Health Canada Santé Canada

Update: Vaccine-Preventable Diseases

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Current News

Varicella-Zoster Virus Disease and Epidemiology: Seeking Better Control Strategies – Part 1

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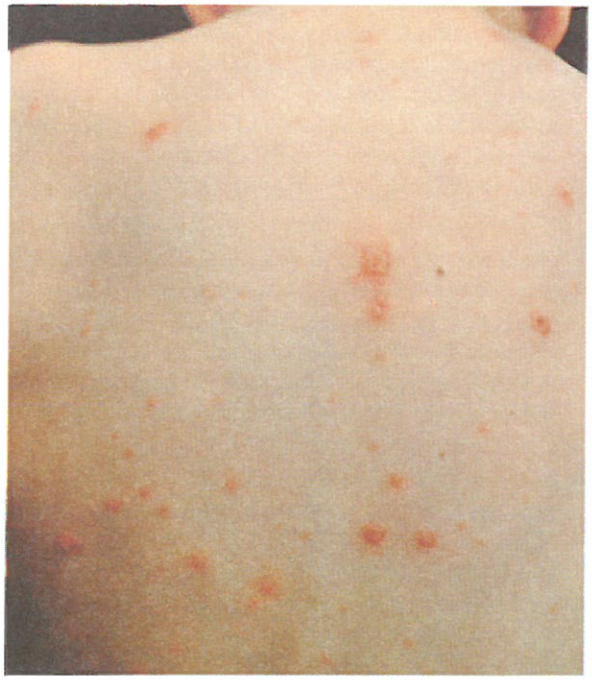
Introduction

The purpose of this two-part series is to review strategies for the control of varicella-zoster virus (VZV) infection and ongoing related public health discussions in Canada. This part focuses on the clinical and epidemiological description of varicella-zoster virus disease and summarizes the epidemiological data available through routine national surveillance in Canada. Part 2, to be published in the next issue of the *Update*, will review strategies for control of VZV infection, including those used in countries where a licensed vaccine is available, as well as highlight developments in Canada for introducing a control strategy.

Historical Perspective and Clinical Features

It is now well recognized that VZV causes two clinical diseases; varicella (chickenpox) and zoster (shingles). In early medical literature, zoster was described as an independent of varicella while the latter was often confused with smallpox until the 1760s when the clinical differentiation between smallpox and chickenpox was made[1]. As recently as 1940, it was taught at Harvard University that zoster and chickenpox were distinct and unrelated[2]. Following its concurrent isolation from patients with varicella and zoster, by Thomas Weller and his colleagues, VZV was definitively described in 1958 as the etiological agent for the two clinical entities[1,2].

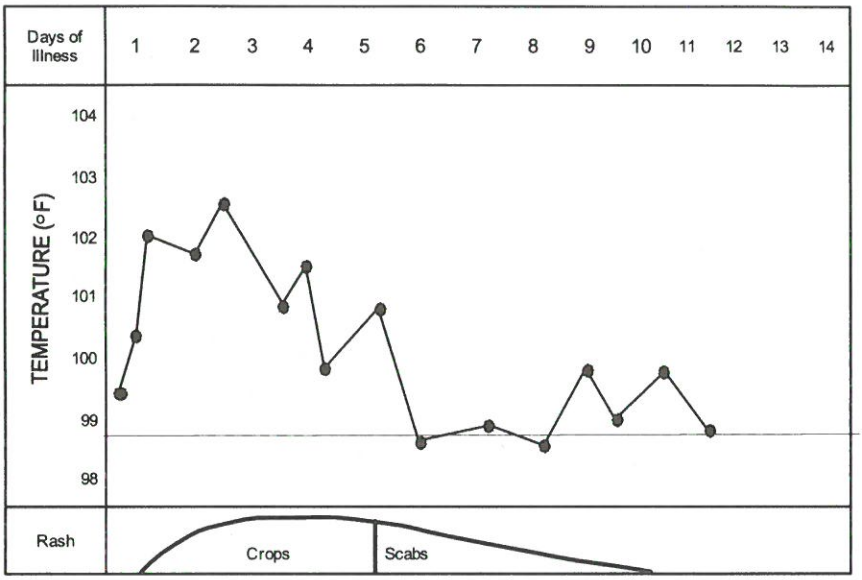
Varicella is a highly contagious disease caused by primary VZV infection and characterized by a short or absent prodromal phase, followed by fever and a characteristic pruritic rash. Figure 1 illustrates the typical clinical course of varicella. The rash appears in crops, progressing rapidly from macules to papules, vesicles, pustules and eventually to crusted lesions. Typically, three successive crops of lesions, ranging between 250 and 500 lesions in total, appear over a 3-day period thus, a combination of all five



Typically, the chickenpox rash appears in successive crops of lesions which progress rapidly from macules to papules, vesicles, pustules and finally to scabs; clinical presentation often includes a mix of the different types of lesions. Courtesy of Centers for Disease Control and Prevention, Atlanta, Georgia.

Canada

Figure 1
Schematic diagram illustrating the typical clinical course of chickenpox



The figure is reproduced with permission from Krugman S, Katz SL, Gershon AA, Wilfert CM eds. *Infectious Diseases of Children*, 9th ed., St. Louis, Missouri: Mosby Year Book Inc, 1992.

Types of lesions may present during the peak of the clinical phase[1,3]. The rash is centrally distributed with lesions concentrated on the trunk, scalp and face. Diagnosis of varicella can be made clinically by the characteristic rash and epidemiological factors, such as a history of susceptibility and known exposure to a person with varicella or zoster. Second attacks may occur but are unusual and mostly mild[3].

