PART 4

VARICELLA (CHICKENPOX) VACCINE

KEY INFORMATION (refer to text for details)

What	• Primary varicella zoster virus infection causes varicella (chickenpox) and reactivated infection results in herpes zoster (shingles). • Complications are more common in adolescents, adults and immunocompromised people. Children with impaired immunity are at risk of severe varicella and death. • Varicella-containing vaccine is available as univalent varicella vaccine or combined multivalent measles-mumps-rubella-varicella (MMRV) vaccine. • Univalent varicella vaccine or varicella zoster immune globulin (VarIg) may be used for varicella post-exposure immunization, depending on the circumstances. • The efficacy of varicella vaccines in children is estimated to be 94.4% following a single dose and 98.3% following a second dose. • Reactions to varicella vaccines are generally mild and include pain, swelling and redness at the injection site in 10% to 20% of recipients; low-grade fever in 10% to 15%; and a varicella-like rash in 3% to 5% of vaccinees after the first dose and 1% after the second dose. • Reactions to MMRV vaccine include pain and redness at the injection site and/or low-grade fever in 10% or more of vaccinees. Rash, including measles-like, rubella-like and varicella-like rash, as well as swelling at the injection site and moderate fever (greater than 39°C), occur in 1% to less than 10% of vaccinees and can occur 7 to 21 days after receipt of vaccine. Febrile seizures following vaccination with a varicella-containing vaccine should be reported as an Adverse Events Following Immunization.
Who	• Univalent varicella or MMRV vaccine is recommended for immunization of healthy children aged 12 months to 12 years of age • Univalent varicella vaccine is recommended for susceptible adolescents (13 to17 years of age) and susceptible adults (18 to 49 years of age). • Priority groups for varicella immunization include susceptible: o Non-pregnant women of childbearing age o Household contacts of immunocompromised people o Health care workers o Adults who may be exposed occupationally to varicella (e.g., people who work with

	young children) o Immigrants and refugees from tropical regions o People receiving chronic salicylate therapy (e.g., acetylsalicylic acid [ASA]). o People with cystic fibrosis o Susceptible adults exposed to a case of varicella • Do not immunize pregnant women with varicella-containing vaccine. Pregnancy should be avoided for at least 4 weeks after receipt of vaccine. • Administer MMRV vaccine in the routine manner to children who have a history of anaphylactic hypersensitivity to eggs. • Univalent varicella vaccine may be considered for patients with select immunodeficiency disorders. MMRV vaccine has not been studied in persons with impaired immune function, including primary or secondary immunodeficiency disorders, and so is not recommended for this group.
How	• For routine childhood immunization, administer the first dose of varicella-containing vaccine (univalent varicella or MMRV) at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter. • For children aged 12 months to 12 years of age not immunized on the routine schedule, the recommended interval between 2 doses of any varicella-containing vaccine is at least 3 months. A minimum interval of 6 weeks between doses of varicella-containing vaccine may be used if rapid, complete protection is required. Adolescents (13 to 17 years of age) and adults (under 50 years of age) who may be susceptible to varicella (refer to *Susceptibility and immunity* for a definition of susceptible) should be tested for antibodies against varicella. If varicella susceptible, administer two doses of univalent varicella vaccine, at least 6 weeks apart. Adolescents and adults (under 50 years of age) who have received only one dose of varicella vaccine should be offered a second dose. For adults 50 years of age and older, refer to *Herpes Zoster (Shingles) Vaccine* in Part 4 for recommendations. • Avoid salicylates (e.g., acetylsalicylic acid [ASA]) for 6 weeks after varicella vaccination. • Varicella-containing vaccine may be administered concomitantly with other routine childhood vaccines at different injection sites using separate needles and syringes.
Why	• Varicella occurs worldwide. • Children up to 12 years of age with varicella disease who are otherwise healthy account for 80% to 85% of varicella-associated physician visits, 85% to 90% of hospitalizations, and nearly 50% of fatal cases.

Since the publication of the *2006 Canadian Immunization Guide:*

- New recommendations have been made regarding a two-dose varicella vaccination schedule for healthy children.
- New recommendations have been made about the use of univalent varicella vaccine in human immunodeficiency virus (HIV)-infected individuals.
- A new combined multivalent vaccine (measles-mumps-rubella-varicella [MMRV]) has become available for healthy children aged 12 months to 12 years of age.
- Changes in the minimum interval between varicella-containing vaccines have been recommended to make the intervals more consistent between varicella-containing products.
- Herpes zoster vaccine has become available for older adults. Refer to *Herpes Zoster (Shingles) Vaccine* in Part 4 for additional information.

For further information, refer to the National Advisory Committee on Immunization (NACI) Statements: *Statement on Measles-Mumps-Rubella-Varicella Vaccine* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-9/index-eng.php); *Updated Recommendations for the use of Varicella and MMR Vaccines in HIV-infected Individuals* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-7/index-eng.php); and *Varicella vaccination two-dose recommendations* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-8/index-eng.php).

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Varicella (chickenpox) is a generalized viral disease caused by varicella zoster virus (VZV), a deoxyribonucleic acid (DNA virus) of the *Herpesvirus* family.

Reservoir

Humans

Transmission

VZV is spread by the airborne route as well as by direct contact with the virus shed from skin lesions. The attack rate among susceptible contacts in household settings is estimated at 65% to 87%. The incubation period is from 10 to 21 days after exposure, usually 14 to 16 days. Infectiousness begins 1 to 2 days before onset of the rash and lasts until the last lesion has crusted.

Risk factors

Varicella has been considered to be a benign disease in otherwise healthy children up to 12 years of age. Risk of severe varicella infection increases with age. Adults and, in particular, pregnant women are at increased risk of severe disease. However, because most infections occur in children up to 12 years of age in unvaccinated communities, the majority of severe cases occur in this age group. Children up to 12 years of age account for 80% to 85% of varicella-associated physician visits, 85% to 90% of hospitalizations, and nearly 50% of fatal cases. Children with impaired immunity are at risk of severe varicella and death.

