

Prevention of varicella in children and adolescents



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Varicella (chickenpox) is a common communicable infection of childhood characterized by a generalized pruritic papulovesicular rash, fever and malaise. In unimmunized populations, the lifetime risk of varicella is 95%, with 50% of cases occurring by five years of age and 90% by 12 years of age (1,2). Varicella may be associated with considerable morbidity, mortality and economic impact in healthy persons and in those with immunocompromising conditions. The risk of invasive group A streptococcus infection is increased 40- to 60-fold in the general population after varicella (3). Before immunization programs were established, previously well children accounted for 85% to 90% of varicella-associated hospitalizations, nearly 50% of fatal cases and 80% to 85% of physician visits (1). The Canadian Paediatric Society (CPS) supports universal immunization programs for children (4), as described by the National Advisory Committee on Immunization (1,5,6) and the National Varicella Consensus Conference (7). At the time of writing, nine provinces and two territories have routine immunization programs at 12 months of age, and some have catch-up programs. The present statement will discuss the prevention of varicella in children given reported changes in epidemiology in regions with high vaccine coverage, and the care of exposed children who have not yet received or are ineligible for the vaccine. For ease of reading, use of the word 'children' throughout this statement includes both young children and adolescents.

PREVENTION WITH ROUTINE IMMUNIZATION PROGRAMS IN CHILDHOOD

Two live, attenuated varicella vaccines are now approved and marketed in Canada (1,6). These products are refrigerator-stable and can be stored at 2°C to 8°C for several months. They are 70% to 90% effective in protecting immunized individuals from varicella of any severity and 95% effective against severe varicella (1,8). Detailed information about vaccine administration and other vaccine provider information is available in the *Canadian Immunization Guide* (8) and on the Public Health Agency of Canada Web site (<www.phac-aspc.gc.ca/im/index.html>).

In the United States, where routine childhood immunization programs began to be implemented almost 10 years ago, a dramatic reduction in disease incidence, morbidity and mortality has been observed (9-13). Outbreaks of chickenpox in immunized children, so-called 'break-through disease', do occur, but both the acuity of illness

and the infectivity of cases are diminished compared with unimmunized children. A two-dose varicella schedule is being considered in the United States for several reasons (14,15). A single-dose schedule is unlikely to achieve further control of varicella. The public health resources required to investigate outbreaks in immunized children are considerable and could be averted if better control were achieved. A combination measles-mumps-rubella-varicella vaccine may be licensed and would facilitate program implementation along with the current routine immunization schedule. Randomized, controlled trials of the two-dose schedule indicate excellent immunogenicity and fewer local and systemic adverse events compared with the one-dose schedule. In Canada, any discussion of a two-dose schedule is premature given that provinces have either a relatively new universal program or no program at all. It may be several years before the epidemiology of disease in this environment becomes clear.

Family physicians and paediatricians will continue to see chickenpox in childhood for some years because not all provinces have catch-up programs for children, and certain children are ineligible for the vaccine because of immunocompromising conditions or a history of anaphylaxis to the vaccine or a component of the vaccine (8). If exposures are identified in nonimmune children, there is still an opportunity to prevent illness and further spread of varicella. The present statement reviews available preventive interventions and makes recommendations for their use in Canadian children. It also reviews which varicella exposures are likely to be high risk for disease transmission and, therefore, warrant intervention.

When is an exposure significant?

Chickenpox is spread by large droplets from the respiratory tract, by secretions from cutaneous lesions and by the airborne route in the 48 h before the rash and early in the illness. Up to 96% of exposed, susceptible household members will develop varicella when exposed to this virus in the home (16). In evaluating the risk of varicella in an exposed person, it is first important to determine if they are immune. A history of chickenpox is considered sufficient evidence of immunity. Serological testing in healthy, vaccinated individuals is not necessary because the vaccine affords a high level of protection and commercially available tests will not identify vaccine-induced antibodies.

Physicians should inquire about the time since the exposure. The incubation period for chickenpox is eight to 21 days, and most prophylactic interventions will be most effective early after exposure.

In nonimmune patients, the following contact situations are considered significant exposures to varicella-zoster virus (VZV) (8):

- continuous household contact (living in the same dwelling);
- playing indoors for more than 1 h with a contagious case; and
- sharing the same hospital room with a contagious patient.

POSTEXPOSURE PROPHYLAXIS

Vaccine

Administration of varicella vaccine to contacts of chickenpox cases within three days, and in some instances up to five days, of exposure has been shown to be effective (17,18) and is recommended to provide individual protection and prevent further spread of disease (8). Vaccine given after this time might attenuate the illness and would not be harmful. All unimmunized children who are eligible should be offered the vaccine.

Passive immunization

During viral infection, specific antibodies enhance host defense by blocking the entry of viruses into cells, neutralizing viruses and promoting antibody-directed, cell-mediated cytotoxicity (19). Both varicella-zoster immune globulin (VZIG) and intravenous immune globulin (IVIG) may prevent or modify illness in nonimmune persons after exposure to varicella.

VZIG, prepared from human plasma with high titres of anti-VZV antibody, has been used since the 1970s to prevent varicella in nonimmune persons at risk for severe complications. It has been shown to prevent the onset of chickenpox or modify the illness if given to nonimmune persons soon after exposure (20).

Although vaccination is the most important intervention in the prevention of varicella, some children are not eligible for the current live virus vaccine because they are younger than one year of age, or because of contraindications to the vaccine. According to the *Canadian Immunization Guide* (8), the following children are eligible for VZIG to prevent severe varicella following a significant exposure:

- immunocompromised patients, including some receiving corticosteroid therapy;
- newborn infants of mothers who develop varicella during the five days before or 48 h after delivery; and
- hospitalized premature infants who are exposed during the first week of life and are less than 28 weeks gestation, or who are 28 to 37 weeks gestation and whose mothers are nonimmune (due to their history or seronegative status).

