Until recently, varicella (chickenpox) was one of many prevalent infectious diseases that primarily affects children who inevitably suffered its unwanted health-related consequences. In early 1995, a then-new and well tested varicella vaccine (Varivax™, Oka/Merck®) was officially licensed for use in the United States. Varivax, however, remained unlicensed for use in Canada.

In May 1999, Health Canada’s Laboratory Centre for Disease Control (LCDC) held a conference to establish control strategies for possible use of Varivax in Canada. At that conference, a domestic cost-benefit analysis was designed and reviewed for proposed universal and routine varicella vaccination throughout Canada. The final recommendation resulting from this conference was that a universal immunization program for young Canadian children should be implemented within 2 years of availability of a refrigerator-stable vaccine. With the LCDC’s recommendation and its potential implementation, the possibility of life without chickenpox could be envisioned. Or was it too good to be true?

In January 1996, Varivax was added to the recommended standard childhood immunization schedule in the United States. In 1997, a comprehensive market survey of pediatricians in the US conducted by Merck found that only two thirds were incorporating the vaccine into the recommended immunization program. The Merck survey result begs the obvious question: why did one third of pediatricians decide not to use the vaccine?

Complications of varicella zoster virus infection
Canadian data from a variety of sources suggest that, during an acute episode of varicella, about 30% to 65% of children see a physician. According to the LCDC, in 1999, specific complications occurred in only 5% to 10% of all varicella cases in otherwise healthy children. Furthermore, about 50% of these complications were secondary bacterial skin infections, such as impetigo, cellulitis, and lymphadenitis. These infections are frequently due to Staphylococcus aureus or group A β-hemolytic streptococci (GABHS). Also, otitis media occurs in up to 5% of all varicella cases. Of more serious concern are the potential secondary infections associated with GABHS, such as bacteremia, osteomyelitis, septic arthritis, endocarditis, necrotizing fasciitis, and toxic shocklike syndrome, which are rare but can occur nonetheless.

A population-based study in Ontario concurred with findings from an outbreak in a day-care centre in Boston and indicated that varicella increases risk of severe GABHS infection among previously healthy children 40- to 60-fold. Moreover, it is estimated that eliminating varicella by an effective immunization program could prevent at least 15% of cases of GABHS in otherwise healthy children.

From 1987 to 1996, the deaths of one to 16 people of all ages each year (total of 53) were attributed to varicella; children younger than 10 years old accounted for 26% of the reported deaths. Most (90%) of the children who died presented with no identifiable risk factors. Interestingly, in both the United States and Canada, varicella is currently the major cause of death due to diseases preventable by vaccines. Varicella in adults is associated with more severe prodromal symptoms, including irritability; headaches; anorexia; arthralgia; myalgia; and elevated, prolonged fever. Lesions are more abundant and deeper with a greater risk of complications, such as pneumonia, encephalitis, and death.

Immunocompromised children might develop progressive varicella, characterized by a more severe prodrome followed by widespread dissemination of varicella zoster virus (VZV). Lesions are larger, deeper, and umbilicated or hemorrhagic. Healing is delayed and associated with substantial morbidity and mortality.
Vaccine-induced immunity
Since development of the varicella vaccine by a Japanese physician in the early 1970s and its subsequent use thereafter, clinical trials conducted in Japan supported the new vaccine’s safety and immunogenicity. In 1986, the vaccine was licensed for universal use in healthy Japanese children, and shortly thereafter was used throughout Korea as well. Seroconversion was obtained at a rate of 91.5% in 8429 vaccine recipients. Only 6.9% reported relatively mild adverse effects, including fever, rash, or local reaction.

Since licensure in Japan, researchers have continued to monitor the vaccine’s long-term effectiveness, particularly as it relates to immunity waning over time. The concern is that, if immunity wanes in those vaccinated, then adults who have a higher potential for complications would consequently be susceptible to acquiring the disease. In fact, a follow-up study of 25 people 20 years after one immunization found that 100% had positive antibodies as measured by fluorescent antibody-to-membrane antigen and 100% had positive cell-mediated immunity indicated by reactions to VZV antigen skin tests. Although the number of participants was admittedly low, it was still encouraging to find that long-term immunity was possible.

Generally, the Oka/Merck vaccine has been safe and effective during its use in the US population since its licensure in 1996. The immune response, however, is approximately 10-fold lower than that acquired by natural infection.

Why the concerns about using the vaccine?
Initially, immunizations were developed to prevent deaths from life-threatening diseases, such as pertussis, rubella, and measles. Vaccinations have nearly eradicated these diseases and have, as a result, successfully saved many lives.

Some argue that implementing the varicella vaccine immunization program was driven by cost savings related to (but not exclusive to) taking time off work. Consequently, the need for a comparatively expensive intervention for a disease that is “relatively benign” can be questioned and debated.

In Canada, a recently completed multicentre study estimated the financial burden of VZV on the basis of medical and societal parameters (including cost of lost productivity and personal expenses borne by caregivers). Independent cost assessments were completed on uncomplicated cases and cases that required hospitalization. Costs were estimated to be $122.4 million or $353 per case. Of this total, 81% was apportioned to personal expenses and productivity costs, 9% to ambulatory medicine, and 10% to hospital-based medical care. Similar studies with highly comparable findings have been conducted in the United States.

One concern with the aging of immunized children pertains to the elimination of naturally circulating VZV in the environment as a result of the vaccine. Without natural, circulating VZV to boost immunity, it might become necessary to revaccinate adults. Some clinicians are concerned about compliance with immune boosting later in life. Interestingly, this same question was posed in the 1970s about immunizing children against measles, mumps, and rubella—all diseases that, like chickenpox, are more serious in adults.

Based on recent data describing trends in cell-mediated immune responses to VZV in Japan, Korea, and the United States, there is no statistically or clinically significant reason to believe that seroconversion for VZV will be any different from that which occurred with previous universal immunization programs. Researchers have seen variations in strains of VZV in different geographical locations and have raised the question about effectiveness of the Oka/Merck vaccine strain in the United States and Canada. At present, this issue is being investigated, and already, new variant forms of the vaccine are being developed to address this concern effectively.

Some health care workers and parents of young children have questioned the safety of the varicella vaccine. Well-documented reactions to the varicella vaccine have been consistently described as “mild” and include injection site reactions (20%), non–injection site rashes (3% to 5%), and low-grade fever (15%). Serious adverse effects, such as pneumonia, febrile seizures, encephalitis, anaphylaxis, and death remained extremely rare. People who become infected with VZV after immunization present with significantly milder courses of illness.

Another documented concern regarding the vaccine is its effectiveness at protecting against herpes zoster (shingles) later in life. The LCDC reports that reactivation of VZV in the form of shingles has occurred in 23 cases per 100,000 people among the adolescent and adult populations studied. The reactivation rate appears to be less frequent, however, and the disease less severe than following natural infection. The long-term effect of vaccination on shingles for those who are already vaccinated is yet to be determined.
Currently, VZV vaccine is being used in a massive research endeavour in the US veteran population older than 60 years and reporting a history of chickenpox in early life. The purpose of this investigation is to see whether a similar VZV vaccine is successful at preventing shingles in this population.13

Vaccination: just do it!
Over the past decade, epidemiologic trends in Canada reveal that, in previously healthy children, varicella-related complications are killing approximately 16 children (younger than 10 years of age) per year, and approximately 1400 children per year require hospitalization for varicella-related complications.9 These rates are sevenfold higher in infants and immunocompromised children.11 How many children will have to suffer the consequences of an apparently routine case of VZV that could have been avoided but becomes unexpectedly worse, even to the point of death?

Extensively studied, the varicella vaccine has already been planned and programmed for implementation in Canada.2 Until a refrigerator-stable vaccine becomes available, however, varicella vaccine will not be incorporated into the recommended immunization schedule in Canada, as most family practice offices cannot maintain the vaccine in the recommended frozen state.

Several key recommendations put forward in the Canada Communicable Disease Report in 19982 have not been adopted yet because of the problems of supply and storage. This results in sporadic and limited availability of the vaccine at local pharmacies. Consequently, costs for the vaccine will be reimbursed by neither the Ontario Health Insurance Plan nor private drug plans in Canada.

Many parents are opting to purchase the vaccine and are willing to assume costs and risks associated with its administration. The potential pathophysiologic problems inherent in “random” and “inconsistent administration” of the varicella vaccine, or any other vaccine for that matter, have been sufficiently described. Achieving the greatest benefits from a universal varicella vaccination program would require a comprehensive public education program dispelling “the myths” previously described and attached by some to the VZV vaccine.

It is important that further research be done on issues of duration of vaccine-induced immunity, potential interference of immune response to VZV vaccine from passively transferred antibodies, potential rare adverse events, long-term epidemiologic impact of vaccination on varicella and herpes zoster, and coverage levels to prevent emergence of susceptible cohorts of elderly people.

Because data pertaining to these issues are currently unavailable, unfounded concerns will probably be raised. It is important, however, to re-emphasize that virtually everyone in Canada will, in fact, acquire the wild VZV strain, a strain that is much more aggressive and capable of inducing more serious physiologic complications than those experienced with the milder vaccine strain. As these more serious physiologic complications can now be safely and virtually eradicated with a universal, routine varicella vaccination program, the answer to the question of whether or not to vaccinate becomes easy: just do it! ♦

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References