Seasonal/temporal pattern

Varicella disease increases during the school year and decreases sharply during summer vacation.

Spectrum of clinical illness

Symptoms of varicella include low-grade fever, mild constitutional symptoms, and a generalized, pruritic rash, with lesions at different stages that progress rapidly from macules to papules to vesicular lesions before crusting. The main complications of varicella include secondary bacterial skin and soft tissue infections, bacteremia, pneumonia, osteomyelitis, septic arthritis, necrotizing fasciitis, toxic shock-like syndrome, cerebellar ataxia, stroke and encephalitis. Varicella increases the risk of severe invasive group A streptococcal infection in previously healthy children by 40- fold to 60-fold. Complications are more common in adolescents, adults and people with conditions that compromise their immune system who have higher rates of pneumonia, encephalitis and death.

Congenital varicella syndrome is rare when infection occurs before the 13th or after the 20th week of gestation. The risk is approximately 2% when infection occurs at between 13 and 19 weeks of gestation. Congenital infection results in a wide clinical spectrum, which may include low birth weight, ophthalmic abnormalities, skin scarring, limb atrophy, cerebral atrophy and a variety of other anomalies. Maternal varicella occurring in the 5 days before to 2 days after birth is associated with severe neonatal varicella in 17% to 30% of infants, with high case fatality for the newborn.

Varicella case fatality rates are highest among adults (30 deaths/100,000 cases) followed by infants under 1 year of age (7 deaths/100,000 cases) and those aged 1 to 19 years (1 to 1.5 deaths/100,000 cases). In Canada, 70% of the 59 varicella related deaths in the years 1987 to 1997 (pre-vaccine) occurred in those over 15 years of age. Between 2000 and 2009, a total of 10 pediatric deaths due to varicella were reported by the Immunization Monitoring Program ACTive (IMPACT) system, with a range of 0 to 3 deaths per year.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

Varicella occurs worldwide and, in countries without vaccination programs, it is mainly a disease of childhood, developing in 50% of children by the age of 5 years and 90% by the age of 12 years. The epidemiology of varicella is similar among developed countries such as the United Kingdom (UK), the United States (US), and Canada. No significant gender difference has been found. People from tropical regions (including South Asia, South East and East Asia) are less likely to acquire immunity in childhood and, therefore, have higher rates of susceptibility as adults.

In the US, there were approximately 4 million varicella cases annually before varicella vaccine was licensed in 1995. The incidence of varicella, as well as varicella-related hospitalizations, has decreased significantly in the post-vaccine era. Varicella-related hospitalizations in the US decreased from 2.3-5 per 100,000 population (1993-1995) to 0.3-1.3 per 100,000 population (2001-2002) and ambulatory care visits for varicella declined by 59%. In 2000, the number of varicella-related deaths in the US had declined by 78% in the under-20-year age group and by 63% in the 20-year to 49-year age group, as compared with the pre-vaccine years, 1990 to 1994.

National

In the pre-vaccine era, it is estimated that there were approximately 350,000 varicella cases and 1,500 to 2,000 varicella-related hospitalizations each year in Canada. However, assessing the effect of varicella immunization programs on the incidence of the disease is difficult as varicella infections are significantly under-reported, with less than 10% of the expected cases reported annually. Canadian studies have found decreases in the burden of varicella following the introduction of immunization programs. Alberta saw a significant decline in disease incidence compatible with a vaccination program effect. Following introduction of publicly funded varicella vaccination in Ontario, varicella-related hospitalizations, emergency department use, and visits to physicians' offices decreased 53%, 43% and 45% respectively.

Information on pediatric hospitalized cases and deaths are available from the IMPACT system for the periods 1990 to 1996 and 1999 to 2009. These data indicate that the majority of hospitalizations occur in previously healthy children. Among these cases, children younger than 10 years of age were mainly affected and accounted for 16.5% (less than1 year of age) and 75.5% (1 to 9 years of age) of the total hospitalizations. Since 2004, the annual average number of varicella hospitalizations at IMPACT centers has dropped from 300 (2000 to 2004) to 114 (2005 to 2009).

PREPARATIONS AVAILABLE FOR USE IN CANADA

VARICELLA-CONTAINING VACCINES

- **VARIVAX® III**: live, attenuated, univalent varicella virus vaccine, (Oka/Merck), Merck Canada Inc. (Var)
- **VARILRIX®**: live, attenuated, univalent varicella virus vaccine, (Oka/GSK), GlaxoSmithKline Inc. (Var)
- **PRIORIX-TETRA®**: live, attenuated, combined measles, mumps, rubella and varicella vaccines, GlaxoSmithKline Inc. (MMRV)

VARICELLA ZOSTER IMMUNE GLOBULIN

- **VariZIG™**: varicella zoster immune globulin (human), Cangene Corporation (Varig)

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the Drug Product Database at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php. Refer to *Table 1* and *Table 2* in *General Considerations* in Part 1 for lists of all vaccines and passive immunizing agents available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

The rate of breakthrough varicella disease in vaccinees following one dose of varicella vaccine has been estimated at 7.2% over a 10-year follow-up period. American data estimate the overall effectiveness of a single dose vaccination program to be between 70% and 90% in preventing varicella disease of any severity, and 95% in protecting against severe varicella for at least 7 to 10 years after immunization. However, despite high vaccination coverage, limitations of the single dose regimen in achieving varicella control have been identified in the US. Primary vaccine failure and waning immunity appear to be responsible for breakthrough disease.

A two-dose primary schedule for children 12 months to 12 years of age has improved varicella control. In a 10-year prospective study, the cumulative risk of breakthrough disease was 3.3-fold lower in children who received two doses of varicella vaccine compared to children who received one dose. The estimated vaccine effectiveness was 98.3% after two doses, significantly higher than after one dose (94.4%). The 2-dose regimen was 100% efficacious against severe varicella.

There are no data regarding the efficacy of MMRV vaccine.

IMMUNOGENICITY

In healthy children 12 months to 12 years of age, a single univalent varicella vaccine dose results in a seroconversion rate of 98% at 4 to 6 weeks after vaccination with antibodies persisting in 98% at 5 years and 96% at 7 years after vaccination. A second dose of a univalent varicella vaccine in children produces an improved immunologic response that is correlated with improved protection. In adults and adolescents 13 years of age and older, two vaccine doses administered 4 to 8 weeks apart result in seroconversion rates of 99% at 4 to 6 weeks after the second dose, with persistence of antibodies 5 years later in 97%.

In a study of 12-month-old children, a single dose of MMRV vaccine resulted in a seroconversion rate for measles, mumps, rubella and varicella of 98%, 97%, 98% and 93%, respectively. The seroconversion rates and geometric mean titres for individual components were not significantly different from those achieved after measles-mumps-rubella (MMR) plus a univalent varicella vaccine or MMR vaccine alone. A study of children receiving two doses of MMRV vaccine during the second year of life noted seropositivity for measles, mumps, rubella and varicella of 99%, 97.4%, 100% and 99.4% respectively by the third year post-vaccination. Long-term persistence of anti-measles, anti-mumps, anti-rubella and anti-varicella antibodies following MMRV vaccinations are under evaluation.

RECOMMENDATIONS FOR USE

HEALTHY CHILDREN (12 months to 12 years of age)

Two doses of varicella-containing vaccine (univalent varicella or MMRV) should be given for routine immunization of children and for immunization of children who have missed varicella immunization on the routine schedule.

Children with a history of varicella disease occurring before 12 months of age should receive routine immunization with two doses of varicella-containing vaccine after 12 months of age, because varicella disease at less than 12 months of age has been associated with an increased risk of a second episode of varicella. Children who receive one dose of varicella-containing vaccine and subsequently develop

laboratory confirmed breakthrough infection do not require a second dose of a varicella-containing vaccine for varicella protection.

ADOLESCENTS (13 to 17 years of age)

Adolescents without contraindications who may be susceptible to varicella (refer to *Susceptibility and immunity* for a definition of susceptible) should be serologically tested for varicella antibodies because the majority of such adolescents will be immune. If the adolescent is shown to be serologically susceptible to varicella, the person should receive two doses of a univalent varicella vaccine (as MMRV is not authorized in this age group) a minimum of 6 weeks apart. In adolescents with documentation of receiving only one dose of a varicella-containing vaccine, a second dose should be offered.

ADULTS (18 years of age and older)

Adults (under 50 years of age) without contraindications who may be susceptible to varicella (refer to *Susceptibility and immunity* for a definition of susceptible) should be serologically tested for varicella antibodies because the majority of such adults will be immune. If an adult under the age of 50 years is shown to be serologically susceptible to varicella, the person should receive two doses of univalent varicella vaccine. Adults (under 50 years of age) who received only one dose of varicella vaccine should be offered a second dose.

In adults aged **50 years and older,** routine serologic testing is not recommended. Nearly all Canadians 50 years of age and older, will have had prior varicella exposure even if the person does not remember having had chickenpox or herpes zoster. In the rare circumstance that an adult aged 50 years and over is known to be serologically susceptible to varicella based on previous testing for another reason, and is without contraindications, the individual should be vaccinated with two doses of univalent varicella vaccine. For other adults 50 years of age and over, refer to *Herpes Zoster (Shingles) Vaccine* in Part 4 for additional information.

Susceptibility and immunity

A self-reported history of varicella is considered a reliable history of varicella disease in individuals born before 2004 (with the exception of health care workers). For children born in 2004 or later and health care workers, a health care provider diagnosis of varicella or herpes zoster is necessary to be considered a reliable history of varicella disease.

Individuals who have one or more of the following are considered immune to varicella. Individuals who do not have ANY of the following are considered susceptible to varicella:

- Self-reported history of varicella if born before 2004 (except for health care workers)
- For those born in 2004 or later and for health care workers, a health care provider diagnosis of varicella or herpes zoster
- Documented evidence of immunization with two doses of a varicella-containing vaccine
- A history of laboratory confirmed varicella infection
- Laboratory evidence of immunity

Recipients of hematopoietic stem cell transplant should be considered susceptible in the post-transplantation period regardless of a history of varicella disease or vaccination, or positive serologic test results.

PRIORITY GROUPS

The following groups are priorities for varicella immunization if susceptible:

- **Women of childbearing age.** Varicella-containing vaccine should not be given during pregnancy. Refer to *Pregnancy and lactation*.
- **Household contacts of immunocompromised people.** Refer to *Immunocompromised persons*.
- **Health care workers** and others who may be exposed occupationally to varicella (e.g., teachers of young children, child care workers). Refer to *Workers*.

- **Immigrants and refugees from tropical regions** who are more likely to be susceptible to varicella. Refer to *Persons new to Canada*.
- People receiving **chronic salicylate therapy** (medications derived from salicylic acid, e.g., acetylsalicylic acid [ASA]) because of an association between wild-type varicella disease, salicylate therapy and Reye's syndrome. Refer to *Drug interactions* for additional information regarding the avoidance of salicylate therapy following varicella vaccination.
- People with **cystic fibrosis**, because varicella disease may cause a transient worsening of lung function.
- **Persons exposed to a case** of varicella. Refer to *Post-exposure immunization*.

Refer to *Schedule*.

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults, who are susceptible to varicella, including those lacking adequate documentation of immunization, should be started on an immunization schedule appropriate for their age and risk factors. Varicella-containing vaccine may be given regardless of possible previous receipt of the vaccine because adverse events associated with repeated immunization have not been demonstrated. Refer to *Immunization of Children and Adults with Inadequate Immunization Records* in Part 3 for additional general information.

PREGNANCY AND LACTATION

Immunity to varicella should be reviewed in women of reproductive age and vaccination should be recommended to susceptible non-pregnant women. Women should delay pregnancy by at least 4 weeks following vaccination with a univalent varicella vaccine.

Varicella-containing vaccine is contraindicated in pregnancy because there is a theoretical risk to the fetus; however, there is no evidence to demonstrate a teratogenic risk from the vaccine. Termination of pregnancy should not be recommended following inadvertent immunization with varicella vaccine on the basis of fetal risks following maternal immunization. Incidents of inadvertent varicella immunization during pregnancy, or of pregnancy occurring within 3 months after immunization with VARIVAX® III, should be reported to the registry maintained by Merck Canada Inc., Medical Services (telephone: 1-800-684-6686). GlaxoSmithKline Inc. does not maintain a pregnancy outcome registry for VARILRIX®.

Women who are breastfeeding and individuals in households where there is a newborn can be vaccinated with a univalent varicella vaccine.

Refer to *Contraindications and Precautions*. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional general information.

PATIENTS/RESIDENTS IN HEALTH CARE INSTITUTIONS

Most residents of long-term care facilities will be immune to varicella. Postpartum women susceptible to varicella should be vaccinated before discharge. Refer to *Immunization of Patients in Health Care Institutions* in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

In general, immunocompromised persons should not receive live vaccines because of the risk of disease caused by the vaccine strains. When considering immunization of an immunocompromised person, approval from the individual's attending physician should be obtained before vaccination. For complex cases, referral to a physician with expertise in immunization and/or immunodeficiency is advised.

In Canada, only VARILRIX® has received authorization for the vaccination of select groups of immunocompromised people; however, VARIVAX® III may also be used. MMRV vaccine has not been studied in persons with impaired immune function, including primary or secondary immunodeficiency disorders, and so is not recommended for this group.

In immunosuppressed people, antibody testing may be considered 6 to 8 weeks after the last dose of univalent varicella vaccine is given. Local antibody assays may not be sensitive enough to detect antibody after vaccination. For the purposes of post-exposure prophylaxis, an immunosuppressed person with a negative test should be considered non-immune. Therefore, if antibody is not detectable, consider offering immunocompromised persons VarIg upon subsequent exposures to wild-type varicella. Refer to *Figure 1*, *Table 1* and *Post-exposure immunization*.

Family or medical history

People who have a suspicious history for immunodeficiency disorders (e.g., known or suspected family history of congenital immunodeficiency disorder or HIV infection, or a history of failure to thrive and recurrent infections) should not be immunized until they have been fully investigated and T cell dysfunction ruled out.

Congenital (primary) immunodeficiency

Live vaccines are generally not recommended for patients with congenital immunodeficiency states although some exceptions exist.

B cell deficiency

Univalent varicella vaccine should be considered if the individual is not receiving regular immune globulin replacement therapy, which may affect the efficacy of the vaccine. People with isolated humoral immunoglobulin deficiency disorders and known intact T cell systems may be vaccinated with two doses of univalent varicella vaccine at least 3 months apart.

T cell, natural killer T cell, and mixed cellular and antibody defects (e.g., Severe Combined Immune Deficiency [SCID])

All live vaccines, including varicella-containing vaccine, are contraindicated in people with defects in T cell function.

Phagocytic and neutrophil disorders (e.g., congenital neutropenia, leukocyte adhesion and migration defects, chronic granulomatous disease)

Children with phagocytic or neutrophil disorders may be vaccinated with two doses of univalent varicella vaccine at least 3 months apart.

Complement deficiency

Persons with complement deficiency disorders may be vaccinated with two doses of univalent varicella vaccine at least 3 months apart. Because immunity can decrease over time, assessment of antibody titres and re-immunization, if needed, should be considered.

Acquired (secondary) immunodeficiency

Malignant hematologic disorders

Varicella-containing vaccine is contraindicated in individuals with severe immunodeficiency due to conditions such as: blood dyscrasias, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Varicella-containing vaccine is contraindicated in people undergoing immunosuppressive treatment for acute leukemia. Children with Acute Lymphocytic Leukemia (ALL) may be vaccinated with univalent varicella vaccine if the disease has been in remission for at least 12 months, the child's total lymphocyte count is at least 1.2×10^9/L, the child is not receiving radiation therapy, and maintenance chemotherapy can be withheld for at least 1 week before to 1 week after immunization. Two doses of univalent varicella vaccine may be given, at least 3 months apart.

Malignant solid tumours

Varicella-containing vaccine is contraindicated in people undergoing immunosuppressive treatment for any malignant solid tumours.

Hematopoietic stem cell transplantation (HSCT- autologous or allogeneic)

- Pre-transplantation: People awaiting HSCT should not receive varicella-containing vaccine. Vaccination of donors immediately before stem cell harvest is not recommended because there is no evidence that immunity can be transferred from the donor to the recipient and there are no safety data.
- Post-transplantation: Antibody titres to vaccine-preventable diseases decline after HSCT if the recipient is not re-vaccinated. Vaccination of seronegative HSCT recipients with one dose of univalent varicella vaccine may be considered at two years or more after transplantation provided there is no evidence of chronic graft-versus-host disease, immunosuppression has been discontinued for at least 3 months, and the person is deemed to be immunocompetent by a transplant specialist. Serologic status should be checked prior to vaccination and vaccine administered to serologically varicella susceptible persons only. Safety and immunogenicity data are not available regarding administration of more than one dose of varicella-containing vaccine after HSCT.

Solid organ transplantation

Varicella vaccination is recommended before transplantation for susceptible (as determined by serology) children and adults. Ideally, and if time permits, two doses of univalent varicella vaccine should be given at least 3 months apart with the last dose being given at least 6 weeks prior to transplantation. If time does not permit administration of a two-dose series, one dose of univalent varicella vaccine should be given and the transplant delayed by at least 4 weeks. The person should not be receiving immunosuppressive treatment at the time of vaccination. Varicella-containing vaccine is not recommended after solid organ transplantation.

Immunosuppressive therapy

Vaccination status for varicella should be reviewed for immunocompetent persons who might be anticipating initiation of immunosuppressive treatments or who have diseases that might lead to immunodeficiency.

If indicated, varicella vaccine should be administered at least 4 weeks before the initiation of immunosuppressive therapy (e.g., high-dose systemic corticosteroids [2 mg/kg per day or more of prednisone or its equivalent or 20 mg/day or more of prednisone or its equivalent] for 14 days or more; chemotherapy; radiation therapy; azathioprine; cyclosporine; cyclophosphamide; infliximab). If this cannot be done, a period of at least 3 months should elapse after immunosuppressive drugs (except high-dose systemic corticosteroids) have been stopped before administration of live vaccines. A period of at least 4 weeks should elapse between discontinuation of high-dose systemic steroids and the administration of live vaccines. The interval between discontinuation of immunosuppressive drugs and varicella vaccine administration may vary with the intensity of the immunosuppressive therapy, underlying disease and other factors. If immunosuppressive therapy cannot be stopped, live vaccines are generally contraindicated, although the risk-to-benefit ratio may favour immunization if only low doses of immunosuppressive drugs are required and there is significant risk of varicella infection.

Corticosteroid therapy is not a contraindication to administering a live vaccine when steroid therapy is short-term (i.e., less than 14 days); or a low-to-moderate dose (less than 20 mg of prednisone or equivalent per day for an adult); or long-term, alternate-day treatment with short-acting preparations; or maintenance physiologic replacement therapy; or administered topically, inhaled, or locally injected (e.g., joint injection).

HIV-infected

An infectious disease specialist/immunologist should be consulted for advice on varicella immunization in HIV-infected people. Varicella vaccine is contraindicated in persons with advanced HIV/AIDS. The safety and immunogenicity of MMRV vaccine in HIV-infected individuals has not been evaluated, and MMRV vaccine is not routinely recommended.

- Children: HIV-infected children 12 months of age and older, and with CDC clinical category N, A, or B and immunologic category 1 or 2 (i.e., CD4 percentage ≥15%) may receive two doses of a univalent varicella vaccine 3 to 6 months apart. Univalent varicella vaccine may be administered concomitantly with measles-mumps-rubella (MMR) vaccine at different injection sites using separate needles and syringes. Refer to *Measles Vaccine*, *Mumps Vaccine* and *Rubella Vaccine* in Part 4 for additional information.
- Adolescents and adults: There are no published data on the use of varicella vaccine in susceptible HIV-infected adolescents and adults. HIV-infected adolescents and adults should be asked for a history of varicella disease or vaccination (refer to *Susceptibility and immunity*), and if negative for both, serology should be requested to confirm susceptibility. Based on expert opinion, immunization with two doses of univalent varicella vaccine administered 3 months apart may be considered for susceptible HIV-infected adolescents and adults with CD4 cell count ≥200 x 10^6/L and CD4 percentage ≥15%.

Household contacts

Susceptible household contacts of immunocompromised people should receive varicella-containing vaccine as appropriate for age and risk factors. If the vaccine recipient develops a varicella-like rash, the rash should be covered and the vaccinee should avoid direct contact with the immunocompromised person for the duration of the rash. Secondary transmission from people with post-vaccination varicella-like rashes can occur rarely.

Refer to *Post-exposure immunization* and *Contraindications and Precautions*. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional general information.

PERSONS WITH CHRONIC DISEASES

Hyposplenism or asplenia

Hyposplenic or asplenic (congenital absence, surgical removal or functional [e.g., sickle cell disease]) individuals should receive two doses of univalent varicella vaccine, at least 3 months apart.

Chronic renal disease/dialysis

Varicella vaccine is recommended for individuals with chronic renal disease or undergoing dialysis. Two doses of univalent varicella vaccine may be given, at least 3 months apart.

Neurologic disorders

People with conditions such as autism spectrum disorders or demyelinating disorders (including multiple sclerosis) should receive all routinely recommended immunizations, including varicella-containing vaccine.

Autoimmune diseases

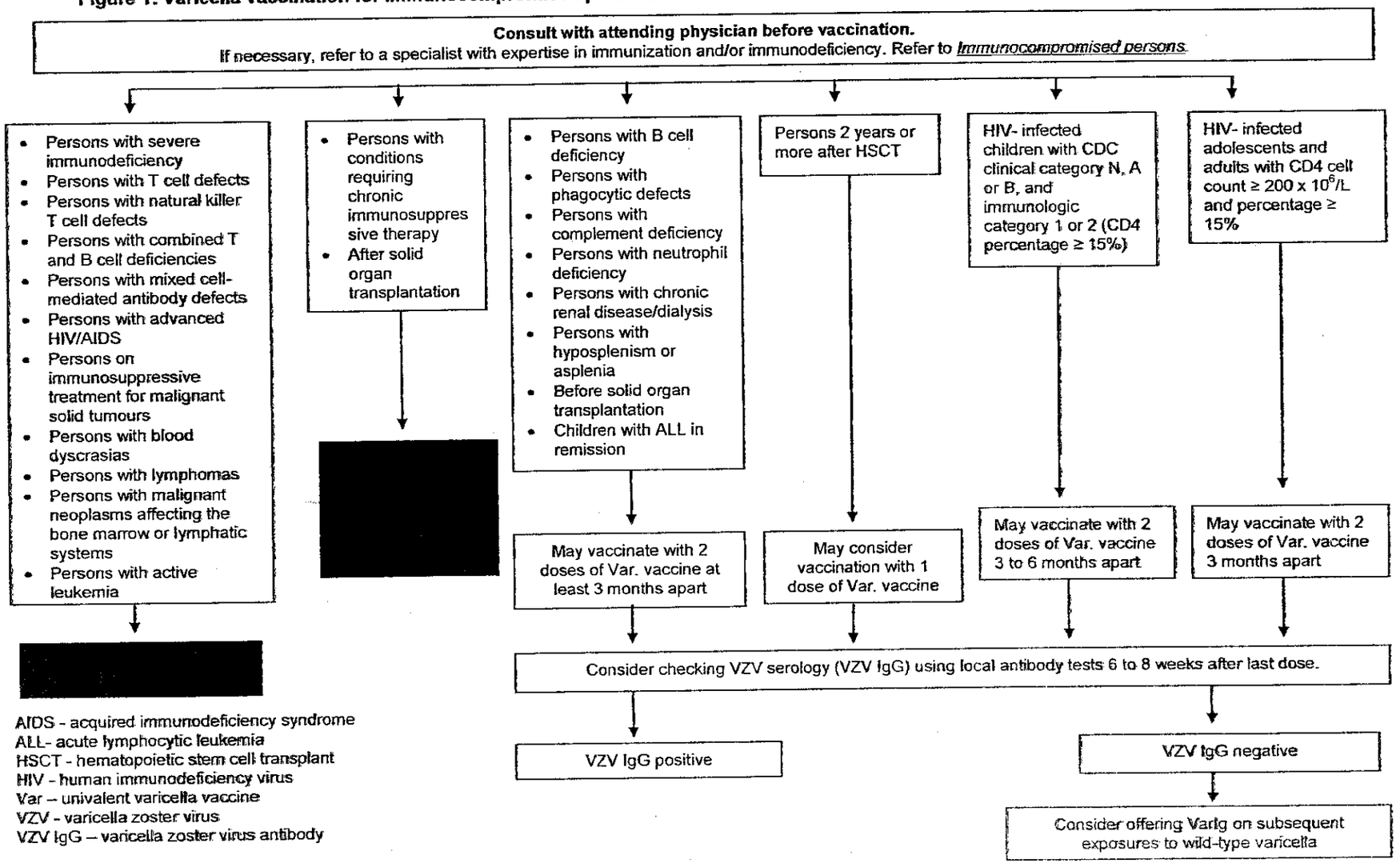
Although definitive data are lacking, individuals with autoimmune disease **not being treated with immunosuppressive drugs** are not considered significantly immunocompromised and should receive varicella immunization following consultation with a physician. The nature of the person's underlying disease should be considered. Rheumatic disease modifying agents such as hydroxychloroquine, sulfasalazine, or auranofin are not considered immunosuppressive.

The safety and efficacy of live, attenuated vaccines during **low dose intermittent or maintenance therapy with immunosuppressive drugs** (other than corticosteroids) for autoimmune disease is

unknown. These drugs include therapeutic monoclonal antibodies, especially the anti-tumour necrosis factor agents adalimumab, infliximab, and etanercept and others (azathioprine, methotrexate, leflunomide, and abatacept). These have been reported to cause reactivation of latent tuberculosis infection and predisposition to other opportunistic infections. Therefore, until additional information becomes available, avoidance of live vaccines during intermittent or low dose chemotherapy or other immunosuppressive therapy is prudent.

Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for additional general information.

Figure 1: Varicella vaccination for immunocompromised persons



AIDS - acquired immunodeficiency syndrome
ALL- acute lymphocytic leukemia
HSCT - hematopoietic stem cell transplant
HIV - human immunodeficiency virus
Var – univalent varicella vaccine
VZV - varicella zoster virus
VZV IgG – varicella zoster virus antibody

PERSONS NEW TO CANADA

Health care providers who see persons newly arrived in Canada should review the immunization status and update immunization for these individuals as necessary. People from tropical regions are more likely to be susceptible to varicella and should be a priority for varicella immunization. Refer to *Immunization of Persons New to Canada* in Part 3 for additional general information.

WORKERS

Varicella immunization should be offered to susceptible workers (refer to *Susceptibility and Immunity* for a definition of susceptible) including health care workers, child care workers, and teachers of young children. These groups are at occupational risk of exposure or may transmit disease to susceptible individuals. For health care providers, a self-reported history of varicella is not reliable to be considered immune. A health care provider diagnosis of varicella or herpes zoster is required for immunity to be considered reliable based on clinical presentation. If a health care provider diagnosis is not available, serologic testing is required to document immunity. Two doses of varicella vaccine are recommended for susceptible workers as is the case for all susceptible adults. A second dose of varicella vaccine should be offered to workers who would have received only one dose of vaccine.

Health care workers with a post-vaccine rash at the injection site may continue to work if the rash is covered. Those with a varicella-like rash not confined to the injection site should be excluded from work in high-risk patient care areas (e.g., where there are premature infants and immunocompromised patients) until lesions are crusted. Vaccinees with a post-vaccination varicella-like rash rarely transmit the vaccine-associated virus.

Refer to *Immunization of Workers* in Part 3 for additional general information.

POST-EXPOSURE IMMUNIZATION (refer to Table 1)

Significant exposures to VZV

The following situations are significant exposures to VZV:

- Continuous household contact (living in the same dwelling) with a person with varicella
- Being indoors for more than 1 hour with a case of varicella
- Being in the same hospital room for more than 1 hour, or more than 15 minutes of face-to-face contact with a patient with varicella
- Touching the lesions of a person with active varicella
- Close exposure to a person with herpes zoster. Refer to *Post-exposure immunization* in *Herpes Zoster (Shingles) Vaccine* in Part 4 for additional information.

Univalent varicella vaccine

Univalent varicella vaccine given as soon as possible and within 3 and up to 5 days after exposure has been shown to be approximately 90% effective in preventing or reducing the severity of varicella and is the post-exposure management of choice for susceptible, healthy, non-pregnant persons. Varicella vaccination is not indicated for post-exposure management of infants less than 12 months of age, as the vaccine is not authorized for this age group and these infants are generally protected by maternal antibodies. Adults who previously received at least 1 dose of varicella-containing vaccine before 12 years of age or two doses thereafter should not be serologically tested as they are likely to be immune to varicella and commercially available antibody tests are usually not sensitive enough to detect post-vaccination antibody concentrations. Those who received only one dose of varicella-containing vaccine should be offered a second dose. There are no data on the use of MMRV vaccine in varicella post-exposure or outbreak situations.

Varicella zoster immune globulin

The decision to administer VarIg should be based on fulfilling all of the following criteria:

- The exposed person is susceptible to varicella.
- There has been a significant exposure to VZV. Refer to *Significant exposures to VZV*.
- The person is at increased risk of severe varicella. Refer to *Persons at increased risk of severe varicella*.
- Post-exposure immunization with univalent varicella vaccine is contraindicated.

If VarIg is being considered, consultation with an infectious diseases/infection control specialist is advised.

Persons at increased risk of severe varicella

VarIg is recommended for the following persons at increased risk of severe varicella if significant exposure has occurred:

- **Susceptible pregnant women** exposed to varicella should be evaluated for a history of varicella vaccination or disease. In the absence of such a history, immunity should be assessed by serologic testing as soon as possible. Exposed susceptible pregnant women should *not* be given vaccine; VarIg should be offered as soon as possible and within 96 hours of exposure to reduce potential maternal morbidity. If serology results cannot be obtained within 96 hours, VarIg should be administered to pregnant women who are presumed to be susceptible. Susceptible pregnant women should be given univalent varicella vaccine after delivery, assuming the recommended interval has passed since VarIg was administered. For recommendations on the interval between administration of VarIg and vaccination with varicella-containing vaccine, refer to *Recent Administration of Human Immune Globulin Products* in Part 1.
- **Newborn infants of mothers who develop varicella** during the 5 days before to 48 hours after delivery.
- **Neonatal or pediatric intensive care settings.** For the management of significant varicella exposure in a neonatal or pediatric intensive care setting, consultation with the infectious diseases/infection control specialist regarding the potential use of VarIg is advised.
- **Susceptible immunocompromised persons.** Those receiving regular monthly infusions of 400 mg/kg or more of intravenous immune globulin and whose most recent dose was within 3 weeks before exposure do not require VarIg. Monthly infusion of intravenous immune globulin maintains concentrations of varicella antibody comparable to that achieved with VarIg. For immunocompromised persons who are outside the 96-hour post-exposure window for VarIg administration, antiviral therapy from days 7 to 14 post-exposure could be considered. Refer to *Immunocompromised persons*.
- **Susceptible HIV-infected persons.** Based on expert opinion, if not severely immunocompromised (CD4 cell count ≥ 200 x 10^6/L and percentage ≥ 15%), post-exposure vaccination is indicated. If only one dose of vaccine had been administered previously, completion of the series with a second dose is indicated. Post-exposure vaccination is contraindicated if severely immune suppressed (CD4 cell count < 200 x 10^6/L or CD4 percentage < 15%); VarIg is indicated in such patients and should be administered as soon as possible, and within 96 hours of exposure to varicella. VarIg is not routinely necessary for HIV-infected persons without severe immune suppression who have completed an appropriate two-dose vaccination series or who have had natural varicella infection. Previously immunized HIV-infected children may demonstrate significant waning of immunity at 1 to 2 years after receiving 2 doses of varicella vaccine; however, it is unknown if this implies an inability to mount an anamnestic response after exposure to varicella disease. In the event of breakthrough varicella, a specialist should be promptly consulted regarding the need for antiviral therapy.
- **Recipients of HSCT** should be considered susceptible in the post-transplantation period regardless of a history of varicella disease or vaccination, or positive serologic test results.

Such persons should be offered VarIg after exposure to varicella. Refer to *Susceptible immunocompromised persons* for additional information.

VarIg is of maximal benefit if administered within 96 hours after first exposure. However, since the exact timing of transmission is unknown, it may be used within 96 hours of the most recent exposure. If more than 96 hours have elapsed since the last exposure, the benefit of administering VarIg is uncertain. Protection conferred by VarIg lasts approximately 3 weeks. Subsequent exposures occurring more than 3 weeks after a dose of VarIg require additional doses of VarIg if the criteria for VarIg administration, as specified above, are met.

The recommended dose of VarIg is 125 IU/10 kg of body weight up to a maximum of 625 IU. The minimum dose is 125 IU. VarIg should be given by the intramuscular (IM) route. Intravenous administration is also possible in certain circumstances but is associated with additional safety considerations. For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the Drug Product Database. If VarIg is being considered, consultation with an infectious diseases/infection control specialist is advised.

Refer to *Passive Immunization* Part 5 for additional general information.