The virus is spread by airborne droplets and by direct contact with respiratory secretions or vesicular fluid, with an incubation period averaging 14 to 16 days (outside limits of 10 to 21 days)[3]. The infection is highly contagious, with infectivity highest 1 to 2 days before the onset of the rash and up to 5 days after the first crop of lesions appear or when all lesions are crusted. It is estimated that in most temperate countries, > 90% of individuals are infected by 14 years of age[4]. Secondary attack rates are estimated at 90% and 96% for susceptible household contacts[1,5,6].

Complications of chickenpox are rare in immunocompetent children, with < 2 deaths per 100,000 cases in children 1 and 14 years of age reported[1,4], while chickenpox-associated complications and deaths (up to 25 per 10,000 cases[6]) are more frequent in adults. In population-based studies in the United States (U.S.), the most common complications in hospitalized persons were secondary bacterial infections, Reye's syndrome, pneumonia and encephalitis in persons < 15 years old and pneumonia and encephalitis in those ≥15 years old[7,8]. Age-specific data for the U.S. from 1972 to 1978 show that persons aged ≥ 20 years old comprised < 2% of cases but accounted for 11.6% of varicella encephalitis and 27.6% of varicella-related deaths[9]. Similar data for 1990-1994 reported < 5% of varicella cases but 55% of varicella-related deaths in persons > 20 years of age[10]. Varicella encephalitis is associated with mortality of about 10% and up to 15% sequelae in survivors[4]. Recent reports of concurrent infection with varicella and invasive Group A *Streptococcus* provide further evidence that the risk of invasive Group A streptococcal disease increases after chickenpox[11,12]. VZV infection in immunodeficient individuals, particularly those with severe impairment of cell-mediated immunity, is often serious and potentially fatal, contrasting with the relatively benign and self-limited illness (lasting 4 to 5 days) in immunocompetent persons in younger age groups.

Zoster results from reactivation of latent VZV acquired during chickenpox. Zoster is characterized clinically by a painful, unilateral, vesicular rash in a dermatomal distribution, lasting a few days to several weeks; occasionally patients with zoster will not have a rash. Although the rash typically remains localized to one to three dermatomes, in a minority of patients it disseminates outside the dermatomal area and causes widespread lesions that resemble varicella. The factors that control whether the virus remains latent are not well understood however a low cell-mediated immunity to VZV in the presence of normal humoral immunity appears to be a necessary but insufficient setting for the development of zoster[1]. Zoster occurs more frequently in the elderly than the young, with a sharp increase in incidence at about 50 years of age, and is also more common in immunocompromised than immunocompetent persons[1]. Postherpetic neuralgia, developing at least 1 month after the onset of the zoster rash and lasting up to 1 year, is described as a dreaded complication of zoster, with severe, lancinating or boring pain. It is believed to be due, at least in part, to scarring of virus-injured nerves undergoing regeneration[1]. There is a strong correlation between postherpetic neuralgia and increasing age of zoster patients. Patients with zoster remain infectious to persons who have not had chickenpox as long as new lesions remain moist; the virus is present in skin lesions but does not appear to be carried to the respiratory tract therefore transmission is by direct contact.

Congenital varicella syndrome occurs uncommonly following maternal infection with VZV during pregnancy; it is estimated to occur in 2% of maternal varicella cases and even more rarely after maternal zoster. The clinical manifestations of congenital varicella syndrome are well documented, consisting typically of dermatomal skin scarring overlying a hypoplastic limb and a variety of neurological defects[1,3]. Infants with the syndrome may develop recurrent vesicular zoster-like skin lesions which may be the only evidence of congenital infection when maternal infection occurs late in pregnancy. Maternal varicella infection within 5 days before or 2 days after delivery greatly increases the risk of severe or fatal infection in the newborn. This is attributed to insufficient protective maternal antibodies and presumably the immaturity of cell-mediated immunity in the newborn[1,3]. The potentially fatal illness in the newborn can be avoided or mitigated by prompt passive immunization with varicella-zoster immune globulin.

Epidemiology of Chickenpox in Canada

Chickenpox was a nationally notifiable disease between 1924 and 1958 and reintroduced on the list of notifiable diseases in 1986[13]. Since 1986 however, reporting of chickenpox to the Laboratory Centre for Disease Control (LCDC) from the 12 provinces and territories has never been universal; the number of jurisdictions reporting cases between 1986 and 1998 has ranged between 8 and 10. Currently incidence data are only available for Newfoundland, Nova Scotia, New Brunswick, Prince Edward Island, Ontario, Alberta, the Yukon and the Northwest Territories, comprising 55% of the Canadian population. The mean crude annual incidence rate of varicella from 1992 to 1996 (based on reporting jurisdictions) is 240 cases per 100,000 population, ranging between 126 and 301 cases per 100,000 population (LCDC unpublished data). The actual number of cases reported annually for 1992-1996 ranged between 17,788 and 50,836; projected to the overall Canadian population the estimated mean annual incidence would be 69,200 cases. Because of the high level of contagiousness, estimates of annual varicella incidence are inferred to approximate the annual birth cohort[1]. Thus, approximately 380,000 varicella cases can be projected in Canada annually, meaning that the current level of reporting in reporting jurisdictions is < 20% of the expected number of cases.

Approximately 34% of reported cases from 1992 to 1996 were < 5 years of age, 86% < 10 years and 95% < 15 years of age. The mean annual age-specific incidence was highest in school-age children 5 to 9 years old (1,874 per 100,000 population) followed by children 1 to 4 years old (1,118 per 100,000 population) those 10 to 14 years old (384 per 100,000 population) and infants < 1 year old (367 per 100,000). The overall age distribution is similar to that reported in Canada in the mid-1980s[13] and in the U.S. for 1980-1990[6]. Physician compliance with reporting may be biased towards younger children, contributing to the higher incidence in younger age groups.