VZIG should be given as soon as possible after exposure to VZV but within 96 h for maximum efficiency. The dose is 125 units/10 kg intramuscular (IM), with 125 units as the minimum dose and 625 units as the maximum dose. Administration of VZIG prolongs the incubation period of chickenpox from 21 to 28 days. The duration of protection after one dose is three to four weeks, and re-exposures during that time are not an indication for re-dosing. The changing epidemiology of varicella in the United States subsequent to universal immunization programs has decreased the demand for VZIG. The sole North American manufacturer (Massachusetts Biologic Laboratories, USA) discontinued production of VZIG in fall 2004. The manufacturer estimates sufficient VZIG supplies, based on previous annual demand from Canada and the United States, to last through April 2006. At the time of writing, Health Canada is making efforts to secure a supply elsewhere. The CPS strongly supports efforts to secure an ongoing supply of VZIG for post-exposure prophylaxis of varicella in nonimmune children at risk for serious complications.

IVIG has titres of VZV antibody of 1:128 or greater and, because of its intravenous route of administration, results in 100% absorption. VZIG has titres of greater than 1:2048 and IM administration results in approximately 50% absorption. Although few studies have been conducted, it appears that IVIG results in VZV antibody levels similar to IM VZIG (21). It is currently recommended that patients on monthly high-dose IVIG therapy (400 mg/kg) do not need VZIG if the last dose was given three weeks or less before exposure (22). If no replacement is found for VZIG, then an alternative prophylactic intervention for nonimmune high-risk children ineligible for vaccine would be one dose of IVIG at 400 mg/kg.

Antiviral drugs

There are four randomized, double-blind, placebo-controlled trials (23) showing that acyclovir treatment within 24 h of onset of chickenpox (10 mg/kg/dose to 20 mg/kg/dose given four times daily for five to seven days) in healthy children offers modest benefits. These benefits include acceleration of rash healing by one to two days, fewer numbers of lesions, and shortened time to defervescence and of new lesion formation. In contrast, few studies support the use of acyclovir in the prophylaxis of chickenpox. There are a number of case reports (24), case series (25-27) and nonrandomized trials (28-30) in which children were given oral acyclovir up to 11 days after exposure in the index case. Because of the methodology used in these studies, one cannot ascertain with certainty whether acyclovir is an efficacious intervention. The long duration between exposure and initiation of the antiviral makes it likely that acyclovir would be acting as an early treatment during the viremic phase and before presentation of the exanthem rather than as prophylaxis. Follow-up studies of children treated with acyclovir late in the incubation period have shown that a humoral immune response can occur without clinical illness.

Treatment during the viremic phase, before rash onset, would clearly be warranted in children with immunocompromising conditions at risk for serious varicella infection (eg, cell-mediated immunodeficiency, lymphoproliferative disorders or in receipt of immunosuppressive therapy) who cannot be given VZIG. Because it is not possible to determine where an exposed immunodeficient child is in the incubation period, it would be reasonable to begin administering antivirals after exposure and continue until the incubation period is complete (up to 21 days after exposure if IVIG has not been given). Antiviral prophylaxis or early treatment is not warranted in the healthy child.

Infection control measures

In the health care setting, transmission of varicella is prevented by isolation precautions of infected individuals using routine practices and transmission-based precautions (contact and airborne). This involves placing children with chickenpox in a single room with negative air flow, using barrier precautions (gowns, gloves and masks, where indicated) and practising good hand hygiene (31). These measures are highly effective in interrupting transmission. Children offered one of the postexposure management strategies described above should be considered to be at risk of developing chickenpox from day 8 to day 21 after exposure because no postexposure intervention is completely efficacious. The hospitalized exposed child should be isolated during days 8 to 21. Children given VZIG should be isolated until day 28 rather than day 21 because the incubation period may be prolonged by another week. The CPS statement "School and daycare exclusion policies for chickenpox: A rational approach" (30) provides guidance for the management of chickenpox in those settings.

RECOMMENDATIONS

- The CPS continues to support the National Advisory Committee on Immunization's recommendation for universal childhood immunization with varicella vaccine beginning at 12 months of age (4), immunization of children who are nonimmune (ie, 'catch-up programs') and immunization of

household contacts of nonimmune children at high risk of serious illness.

- The CPS recommends ongoing surveillance of varicella to determine whether the currently recommended program will achieve national goals. A two-dose schedule may be warranted in Canada in the future when there are established universal programs, the epidemiology of chickenpox and VZV becomes clearer, and based on the national goals for varicella control.
- Children who are nonimmune in whom vaccine is not contraindicated should be offered postexposure vaccination. This is most likely to be effective if given as soon after exposure as possible, preferably within 96 h (four days).
- Nonimmune children at risk for serious disease who are not candidates for vaccine should be offered VZIG as soon as possible and within 96 h of exposure. If VZIG is not available, clinicians should consider prophylaxis with one dose of IVIG at 400 mg/kg.
- Immunocompromised children at risk for serious varicella should be considered for antiviral prophylaxis. There is insufficient evidence to recommend antiviral prophylaxis in normal children at the present time.
- Infection control precautions should be implemented in the hospital setting to prevent varicella transmission (31,32).
- A child with mild illness should be allowed to return to school or daycare as soon as he or she is well enough to participate normally in all activities, regardless of the state of the rash.
- Physicians of immunosuppressed patients should inform parents to contact them immediately if their child has been exposed to chickenpox.
- Parents of immunosuppressed children should request that they be notified by the schools that chickenpox is in the classroom and be provided with information on the VZV incubation period and how to detect early varicella (32).

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate.