. For serogroup C, short-term clinical protection is high in adolescents and adults, modest in children, and non-existent in infants. To overcome these deficiencies, new meningococcal conjugate vaccines (MCVs) have been developed, which contain serogroup A, C, Y, and W-135 polysaccharides chemically conjugated to protein carriers. MCVs induce higher titres of anticapsular and bactericidal antibodies than those produced by MPVs at similar ages, and immunologic memory has been observed after revaccination, a feature of a T-dependent immune response. In individuals previously immunized with serogroup C MPV, hyporesponsiveness to subsequent doses is partially overcome using MCV.

The safety profile of MCVs is similar to that of other conjugate vaccines. Although their clinical efficacy has never been tested in a randomized trial, a mass immunization campaign using different serogroup C MCVs is under way in the United Kingdom, and preliminary results are encouraging.

■ **New Influenza Vaccines – Public Health Applications**

Dr. Paul Glezen

Influenza Research Center, Baylor College of Medicine

Influenza viruses are classified on the basis of their surface antigens, hemagglutinin (H) and neuraminidase (N). It is because of the virus's ability to change its antigenic composition that annual immunizations against influenza are necessary. Influenza A virus is the one usually responsible for major epidemics of the disease, and so far the H3N2 strain has had the most severe consequences in terms of death and illness. For each death caused by influenza, there are 10-15 hospital admissions, most commonly among children < 5 and those aged 65+. Children are recognized to be the spreaders in the community and responsible for introducing the infection into the household. Mortality rates are highest in the 65+ age group. Although immunization among older people is effective and cost saving, the response of these individuals is not optimal.

A new, live attenuated influenza vaccine administered by nasal spray has been developed (not yet licensed), which has been found to be well tolerated and efficacious in young children. The efficacy in a St. Louis trial was 92% for influenza A and 91% for influenza B. The vaccine was also found to result in a decrease in acute febrile respiratory illness and in the use of antibiotics; there was an overall reduction of 30% in otitis media. Side effects were mild.

A large field trial in Texas is now nearing completion. Immunization of 4,298 children took place in year 1 and 5,250 in year 2. The children were used as their own controls (before and after immunization) for assessment of the vaccine's safety. In the first year, 8 subjects were hospitalized, for reasons not related to the vaccination, and the figure was similar for the second year. For a subset of children with a history of wheezing, there was no increased relative risk for medically attended acute respiratory illness. No serious adverse events occurred. The vaccine was found to be effective during the first year, and analysis of the second year data are under way to investigate indirect protection of community contacts.

■ **Acellular Pertussis Vaccine – Public Health Applications in Adolescents and Adults**

Dr. Scott Halperin

Head of Infectious Diseases, IWK Grace Health Centre

From 1986 to 1997 the number and proportion of pertussis cases has increased the most rapidly among adolescents and adults. Furthermore, this is true not only in Canada: in countries with both high and low childhood immunization rates pertussis is on the increase in these groups. The severity of the disease varies, from mild cough to typical pertussis

profile. It is believed that adolescents contract it from within the community, and parents are infected by their children.

Two vaccines against pertussis have been manufactured for adults and adolescents, combining pertussis vaccine with diphtheria and tetanus toxoids. The vaccine that is available in Canada is Adacel (Aventis Pasteur). It has been shown to be safe, with only mild adverse events, and immunogenic, producing antibody levels in excess of those in immunized children, and yet it is rarely used in Canada. The reason for this may in part be cost and lack of efficacy data. A pertussis immunization program for adolescents and adults may be cost-beneficial, but there are too many poorly defined parameters to state that it would be cost-effective. Another potential disadvantage that has not been thoroughly evaluated is that the vaccine may put adults at higher risk by delaying disease until adulthood (as with varicella).

Newfoundland is the only province/territory in which adolescents are routinely given the new pertussis vaccine, and surveillance of pertussis epidemiology in that province may help address some of these issues.

■ RSV Vaccines – Public Health Applications

Dr. Joanne Langley

Medical Director, Infection Control Services, IWK Grace Health Centre

Respiratory syncytial virus (RSV) is recognized as the leading cause of lower respiratory tract infection (LRTI) (bronchiolitis and pneumonia) in young children. A community study carried out in Rochester, New York, found that RSV was responsible for 50%-80% of LRTI in young children. Later studies have estimated that 100% of children are thought to have been infected by the age of 2 years, and reinfection is common throughout life, usually resulting in less severe disease. RSV is spread through contaminated respiratory secretions. The incubation period is 4-6 days.

Risk factors for severe RSV infection in infancy are prematurity, congenital heart disease, chronic lung disease and immunocompromise. About 1% of episodes require hospital admission. A 1993-94 study carried out by the Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC), involving 1,512 children admitted to hospital with RSV, found that the largest group of infected children had been previously healthy, and the two other largest groups comprised premature infants (37 weeks' gestation or less) and the very young (6 weeks or less). Up to 25% of the children were admitted to the intensive care unit, and up to 15% needed mechanically assisted ventilation. The overall mortality rate was about 1%. RSV also has implications for elderly people, contributing as much to illness and death as does influenza. Studies of long-term care facilities indicate that once RSV is introduced into a facility the attack rate is up to 40%, and up to 53% of residents die.

Two products available for passive immunization are RSV immune globulin (polyclonal) and a humanized mouse monoclonal RSV antibody, both given monthly during the respiratory season and both expensive. The Canadian Blood Services provides access to the products under specific conditions. With respect to a vaccine, two of the virus polypeptides (F and G) have been targeted for vaccine development. There is a need for a vaccine to lead to a greater immune response than does natural infection and to be effective in the high-risk groups such as premature infants and the immunocompromised. Two strategies for development have been to use live attenuated virus and RSV proteins, and trials are under way.

■ Vaccines for Sexually Transmitted Diseases – Public Health Applications

Dr. Stephen Sacks

Viridae Clinical Sciences

Problems encountered in developing a vaccine against sexually transmitted infections (STIs) are the ability of the viruses to endure and adapt to the host's immune system and the possibility of re-infection after cure. Currently available are vaccines against hepatitis A and hepatitis B, and one against herpes simplex virus 2 for selected groups. The hepatitis B vaccine was the first effective vaccine developed against STIs; it is given routinely to grade 6 children and can also be used in neonates.

With regard to bacterial STIs, the porin protein and the pilus have been investigated as potential candidates for a vaccine against gonorrhoea, although trials have so far failed. Whole killed virus vaccine was found to be partially effective against chlamydia, but the protection was short-lived. Vaccine developers are looking at the major outer membrane protein (MOMP) and DNA-based MOMP. Animal studies have shown partial efficacy against syphilis with killed treponemes. More recently, it has been suggested that cloned antigens may give partial protection.

A vaccine against human papillomavirus (HPV), a non-enveloped virus, is considered a priority, because it has been estimated that up to 50% of young sexually active women may be infected with HPV, which may result in no disease, or in benign (genital warts) or malignant (cervical cancer) disease. There are many current candidates for a vaccine, some of which use virus-like particles. Three phase 1 studies have been completed. Herpes is an enveloped virus. The incidence of herpes infection continues to rise and is affecting younger age groups. Many different approaches to vaccine development have been taken. One vaccine has proved successful, but only in women who are seronegative for herpesvirus. With regard to HIV, many vaccines are under study, but there are problems to be overcome: the challenge is to enhance the immunogenicity of antigens, improve the use of adjuvants, to use primate models better, make use of the latest developments in

biotechnology genomics, to use novel vectors, and to understand the effects on the immune system.

■ **Current Status and Use of Varicella and Hepatitis A Vaccine in Canada**

Dr. Barbara Law

University of Manitoba

Hepatitis A immunization is offered as a risk-based program in Canada. Recommendations from NACI in 2000 were that the booster dose does not have to be the same product as the original vaccine used; a single dose should be used for outbreak control; and vaccine is preferable to immune globulin for post-exposure prophylaxis. A survey of epidemiologists and medical officers of health revealed that Saskatchewan is the first province to target hepatitis A immunization at children (1-15 years) in communities at high risk. Most provinces have focused their efforts on individuals with chronic liver disease, primarily those with hepatitis C, as well as intravenous drug users.

The recommendations on varicella immunization from a 1999 consensus conference were as follows:

- routine immunization for children \geq 12 months of age
- followed by susceptible children $<$ 13 years
- and then at-risk adult groups (e.g. health care workers, teachers, day care providers).

The goal was set for routine immunization programs to be in place by 2005 or within 2 years of development of a refrigerator-stable vaccine.

Varivax (Merck & Co.), the first vaccine licensed, was a live, attenuated Oka strain that was stable in the refrigerator for only 72 hours. In June 2000, Varivax II was introduced, and this vaccine is refrigerator stable for up to 90 days, although it still has to be used within 30 minutes when reconstituted. Despite the recommendations, Prince Edward Island is the only province/territory to date that has begun routine administration of the vaccine. Alberta's program is planned to begin in January 2001, and other provinces/territories are at the planning or preparation stage. With regard to surveillance of varicella and herpes zoster, there has been some progress in enhancing laboratory capacity for detection, but limited movement in other surveillance targets.

In the United States, there has been a move recently to strengthen the recommendations on varicella immunization programs. Already, 20 or more states require proof of varicella immunity when children enter school. The safety record in the United States is 67.5 cases per 100,000 of minor adverse events (mostly rash) and 2-9 per 100,000 serious adverse events over 3 years' postmarketing surveillance. There seems no reason why Canada should not move forward more quickly with varicella immunization programs.

Immunization Programs: Choices and Inertia

■ How Do We Decide? (New Programs)

Dr. Bernard Duval

Institut national de santé publique du Québec

In considering how to implement effective immunization programs as soon as possible after vaccine licensure, the role of public health in the decision-making process must be defined. Part of the role is to provide technical information to the decision-makers, although this information is often not available or is not in the right form. Technology assessment is a form of policy research: it is policy oriented, has interdisciplinary content and process, examines databases, synthesizes information, and disseminates information tailored to different target audiences. Unfortunately, public health has little of the policy-oriented research capacity needed for technology assessment. Some of the considerations that decision-makers rely on to do their job are acceptability to key stakeholders, cost implications, acceptability to consumers, strength of evidence regarding effectiveness and usefulness, and evidence of need.

A decision-making model that may be valuable in strengthening the influence of public health in policy decisions includes six categories molecular biology, microbiology, clinical aspects, epidemiology, health services/economic costs, and policy ranging along a continuum from reductionism to holism. Public health scientists need to better document these different elements of the process, and will require the human and financial resources to carry out the appropriate studies. When the decision is well documented for all the components of the model, it will be easier to convince decision-makers to allocate the rather large sums required for new vaccination programs.

■ Evaluation of Immunization Programs

Dr. Gaston De Serres

Institut national de santé publique du Québec

It is important to remember that immunization programs are instituted on the basis of information obtained from clinical trials, in which conditions are optimal, participants' immune systems are healthy, and thus the maximum benefit is gained from the vaccine. The effectiveness of immunization is likely to be lower in the community. Vaccine coverage will be determined by the acceptability of the product, which in turn is influenced by its safety, accessibility, and promotion, as well as the perception of risk associated with the disease.

Evaluation of vaccine effectiveness involves surveillance of disease and analysis of trends. However, there is no formal mechanism in place; rather, an analytic approach is taken,

and studies evaluating effectiveness tend to be carried out only when there is a crisis. The long-term impact of the vaccine has tended to be overlooked. With respect to safety, there is a passive reporting system of adverse events, but this is not very sensitive. The active surveillance system (IMPACT) does not provide information about the denominator, only the numerator. The Advisory Committee on Causality Assessment is a tool for evaluating safety, but again is not very sensitive and has low capacity. Vaccine coverage is evaluated according to the number of doses distributed, and this is inadequate. Moreover, it is impossible to know the coverage for travellers. Information management systems will help, but will only be fully operational in a few years. Suboptimal coverage must be investigated by epidemiologic studies. Promotion of the vaccine and immunization program is necessary for providers and the public. In the United Kingdom, regular surveys of the public are carried out, and when a new program is being planned, a marketing study is initiated.

Public health is responsible for program evaluation. Problems will arise with the implementation of universal immunization programs, and public health must ensure that there is adequate follow-up. The same scientific rigour must be applied as in basic research. However, not all provinces/territories have the resources or capacity for such evaluation. Health Canada must take the lead in program research and dedicate more resources to this crucial aspect of immunization.

Breakout Sessions

Travel immunization: This session covered developments in the delivery of vaccines against yellow fever, hepatitis B, influenza and rabies. A Health Canada survey of 51/197 yellow fever clinics revealed that a significant minority had major deficiencies; no clinic received a perfect score, and one was decertified. Accelerated schedules for hepatitis B will provide rapid serologic responses and improved protection in the short term; however, long-term immunity may be compromised without further boosters. With regard to influenza, large numbers of travellers are at risk, and there are many factors that contribute to transmission. “Northern” and “southern” influenza vaccine cocktails exist but are not readily available. Repeat immunization with the northern trivalent vaccine may be appropriate. Pre-exposure immunization against rabies is very expensive. There is no significant difference between the Canadian (intramuscular) formulation and the U.S. (intradermal) formulation. The intradermal route can elicit excellent antibody responses, and can be considered for use in high risk Canadian travellers if there is appropriate attention to technical concerns and verification of titres.

Immunization of health care workers: This session opened with results from a recent survey conducted by the Division of Immunization, Health Canada. All of the 11 provinces and territories who responded recommend influenza immunization for health care workers (HCWs), 10 recommend rubella immunization, 9 recommend measles and hepatitis B immunization, and 3 recommend varicella immunization. The concerns expressed by the provinces related to lack of public funding for certain vaccines, HCW resistance to immunization, and issues of mandatory immunization. A survey in Quebec found that only 59% of nurses were strongly favourable towards immunization programs, as compared with 87% of family physicians and 92% of pediatricians. In Ontario, a provincial protocol requires long-term care facilities to develop policies to provide vaccine annually and to exclude unvaccinated HCWs during influenza outbreaks unless they are willing to take antiviral medication. Influenza vaccination Coverage in Ontario long-term care facilities rose from 44% in 1998/1999 to 86% in 1999/2000. Higher rates were associated with facilities having a written policy stipulating exclusion without pay of unvaccinated workers who refuse immunization, use of group and individual educational sessions, and provision of on-site clinics. Ethical analysis of HCW immunization issues suggests that if immunization poses only minimal risk to HCWs and is necessary to lessen serious harm to patients, then priority to patient well-being (as per the professional code of ethics) suggests that HCWs should accept immunization.

Emergency response immunization issues: Emergency situations involving vaccination products were discussed in this session. Canada's decision to accept refugees from Kosovo forced public health authorities in Nova Scotia to quickly organize procedures for receiving them, including the updating of refugees' immunization status. This type of intervention required clarification of the roles and responsibilities of the partners, the setting up of databases and a recall system, and efficient and open communication mechanisms. In particular, all possible health risks for the people participating in the project had to be taken into account. Analysis of the decision-making process during flare-ups of invasive meningococcal type C disease in Quebec revealed the difference in approach between scientists and politicians: the first deals with the unknown and is without social value, whereas the political perspective takes into account the context of the decision, the feasibility of the intervention, and popular perception. The plan that has been prepared for the expected influenza pandemic, calling for mass immunization campaigns, helped to illustrate the organizational principles of who, where, how and with what product such campaigns will be conducted. Prior preparation and good management of an emergency situation are the basic conditions for an adequate public health response.

Vaccine research: new products in the pipeline. Four companies made presentations on vaccine developments in the "middle distance". ID Vaccine is developing a vaccine against group A streptococcal infection, which causes over 10 million cases of pharyngitis and 10,000 cases of invasive disease annually in the United States. The candidate vaccine is based on the surface M protein. A recent phase I trial in the United States confirmed the

safety and immunogenicity in adult volunteers of a 6-valent protein vaccine. Plans were described for testing a 26-valent vaccine at Canadian sites. Coley Pharmaceuticals, of Ottawa, is participating in work that aims to optimize DNA-based vaccine formulations for humans. These candidate vaccines have the potential to be inexpensive, stable, and safe, but results in humans have not so far matched those in animals. Human trials of a novel nicotine vaccine, developed by Nabi, are planned for 2001. The conjugate vaccine is intended as an aid to smoking prevention and cessation. It elicits antibodies that soak up nicotine, then release it slowly, thus reducing the amount reaching the brain. Nicotine by itself does not provoke an increase in antibodies or tissue inflammation. SmithKline Beecham Biologicals (now GlaxoSmithKline Biologicals) is developing a human rotavirus vaccine that is expected to pose less risk of intussusception than occurred with the tetravalent rhesus rotavirus vaccine. Studies in human infants have been favourable, so expanded trials are planned, involving sites in Canada.

Wednesday, December 6

Keynote Address

Dr. Noni MacDonald

Dean of Medicine, Dalhousie University

Immunization has not been a prominent item on the curricula of either medical or nursing schools, despite its proven public health benefits over the years. This gap can be likened to attention deficit hyperactivity disorder. Clearly, little attention is paid to immunization in the second report on the health of Canadians (*Toward a Health Future*), in which the topic is “covered” in two paragraphs out of 200 pages. In medical and nursing schools, students learn about the risks of immunization, response to the vaccine, immunization schedules, and so on. The benefits are hardly touched upon: for instance, in 1924 there were more than 9,000 deaths in Canada from diphtheria, one of the major killers of children, but since 1983 there have been 0 cases each year. Students need to be told about this because they have not learned it from their own experience, and they need to know that immunization is cost-effective.

One of the features of hyperactivity is that concentration is not focused on matters of importance. What is important is to combat attacks on the benefits of immunization. The headline “Too Many Vaccines for Kids” must be anticipated, planned for, and responded to with equally arresting headlines. The public needs to be informed that a temporal association does not equal causality. For example, it was once claimed that DPT was associated with SIDS, and yet we know this to be untrue and can show it to be untrue by providing the evidence: a reduction in the rates of SIDS following the strategy of laying babies down on their backs rather than their stomachs.

Correcting the deficit in immunization education will require efforts by a number of groups. Provision of the relevant information is of primary importance, and this will include the benefits of immunization — e.g. immunization of health care workers against influenza leads to increased survival in patients — the cost-effectiveness, indications, schedules, adverse events, true contraindications, causality assessment, and influences affecting compliance. For doubters, the “teachable moment” can be exploited, with descriptions of the illness and its effects. People’s logic is not always perfect, and so assumptions cannot be made about their conclusions. As well, students need to learn communication skills: how to make sure that the information they provide is relevant and will be attended to and the best format in which to do this.

National curricula for medical and nursing schools are necessary that include all these elements. Moreover, if programs were established in high schools this would ensure that children become aware of the rationale for being immunized and carry that message home. It is time for a Task Force to be set up that would develop such curricula, so that our future health professionals’ commitment to immunization is not left to chance.

Education and Curriculum

■ Getting Immunization on the Medical School Agenda

Dr. Yves Robert

Laboratoire de santé publique du Québec

Immunization is the most common medical procedure carried out: in Quebec alone there are 3 million vaccinations each year, or one dose every 10 seconds. Medical students find this hard to believe; for all its frequency, immunization is given scant attention in medical schools. In a 1997 survey (Sciberras J et al., unpublished data), at least two-thirds of medical schools reported that they devote some time to the topic of immunization (an average of 1-2 hours), and 92% felt that they do not allow sufficient time.

Surveys show that the public prefers to receive its health information and advice from a health care provider, so it is important that medical students receive the relevant information and can pass this on when they are in medical practice. Unfortunately, with the increasing number of complex vaccines coming on the market, what is taught currently will be out of date in the next few years, and physicians have little time to spare for keeping up to date.

A recent survey of pediatricians, nurses, and other health care workers carried out by a Quebec group found that up to 10% of doctors were lukewarm about the idea of immunizing children and called into question the relevance of these programs. It is crucial for the

major controversies about immunization to be brought out into the open and responded to. Students should be taught not only the techniques used for injection and how to manage vaccines (e.g. storage temperatures) but also the cost-benefits and the logic of the program, how to manage adverse events, and how to counter arguments opposing immunization. Physicians are important sources of information for their patients and a fundamental element in bringing about behaviour change. They must take every opportunity to do so when appropriate.

■ Getting Immunization on the Nursing School Agenda

Ms. Agnes Honish

Senior Communicable Disease Control Lead, Alberta Health and Wellness

Large proportions of client immunizations in Canada are administered by registered nurses, who provide front-line health services in a variety of settings. Because the role that nursing schools assume in the educational preparedness of nurses who vaccinate is not known, the Canadian Nurses Coalition on Immunization carried out a survey earlier in 2000 to obtain information on the characteristics of nursing schools, the format and length of time devoted to immunization education, and any practical experience provided.

Of 124 schools invited to participate, 71 responded (57%). Some of the results regarding immunization were as follows: time spent on immunization (except injection technique) was < 1 hour (13%), 2-4 hours (53%), 4-6 hours (19%) and > 6 hours (15%); the material covered included immunization types, schedules, and adverse events (90% of nursing schools), vaccine administration (88%), documentation (60%), and adult immunization (57%); concepts taught included risks and benefits (90%), vaccine-preventable diseases (77%), information communication (77%), and opposition to immunization (57%); regarding the practice of vaccination, 53% of students had no opportunity to observe or practise immunization, 40% had the opportunity, and 7% did not respond; and 73% of nursing schools felt the content of the program was inadequate, 63% felt that the time was inadequate, 63% that the resources were inadequate, and 39% that the clinical aspects were inadequate.

Overall, the key issues arising from the survey were the focus of nursing education on the care of patients in facilities rather than on community care. There was a lack of resource material on universal immunization, and few immunization experts in the nursing schools. Most markedly, there were very few clinical opportunities for students to observe, let alone practise, immunization techniques.

■ Getting Vaccine Research on the National Agenda

Dr. David Scheifele

Director, Vaccine Evaluation Centre, British Columbia

The increasing rate at which new vaccines are being developed is welcome, but it does reveal significant weaknesses in the scientific foundations needed to plan and run Canada's immunization programs. Vaccine research — which is rather more than product development — is supportive research that will help to strengthen these foundations. It will provide information about the burden of disease to be prevented in order to build the rationale for vaccination, shape programs, and measure their effectiveness over extended periods; as well, there will be continuous and meticulous documentation of vaccine safety to maintain public confidence in immunization.

Some of the elements of supportive research include disease epidemiology, the burden of disease, costs of disease and immunization, target groups, optimal uptake of programs for disease control, refinements to immunization schedules, product compatibility, choice between products, barriers to be overcome, and ways of motivating consumers. Research on safety and effectiveness will help to assess the impact of programs on disease, the duration of protection, short-term and long-term safety, and whether or not a program is warranted.

There is no overall body that organizes supportive research in Canada, yet such research is essential, given the many new vaccines emerging and the increasing scepticism of consumers. On December 2, 2000, establishment of the Canadian Association for Immunization Research and Evaluation (CAIRE) was formalized, with the goal of conducting supportive research in Canada. Over 50 top researchers have committed themselves to this alliance, which will be one of the planks of a Canadian National Immunization Strategy.

Late Breakers

■ Influenza Immunization and Oculo-Respiratory Syndrome

In mid-October, a number of people in Alberta and British Columbia reported the development of conjunctivitis or respiratory symptoms a few hours after having been immunized against influenza. At the Immunization Conference, a panel of four speakers presented up-to-date information on aspects of this oculo-respiratory syndrome.

Dr. Eleni Galanis, Health Canada, described the events that followed the alert. A teleconference of provincial epidemiologists on October 25 revealed that 82 cases of oculo-respiratory syndrome associated with influenza immunization had been reported

in four provinces. A case definition was developed, and enhanced surveillance began within a week. By mid-November there were an extra 318 cases and, as of the first week in December, 921 cases had been reported altogether, four requiring hospital admission for the respiratory symptoms. There were no deaths. Most cases resolved spontaneously within 48 hours. By comparison, 287 adverse events were reported after influenza immunization in 1999. Most of the cases (472) in the present outbreak occurred in Quebec, and British Columbia was next in frequency. Three-quarters of those affected were women. There followed frequent communications between governments and manufacturers, press releases, news briefs, letters to physicians, and an article in the *Canada Communicable Disease Report*. As well, the forms for informed consent were modified in accordance with this new information. Epidemiologic, immunologic, and product-related investigations were initiated. Although a causal connection seemed likely, it was agreed that since the syndrome was mild, the benefits outweighed the risks and the program should continue.

Mme Nicole Boulianne, Université Laval, reported on two small studies that were carried out in Quebec to investigate the incidence of oculo-respiratory syndrome in association with influenza immunization. In the first, 422 of 477 subjects responded to a telephone interview and, of these, 28 reported symptoms of the syndrome: in 9 the eyes were affected, in 10 there were respiratory symptoms, and in 9 both were observed. No one was admitted to hospital, but four subjects visited the doctor. In a second survey, of 799 people in four regions, the attack rate was 7% in the under-60 age group. The risk was higher among females and decreased with age. Symptoms resolved within 48 hours. There did not appear to be an association with previous immunization.

A study has been proposed to investigate the immuno-allergic mechanisms behind this oculo-respiratory syndrome. Dr. Danuta Skowronski, BC Centre for Disease Control, described it as a collaboration of several provinces, with the objectives of confirming the association with immunization; identifying the trigger components; determining whether this is a cell-mediated (hypersensitivity) response and, if so, of what type; identifying the manufacturing stage at which the trigger is introduced; assessing whether other vaccines could lead to the same syndrome; and determining the implications for the overall protection provided by the immunization. It is hoped to study three groups of subjects from British Columbia and Quebec: those immunized who experienced the reaction, those immunized who did not, and a group of non-immunized subjects. Skin tests will be carried out with the implicated as well as some non-implicated products. Subjects with positive reactions will undergo skin biopsy to determine the cell type and immunohistologic characteristics.

Dr. Greg Hammond, of Manitoba Health, described the oculo-respiratory syndrome from the perspective of the recommendations developed at a November conference on vaccine safety, held in Montreal. Vaccine safety is one of the five components of a National Immunization Strategy, and the conference recommendations will be forwarded to the Conference of Federal/Provincial/Territorial Deputy Ministers of Health. The recommendations can be

grouped into those involving surveillance, infrastructure, public health action, communication, and research. Dr. Hammond's analysis showed that although reaction to the outbreak was swift, there were several gaps in the current resources available to deal with it. It is hoped that these limitations will be addressed with the further development of the Strategy.

Closing Remarks

Dr. Robert McMurtry

Visiting Assistant Deputy Minister of Health, Population and Public Health Branch, Health Canada

Dr. McMurtry spoke from personal recollection of the fears of disease before the vaccine era: almost everyone had a family member/friend with polio or knew of someone afflicted with the disease. He could readily understand, now, how conference participants and those people committed to the benefits of immunization must be baffled in the face of unsubstantiated attacks on this most successful of public health measures. The question of why we are having to re-defend what appears to be a very fundamental principle — the success of immunization programs — is difficult to answer.

Health literacy, a fundamental knowledge and understanding of what keeps us healthy, may be part of the answer. This conference's emphasis on education is completely fitting in this respect. Accountability is another facet. A record of vaccinations, immunization registries, and accountability by individual physicians' of their immunization practices are all important elements of this. Third, the vast proportion of health care resources goes towards the restoration of health once people become ill, but an affordable, publicly funded health care system in Canada must switch to a proactive rather than a reactive focus: it must get upstream.

Dr. McMurtry thanked everyone for their dedicated work in the field of immunization and their participation at this conference.