Prevention of Varicella

In Canada, the post-exposure management of varicella continues to consist of the administration of varicella-zoster immune globulin to susceptible individuals whose risk of serious morbidity or mortality is substantially increased and the use of antiviral therapies. A live attenuated Oka-strain varicella vaccine was first developed in 1974 and vaccines are licensed in Japan, Korea, several European countries and the U.S. The safety, immunogenicity and efficacy of the vaccine have all been reported as favourable in both healthy and leukemic children[6,14,15]. The post-licensure effectiveness of the U.S.-licensed varicella vaccine has been estimated as 86% against all forms of varicella and 100% against moderate-to-severe disease[15]. There is currently no licensed vaccine in Canada. LCDC plans to hold a consensus conference in collaboration with various public health partners in early 1999 to discuss control strategies for varicella in Canada. It is also expected that the results of cost-benefit analyses of routine varicella vaccination in the Canadian health care system will be available by early 1999.

Public Health Significance

The burden associated with varicella and zoster in Canada have not been well documented in the published literature. Childhood chickenpox is often associated with school absence for the child as well as loss of work days (and lost productivity) for primary caregivers. One study in the U.S. reported lost work days for two-thirds of working mothers (average of 2.5 days) and one-third of working fathers (average of 0.8 day) during a 12-month period[16]. Lost work days are even more prolonged with adult chickenpox because of more severe illness and the likelihood of hospitalizations for complications. Uncomplicated cases of varicella or zoster can also lead to work loss for susceptible or infected health care workers who present a danger to immunocompromised patients; furloughing of such employees can be a real strain on health care and hospital budgets. Additional health care costs to individuals or society accrue from hospitalizations for complicated cases. Finally, cases of congenital varicella syndrome, while rare, can be associated with prohibitive lifetime costs. All of these factors add to the total burden of VZV which may be substantially reduced if disease incidence and morbidity can be reduced through vaccination.

In a historical and clinical review paper on varicella published in 1996, Thomas Weller, who with his colleagues first isolated VZV noted[2]: "VZV can no longer be classified as producing a benign disease. As we discuss indications and the need for varicella vaccine, the increasing importance of the illnesses produced by this reclusive virus per se constitute a persuasive argument for its use."

This observation may be particularly relevant to the Canadian public health community as we debate the potential for introducing routine vaccination against varicella. Whether a routine vaccination program will be introduced and what the targeted population will be for a publicly funded program will be influenced not only by vaccine licensure but also by a number of the usual considerations for implementation of public health programs; desired program objectives, benefits and risks of the vaccination program, program costs in relation to benefits, and competing budgets for introducing or expanding other vaccination and public health programs. The second article in this series will highlight some of the arguments for and against introducing routine varicella vaccination (including vaccine effectiveness,

vaccine safety and cost-benefit considerations) based on the experience of other countries.

Acknowledgements

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Editorial Note

Additional epidemiological data are available for cases hospitalized in 11 paediatric hospitals which comprise the IMPACT (Immunization Monitoring Program ACTive) surveillance system and are due to be published by the IMPACT investigators. As well, a number of studies on the epidemiology of VZV infections and their public health impact in Canada are ongoing and will be a valuable source of further information. The editors take this opportunity to invite and encourage readers to share information on varicella epidemiology or control strategies. Submission of preliminary or final reports on research studies as well as discussion papers to the *Update* are welcome.

References

1. Takahashi M, Gershon AA. *Varicella Vaccine.* In: Plotkin SA, Mortimer EA, eds. *Vaccines*. 2nd ed., Philadelphia: W.B. Saunders Company, 1994:387:417.
2. Weller TH. *Varicella: historical perspective and clinical overview.* J Infect Dis 1996;174(Suppl 3):S306-9.
3. Gershon AA, LaRussa P. *Varicella-zoster virus infections.* In: Krugman S, Katz SL, Gershon AA, Wilfert CM, eds. *Infectious Diseases of Children*, 9th ed., St. Louis, Missouri: Mosby Year Book Inc, 1992:587-614.
4. Fairley CK, Miller E. *Varicella-zoster virus epidemiology – a changing scene?* J Infect Dis 1996;174(Suppl 3):S314-19.
5. Tarlow MJ, Walters S. *Chickenpox in childhood – a review prepared for the UK Advisory Group on chickenpox on behalf of the British Society for the Study of Infection.* J Infect 1998;36(Suppl 1):39-47
6. CDC. *Prevention of varicella – recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 1996;45(RR-11):1-36
7. Guess HA, Broughton DD, Melton III LJ et al. *Population-based studies of varicella complications.* Pediatrics 1986;78(Suppl):723-27.
8. Choo PW, Donahue JG, Manson JE, et al. *The epidemiology of varicella and its complications.* J Infect Dis 1995;172:706-12.
9. Preblud SR. *Age-specific risks of varicella complications.* Pediatrics 1981;68:14-7.
10. Watson B, Goodnow K, Levenson R et al. *Varicella-related deaths among adults – United States, 1997.* MMWR 1997;46:409-12.
11. Davies HD, McGeer A, Schwartz B et al. *Invasive group A Streptococcal infections in Ontario, Canada.* N Engl J Med 1996;335:547-54.
12. Barry MA, Matthews K, Tormey P. *Outbreak of invasive Group A Streptococcus associated with varicella in a childcare center – Boston, Massachusetts, 1997.* MMWR 1997;46:944-48.
13. Varughese PV. *Chickenpox in Canada, 1924-87.* CMAJ 1988;138:133-34.
14. Asano Y, Suga S, Yoshikawa T et al. *Experience and reason: twenty-year follow-up of protective immunity of the Oka-strain live varicella vaccine.* Pediatrics 1994;94:524-26.
15. Izurieta HS, Strebel PM, Blake PA. *Postlicensure effectiveness of varicella vaccine during an outbreak in a child care center.* JAMA 1997;278:1495-99.
16. Lieu TA, Black SB, Rieser N et al. *The cost of childhood chickenpox: parents' perspective.* Pediatr Infect Dis J 1994;13:173-7.

Maintaining Public Trust in Immunization

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In this installment of the *Vaccine Safety Notes*, we are reprinting with permission, a speech delivered on July 21, 1998 during the opening plenary of the U.S. National Immunization Conference held in Atlanta, Georgia. It was given by the Honorable Dr. Louis W. Sullivan, President of the Morehouse School of Medicine in Georgia and former Secretary of the U.S. Department of Health and Human Services (HHS). As head of HHS, Dr. Sullivan managed the Federal agency responsible for the major health, welfare, food and drug safety, medical research and income security programs serving the U.S. population.

Dr. Sullivan is also co-chair of the Vaccine Initiative, along with Dr. Samuel Katz, who is the Wilburt Cornell Davidson Professor and Chairman emeritus of Pediatrics at Duke University and has chaired the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. This initiative, just underway, is sponsored by the Infectious Diseases Society of America and the Pediatric Infectious Diseases Society. It is designed, through surveys and studies of the public's perception of the risks and benefits of immunization, to ensure that public dialogue on immunization progresses with adequate information. Its goals will include public and media education and the identification of areas that require more scientific attention.

As expected, these remarks are focused on the current situation in the U.S. However the messages are clearly applicable to the progressing vaccine safety climate in Canada. We can all learn from these valuable and vital lessons.

"Maintaining the Public's Trust in Immunization"

Dr. Louis W. Sullivan

I'm honored to be with you this morning to help kick off this exciting and important conference.

During the next several days you will be reminded, many times of the progress, that we have made through vaccination in the prevention and control of infectious diseases. As this audience knows better than any, vaccine-preventable diseases are at an all time low level in the United States – and in many areas of the world.

It is the most remarkable public health success story of this century. You in the fields of public health and immunization, your colleagues and predecessors are to be credited and thanked for helping to write this story.

But the story is not over. We have many more chapters ahead. There is still a long way to go before we reach the happy ending we seek – the total elimination of all vaccine-preventable diseases.

We must continue to do everything we can to knock down the barriers that prevent access to immunizations. If the issue is education, we must address it through outreach programs. If the issue is convenience, we must provide early morning or after hours clinics, including nights and weekends. If the problem is cost, we must reduce the cost of, or improve access to vaccines for those that cannot afford them.

At the same time we face another challenge that is more subtle, but equally or even more important – ***to maintain and strengthen the public's trust in vaccines and in our immunization programs***. Not only is this critical to the continued success in our fight against infectious diseases, but to all of public health. Our immunization programs are the most visible public health programs that we have. When we think of public health, immunization is often the first thing that comes to mind.

It is the ultimate irony that as we celebrate the prevention of epidemics of diseases, that just a few generations ago sent fears through the community – meningitis, polio, diphtheria, congenital rubella, measles – we must also acknowledge growing misconception that vaccines cause more harm than good. Imagine!

We are in danger of becoming a victim of our own success. As these serious diseases fade from memory, their threat is no longer perceived as real. At the same time, anti-vaccine forces, fueled by the media and greatly empowered by the new global information age, are focusing public attention on the risks, both real and perceived, rather than the enormous benefits of immunization.

Many of our citizens can't remember seeing a child with measles or polio, but they are constantly reading and hearing about the adverse reactions linked to the vaccines that have nearly vanquished these threats in the United States.

The diseases are seldom in the news; but stories of adverse reactions to vaccines are. This is creating public concerns about the vaccines and a climate for the erosion of public trust, confidence and interest in immunization.

Like a clinician taking a history, we cannot ignore these concerns. If we do, we are likely to lose the confidence of our patients and they are likely to question all that we do. To extend the metaphor, many may choose to find another doctor. Rather, we need to listen to the concerns and take the time to discuss them.

As a colleague explained: "If parents have no fear of vaccine, but fear of disease, the argument in favor of vaccination is clear-cut. If they have no fear of vaccine, but also no fear of disease, there may be inertia. When they have no fear of disease, but fear of vaccines, parents are likely to refuse immunization."

It is a quirk of history that the decline in vaccine-preventable diseases has coincided with the explosion in information technology and communications. Anyone with a computer and a modem can have a voice on the Internet and a competitive media environment is constantly trying to beat the competition in the race to

be first to announce a story. As a result, questions and concerns that we fail to address are taken to another platform and another level.

Reports in the lay press question the safety of routine immuni-zation, alarming parents with unsupported accounts of the dangers of vaccines and affording as much credence to unsubstantiated hypotheses as they do to the weight of the scientific data. Over the past several months, one major national television network broadcast a feature piece that linked diabetes to childhood immunizations

On another, the unfounded hypothesis that links multiple sclerosis to the receipt of the hepatitis B vaccine has also rippled around the country as "news."

Unfortunately, the prevention of more disease isn't as newsworthy or sexy to the media, as a claim that something we thought was good might not be. What percentage of the United States population knows that smallpox was eradicated over 20 years ago?; or that last year only 135 cases of measles were reported in the U.S., compared to the 3-4 million cases that occurred before vaccinations?; or that we are on the verge of eradicating polio from the planet by the end of the millennium?

Yes, success is short lived.

While we must not lose our vigilance for the use of vaccines, we must not allow our dedication to this cause to interfere with the goal itself. There are indications that it might.

- I was the Secretary of the Department of Health and Human Services during the measles epidemic in 1989-1991. During these 3 years over 55,000 cases were reported and there were more than 11,000 hospitalizations and 123 measles-related deaths. Ninety percent of the fatal cases had no history of vaccinations.
- Earlier this month, the *San Francisco Chronicle* reported two infants that died from pertussis and noted a four-fold rise in pertussis cases in the Bay area, largely in a community where "as many as half the schoolchildren are unvaccinated at the insistence of their parents." Imagine!

These issues are not unique to the United States.

- An article in the *Economist* magazine in April of this year reported an upsurge in parental resistance and a decline in the acceptance of the MMR vaccine following major news stories in England that falsely linked this vaccine to inflammatory bowel disease and autism.
- Earlier this year, my colleague, Dr. Gene Gangarosa of Emory University published an article in the *Lancet* [1] that took a global perspective and described the impact of anti-vaccination movements on pertussis control. He concluded, "pertussis incidence was 10 to 100 times lower in countries where high coverage was maintained than in countries where immunization programs were compromised by anti-vaccine movements."

Indeed we have entered a new era. With the decline in disease, we must improve our efforts to respond to concerns about our vaccines and all that we know about their safety and effectiveness. We must also improve our effort to communicate all that we know about the value of vaccines to individuals and to the community at large. I'm afraid that many of us have not put as much energy toward listening to and answering the questions of our patients as we have in reaching the goals that we have attained.

This is the era of communication. Therefore, we must ensure that we do more than just providing the information about the risks and benefits of our vaccines. We must do what we can to better understand the nature of these concerns.

With this in mind, I want to tell you about a new effort we hope will help to put the benefits and risks of vaccines back into perspective. I am proud to have been appointed as a co-chair, along with my distinguished colleague Dr. Samuel Katz of Duke University, of the Vaccine Initiative. This is a special project of the Infectious Diseases Society of American in conjunction with the Pediatric Infectious Diseases Society.

Recognizing that:

1) Immunization advocates currently have a "low share of voice" with the public and the media;

2) The public dialogue is proceeding without adequate regard for the credibility of the source and,

3) The facts about immunization are complex and need to be simplified to make good decisions;

the goal of this Initiative is to communicate the value of vaccines to health care providers, parents and the public. In this way we reinforce our commitment to the immunization of infants, children and adults as the optimal strategy for preventing infectious diseases in individuals and the community. By enhancing the understanding of the benefits of immunization we believe this effort will increase support for compliance with recommended schedules. We also hope that this effort will preempt legislative efforts that may inadvertently harm the public's health.

We are beginning with a research project to better understand the public's perceptions about the benefits and risks of immunization and a national survey to quantify the extent of this concern. We also will engage both the press and policymakers to make them aware of the issues and the scientific basis of our immunization policies. We will make ourselves available to discuss concerns about vaccines when they arise. When we identify areas in which the science is lacking, we will push for the best science to provide the best information. Finally, we hope to develop an alliance with our many partners, many of you that are here today, to help you to better communicate with your many constituents.

Our task is a formidable one that no one can do alone. We look forward to working together with you not only to continue to expand our victory over infectious diseases but also to maintain and strengthen the public's confidence in our immunization and public health programs.

As I said earlier, immunization is a success story that is not yet over. As we look toward the new millennium, the total eradication of vaccine-preventable diseases is a realistic goal. Together we can write that happy ending to our story. Thank you.

Reference

1. Gangarosa EJ, Galazka AM, Wolfe CR et al. *Impact of anti-vaccine movements on pertussis control: the untold story.* Lancet 1998;351:356-61.

Measles Virus: Standardization of genotyping nomenclature

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The purpose of this article is to outline the new genotypic classification of measles virus isolates.

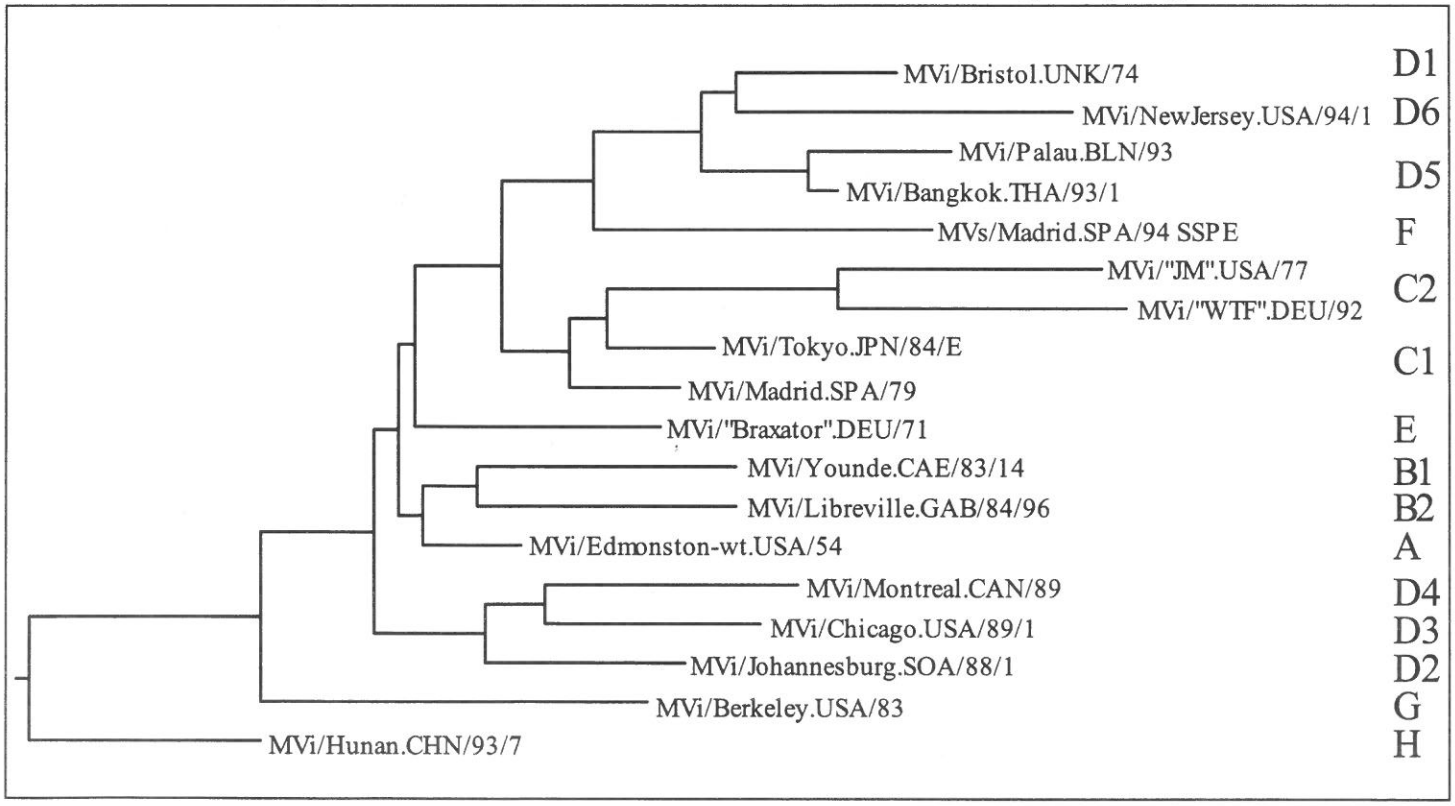
The World Health Organization (WHO) may be looking towards global elimination of measles with the progress of the Pan American Health Organization (PAHO) led measles elimination effort in the Americas[1]. Virus isolation and genotyping for the purposes of molecular surveillance has proven to be an important aspect of the PAHO measles elimination program[2]. There have been numerous research publications describing the genotyping of wild-type measles virus isolates, but there has not been a uniform analysis protocol for describing these isolates. Therefore, WHO held a meeting in May 1998 to establish a standard analysis protocol and nomenclature for describing wild-type measles virus isolates. The resulting guidelines for naming wild-type measles virus isolates have been published[3] and are summarized here.

The gene encoding the hemagglutinin protein (H-gene) and the gene encoding the COOH-terminus of the nucleoprotein (N-gene) are the two most variable regions of the measles virus genome showing up to 7% and 12% nucleotide variability respectively. Distinct genetic groups of wild-type measles viruses can be determined from analysis of either of these regions. Nucleotide sequence analysis of the 450 nucleotide COOH-terminal coding region of the N-gene and the entire 1854 nucleotide H-gene is recommended. The term genotype is the basic taxonomic unit while the term clade indicates the relationship between the genotypes (figure 1). At the present time, there are 15 genotypes (A, B1, B2, etc) grouped into 8 clades (A, B, C, D, etc). Reference strains for each genotype have been chosen based on the earliest isolate of a particular genotype. Table 1 lists the genotype reference strains as well as previous genotypic designations.

The naming of measles virus isolates is to be standardized as follows:

e.g., MVi/NewYork.USA/03.98/2 [D2]
MVi = measles virus isolate or
MVs = measles virus sequence determined from RNA extracted from clinical material
NewYork.USA = location of isolation including three letter WHO designation country code
03.98 = date of isolation consisting of epidemiological week and year
2 = isolate number if more than 1 per week
[D2] = genotype

Figure 1
Phylogenetic tree showing measles virus reference strains and the designated genotypes



additional designations such as SSPE (subacute sclerosing panencephalitis) or MIBE (measles inclusion body encephalitis) can also be added.

Recent Canadian isolates from 1996 to 1998 belong to genotypes C2, D5 and D6. Genotypes C2 and D6 are commonly found circulating in Europe and D5 is commonly found in Japan[2].

Table 1: Measles Virus Reference Strains

Genotype	Previous Designations	Reference Strains (MVi)
A	1, A	Edmonston-wt.USA/54
B1	6, H, B1, B2	Younde.CAE/83/14
B2	6	Libreville.GAB/84/96
C1	C1, A	Tokyo.JPN/84/E, Madrid.SPA/79
C2	5, C2, II, C	"JM".USA/77, "WTF".DEU/92
D1	D1, I	Bristol.UNK/74 (MVP)
D2	D5	Johannesburg.SOA/88/1
D3	2, type2, B, D2, III	Chicago.USA/89/1
D4	7, I	Montreal.CAN/89
D5	3, type1, C, B, D4, III	Palau.BLN/93, Bangkok.THA/93/1
D6	4, D3, I	NewJersey.USA/94/1
E	E	"Braxator".DEU/71
F	F	MVs/Madrid.SPA/94 SSPE
G	G	Berkeley.USA/83
H	8	Hunan.CHN/93/7

References

1. CDC. *Advances in global measles control and elimination: summary of the 1997 international meeting*. MMWR 1998;47:1-23.
2. Bellini WJ, Rota PA. *Genetic diversity of wild-type measles viruses: implications for global measles elimination programs*. Emerg Infect Dis 1998;4:29-35.
3. WHO. *Standardization of the nomenclature for describing the genetic characteristics of wild-type measles viruses*. Weekly Epidemiological Record 1998;73:265-69.

International Notes

Varicella-Related Deaths Among Adults – United States, 1997

(Adapted from MMWR, Vol 46, No 19, 1997)

During January-April 1997, state health departments reported three fatal cases of varicella (chickenpox) to the Centers for Disease Control and Prevention. All three cases occurred in young adult women who were unvaccinated and susceptible to varicella and who were infected by exposure to unvaccinated preschool-aged children with typical cases of varicella. This report summarizes these three cases, which indicate that preventable varicella-related deaths continue to occur in the United States.

Case 1

On January 19, 1997, a 23-year-old woman in good health had onset of a classic varicella rash. In early January, her 2- and 5-year-old unvaccinated children had had varicella. On January 22, she had onset of shortness of breath and hemoptysis. When she was admitted to a local hospital on January 23, a chest radiograph indicated diffuse alveolar density consistent with varicella pneumonia, and treatment was initiated with oxygen and intravenous acyclovir. Her condition worsened, and she required intubation several hours after admission. Because of increasing respiratory distress, she was transferred to a referral hospital where treatment continued with oxygen, antibiotics, and intravenous acyclovir. On January 31, her rash became hemorrhagic, and she developed disseminated intravascular coagulation (DIC) and renal failure, followed by progression to multiple system failure; she died on February 2. Varicella-zoster virus was cultured from skin lesions and from a tracheal aspirate.

Case 2

On March 11, 1997, a 25-year-old woman in good health had onset of a classic varicella rash, fever, and headache. Her 4-year-old unvaccinated child had had onset of a varicella rash on February 23. On March 12, the woman had onset of cough, and on March 13, shortness of breath. On March 14, she sought care

at a local emergency department (ED) because of increasing respiratory difficulty and confusion. Chest radiograph indicated bilateral infiltrates consistent with varicella pneumonia, and arterial blood gases indicated hypoxemia. Varicella encephalitis and pneumonia were diagnosed; she was admitted to the hospital, and treatment was initiated with oxygen and intravenous acyclovir. Four hours after admission, her respiratory difficulty increased, and she required intubation. On March 15, a computerized tomography of the brain revealed severe, diffuse cerebral edema, and she developed renal failure and coma. On March 16, she was transferred to a referral hospital for renal dialysis; an electroencephalogram indicated absence of electrical brain activity, and repeat chest radiographs indicated diffuse infiltrates. She died on March 17.

Case 3

On April 3, 1997, a 32-year-old woman with Crohn's disease sought medical evaluation at a local ED because of an onset of abdominal and back pain. On March 7, therapy had been initiated with 40 mg prednisone daily for an exacerbation of her Crohn's disease. By April 3, her steroid therapy had been tapered to 20 mg prednisone daily. On physical examination, she had mild, generalized abdominal tenderness with no specific signs or abdominal guarding. She was afebrile, and a white blood cell (WBC) count was normal. A benign abdominal syndrome was presumptively diagnosed, and she was discharged. Her symptoms persisted, and on April 4, she sought medical evaluation at the office of her health-care provider. Findings on physical examination were unchanged. Although an abdominal radiograph, abdominal and pelvic ultrasounds, and a WBC count were normal, because of her underlying medical condition, she was referred for surgical consultation. On April 5, the abdominal pain persisted, and she returned to the ED for evaluation. A WBC count was 15,000/mm^3 (normal: 3200-9800/mm^3), and she was admitted to the hospital. Diagnoses of colitis and ileitis with possible perforation and intraabdominal abscess were considered, and treatment was initiated with broad-spectrum antibiotics. On physical examination, a maculopapular, vesicular rash with crusted lesions was observed on her trunk, head, and neck. Varicella was presumptively diagnosed, and she was placed in isolation. The patient reported that she had had onset of a mild macular, nonpruritic rash on her back on April 3 and that she had been exposed on March 12 and 13 to her 4-year-old unvaccinated niece with varicella. On April 6, the vesicles became hemorrhagic, and she began bleeding from intravenous sites. She rapidly developed hypotension and DIC, and died from shock the same day. On autopsy, evidence of viral inclusion bodies in multiple organs was consistent with varicella, and varicella was determined to be the cause of death.

Varicella-Related Deaths Among Children – United States, 1997

(Adapted from CCDR 1998;24:108-11)

During the first quarter of 1998, the Texas Department of Health and the Iowa Department of Public Health notified the United States Centers for Disease Control and Prevention of three fatal cases of varicella (chickenpox) that occurred in children during 1997. All three children were unvaccinated. Two children contracted chickenpox from unvaccinated siblings, and the mode of exposure was unknown for the third. This report summarizes these cases and indicates that varicella-related deaths continue to occur among children in the United States despite the availability of vaccine and recommendations for its use in all susceptible children[1,2].

Case 1

On February 28, 1997, a previously healthy, unvaccinated 21-month-old boy developed a typical varicella rash. He had no reported exposure to varicella. On March 1, he was taken to a local emergency department (ED) with a high fever and was started on oral acetaminophen and diphenhydramine. On March 3, his primary-care physician prescribed oral acyclovir. On March 4, his mother noted a new petechial-like rash. The next morning, his primary-care physician noted lethargy, a purpuric rash, and poor perfusion. He was transferred to a local ED. Fluid resuscitation and intravenous ceftriaxone were initiated, but the child continued to deteriorate rapidly, requiring intubation, mechanical ventilation, and inotropic support with dopamine. Blood cultures were negative for bacterial pathogens. Laboratory tests indicated disseminated intravascular coagulation and severe dehydration. Approximately 1½ hours after arrival at the ED, he was transported to a tertiary-care centre. Within 10 minutes of arrival, he suffered cardiac arrest and died. The death was attributed to varicella with hemorrhagic complications.

Case 2

On December 21, 1997, a 5-year-old unvaccinated boy with a history of asthma was taken to a local ED with a fever of 40.3° C and a typical varicella rash in multiple stages of healing. The child was treated with antipyretic and antipruritic medications, and discharged.

That evening, the boy developed mild dyspnea and was treated at home for a presumed asthma attack with metered-dose inhalers and one dose of oral prednisone. He returned to the ED on December 22, with shortness of breath and a 4-hour history of abdominal and leg pain. On presentation to the ED, one of the patient's siblings had active varicella and another had recently recovered from varicella. Physicial examination revealed numerous chickenpox lesions, one of which appeared infected. He was tachypneic, and his extremities were mottled consistent with peripheral septic emboli. Chest and abdominal radiographs revealed a right pleural effusion, pneumonia, and mild ileus. Thoracostomy produced pleural fluid containing gram-positive cocci, confirmed 8 hours later to be group A *Streptococcus* (GAS). A peripheral blood sample revealed gram-positive cocci. He was admitted to the hospital and treated with intravenous ceftriaxone, nafcillin, and acyclovir.

After admission, his breathing became labored and his extremities increasingly mottled. He rapidly developed hypotension, obtundation, and bradycardia. Despite efforts at cardiopulmonary resuscitation, the child died 5 hours after arriving at the ED. A post-mortem examination attributed the death to GAS septicemia, pneumonia, and pleural effusion, complicating varicella infection.

Case 3

On December 14, 1996, a previously healthy, unvaccinated 23-month-old boy developed fever and a typical varicella rash. Approximately 1 to 2 weeks earlier, his unvaccinated 4-year-old sibling had contracted varicella. He was taken to his physician on December 17, because of persistent fever and cellulitis of the left foot, and he was hospitalized on December 19, for failure to improve on an unspecified outpatient antibiotic regimen. Because his condition deteriorated despite intravenous methicillin and ceftriaxone, he was transferred to a regional hospital on December 21. Sepsis, possible viral meningoencephalitis, and mild pleural effusion were diagnosed. A cerebrospinal fluid examination revealed lymphocytic pleocytosis, and blood and urine cultures grew penicillin-resistant *Staphylococcus aureus*. Antibiotics were changed to nafcillin and gentamycin, and intravenous acyclovir was added on December 23. On December 24, the child developed an aortic insufficiency murmur, and an echocardiogram revealed a 9×9 mm vegetation on the aortic valve, consistent with bacterial endocarditis. Serial echocardiograms displayed growth of the vegetation and development of a pericardial effusion. He was transferred to a cardiac surgery centre on December 26. While awaiting surgery, he developed refractive heart failure secondary to staphylococcal endocarditis. He became incoherent, probably secondary to a major embolic neurologic event, and died on January 8, 1997.

Editorial Note: The original reports on varicella-related deaths among adults and children in the United States, 1997, provide further information, in an editorial note, on the epidemiology of varicella in the United States. As well, the editor(s) include a discussion of the recommendations for the use of varicella vaccine (licensed in the United States since March 1995) and other recommended strategies for preventing varicella in the United States.

Measles: Argentina, Bolivia

Infectious Diseases News Brief (week ending September 4, 1998) prepared by the Division of Disease Surveillance, Bureau of Infectious Diseases, LCDC (adapted from the PAHO web page)

The Pan American Health Organization's (PAHO) campaign to eliminate measles from the Americas by the year 2000 has cut the number of cases from 250,000 in 1990 to 2,109 in 1996. Accordingly, PAHO has issued an alert on measles epidemics in Argentina and Bolivia, noting that Argentina has more than 3,000 confirmed cases, mostly in Buenos Aires. So far, 11 children have died in Argentina. In Bolivia, the epidemic began in the area of Yacuiba, on the border with Argentina in May, and 111 cases have been confirmed, with no deaths reported. In both countries, those most severely affected have been infants and children ≤ 4 years of age. Brazil, the site of a large outbreak last year with more than 51,000 cases, has reported 1,093 cases this year. Thus far in 1998, the United States has reported 47 cases, Canada 7, Colombia 7, Venezuela 3, Paraguay 2, and Guatemala 1. PAHO is recommending that all countries take the following measures: 1) intensify vaccination efforts, especially where there are high numbers of children susceptible to measles; 2) strengthen surveillance for early detection of measles cases and rapidly investigate any suspected cases; 3) strengthen their laboratories' capacity to handle measles samples for serology and virus isolation; and 4) obtain political commitment and resources to carry out vaccination programs.

Vaccine-Preventable Diseases Summary

Cumulative number of cases reported* for selected vaccine-preventable diseases, Canada
January 1996 – August 1998

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

Disease	1996	1997	1998
	Jan-Aug	Jan-Aug	Jan-Aug
Diphtheria	0	1	1
Haemophilus influenzae type b	28	37	30
Measles§	313	556	14
Mumps	230	213	67
Rubella¶	174	3,410	60
Congenital rubella syndrome	0	1	1
Pertussis	2,750	2,225	2,709
Paralytic poliomyelitis	0	0	0
Tetanus	3	2	1

* Based on cases reported to the Notifiable Disease Reporting System, Division of Disease Surveillance, LCDC; 1997 and 1998 data are provisional. Also cumulative totals for the current year to date may not represent national totals due to incomplete reports from the provinces/territories.

§ Measles data are based on cases reported to the Enhanced Measles Surveillance System, Division of Immunization. The majority of cases in 1997 were reported from British Columbia (47%) and Alberta (43%).

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

Errata

- In the last issue of the *Update: Vaccine-Preventable Diseases* (Vol 6 No 3), there was an error in the fax number provided for the Division of Immunization with the announcement on the Canadian National Report on Immunization. **The announcement should have read:** Copies of the Canadian National Report on Immunization, 1997, may be obtained from the Division of Immunization, LCDC, Tel.: (613) 957-1340, **Fax: (613) 952-7948.**

- We also wish to bring to our readers' attention that the third column of the table for Vaccine-Preventable Diseases Summary was labelled wrongly in the French part of the last issue of the *Update: Vaccine-Preventable Diseases* (Vol 6 No 3). **The correct column label is 1998.**

Any inconvenience caused by these errors is regretted.

Announcement

3rd Canadian National Immunization Conference

Partnerships for Health Through Immunization

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

Organized By

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

Objectives

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

To access conference-related information, visit the Conference Website at:

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

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

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

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

Submissions of pertinent reports/epi notes are welcome and the success of this endeavor depends upon the readers' interest and cooperation. Priority for inclusion in the newsletter is determined by the article's relevancy. This is not a formal publication, and the views and interpretation may not necessarily reflect Health Canada's position. Distribution is free of charge. Anyone wishing to receive a copy on a regular basis should contact the Division of Immunization, Bureau of Infectious Diseases, LCDC, Ottawa, Ontario, K1A 0L2; telephone (613) 957-1340; FAX (613) 952-7948. This publication can also be accessed electronically via Internet using a Web browser at http://www.hc-sc.gc.ca/hpb/lcdc

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