Table 1: Varicella post-exposure management for susceptible* individuals

Post-exposure intervention	Individual		
	Healthy, non-pregnant (12 months of age** and older)	**Pregnant**	**Immunocompromised****
Vaccinate with varicella vaccine	Yes	No	No
Check VZV IgG	No	Yes	Yes
If VZV IgG negative, administer VarIg***	Not applicable	Yes	Yes

* Refer to *Susceptibility and immunity* for definition of susceptible.
** Refer to *Varicella zoster immune globulin* for information regarding newborns of mothers who develop varicella during the 5 days before to 48 hours after delivery.
*** If serology results cannot be obtained within 96 hours, VarIg should be administered
**** In case of hematopoietic stem cell transplant (HSCT), administer VarIg regardless of VZV IgG result

OUTBREAK CONTROL

Post-exposure immunization is useful in preventing or limiting varicella outbreaks in hospitals, child care facilities and homeless shelters. Serologic testing for susceptibility is not necessary prior to immunization in an outbreak situation. There are no data on the use of MMRV vaccine in outbreak situations. Refer to *Post-exposure Immunization*.

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VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE (refer to Table 1)

Dose

Each dose is 0.5 mL.

Route of administration

Univalent varicella vaccine should be administered subcutaneously (SC). Although the intramuscular (IM) route is not recommended, there is evidence that it is not necessary to repeat a dose of univalent varicella vaccine if it is inadvertently given IM. MMRV vaccine should be administered SC or IM. Refer to *Vaccine Administration Practices* in Part 1 for additional information.

Schedule

Healthy children (12 months to 12 years of age)

For routine immunization of children aged 12 months to 12 years, two doses of varicella-containing vaccine (univalent varicella or MMRV) should be administered. The first varicella-containing vaccine dose should be administered at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter. The recommended interval between two doses is at least 3 months, however a 6-week interval can be used if rapid complete protection is required.

Two doses of varicella-containing vaccine (univalent varicella or MMRV) should be administered to children less than 13 years of age who were not routinely immunized with varicella-containing vaccine. The recommended interval between doses is at least 3 months. A minimum interval of 6 weeks between doses of varicella-containing vaccine may be used for catch-up immunization if rapid, complete protection is required. In deciding on the timing of the second dose, vaccine providers should consider factors such as the prevalence of varicella in the community, the current age of the child and attendance at a child care centre or school. The choice of vaccines and minimum interval for the second dose will depend on the vaccines and number of doses previously administered. Refer to *Table 2* and *Table 3*. The minimum interval between doses of varicella-containing vaccines has been simplified and differs from previous NACI statements.

Table 2: Recommended options for children (12 months to 12 years of age) not routinely immunized with varicella-containing vaccine

Prior immunization	Recommended options for immunization
0 dose MMR & 0 dose univalent varicella	2 doses MMRV (with the two doses at least 3 months apart[+]) OR 2 doses of MMR* and univalent varicella* (with the two doses at least 3 months apart[+])
1 dose MMR & 1 dose univalent varicella	1 dose MMRV (at least 3 months after univalent varicella[+]) OR 1 dose of MMR* and univalent varicella* (at least 3 months after prior univalent varicella[+])
1 dose MMR & 0 dose univalent varicella	1 dose MMRV (at least 6 weeks after the prior MMR), followed by 1 dose univalent varicella (at least 3 months after MMRV[+]) OR 1 dose univalent varicella (at least 4 weeks after the prior MMR), followed by 1 dose MMRV (at least 3 months after univalent varicella[+])
2 doses MMR & 1 dose univalent varicella	1 dose univalent varicella (at least 4 weeks after the last MMR AND at least 3 months after the prior univalent varicella[+])
2 doses MMR & 0 dose univalent varicella	2 doses univalent varicella (given at least 4 weeks after the last MMR, with a minimum interval of 3 months between the two doses of univalent varicella[+])
1 dose MMRV & 0 dose univalent varicella	1 dose MMRV (at least 3 months after the prior MMRV[+]) OR 1 dose each of MMR* and univalent varicella*(at least 3 months after the prior MMRV[+])
1 dose MMR & 1 dose MMRV	1 dose of univalent varicella (at least 4 weeks after prior MMR or at least 3 months after the prior MMRV[+])

* MMR and univalent varicella vaccines may be given concomitantly at different injection sites using separate needles and syringes. If not given concomitantly, administration of MMR and univalent varicella vaccines must be separated by at least 4 weeks.

[+] If rapid, complete protection against varicella is required, a minimum interval of 6 weeks between 2 doses may be used.

Adolescents (13-17 years of age)

Adolescents with unknown susceptibility status should be serologically tested for varicella antibodies because most will be immune. Healthy, varicella-susceptible adolescents should receive two doses of univalent varicella vaccine given at least 6 weeks apart.

Adults (18 years of age and older)

Adults, under 50 years of age, with unknown susceptibility status should be serologically tested for varicella antibodies because most will be immune. Healthy, varicella-susceptible adults should receive two doses of univalent varicella vaccine administered at least 6 weeks apart. Refer to *Recommendations for use*.

In general, adults 50 years of age and older, are presumed to be immune to varicella. . Routine serology is not recommended in this age group. Herpes zoster vaccine is recommended in people 60 years of age and older without contraindications and may be used in people 50-59 years of age without contraindications. Refer to *Herpes Zoster (Shingles) Vaccine* in Part 4 for additional information.

Table 3: Recommended number of doses of varicella-containing vaccine and minimum intervals for selected groups, by vaccine

Group	Vaccine	
	Univalent Varicella	MMRV
Healthy children 1–12 years of age	2 doses ≥ 3 months apart*	
Healthy adolescents ≥ 13 years of age & adults	2 doses ≥ 6 weeks apart	No data, not recommended
Catch-up (unimmunized) aged ≥ 12 months–12 years	2 doses à ≥ 3 mois d'intervalle*	
Post-exposure (unimmunized) aged ≥ 12 months–12 years	2 doses ≥ 3 months apart*	No data, not recommended
Select immunocompromised groups meeting prerequisites, aged ≥ 12 months	2 doses ≥ 3 months apart	No data, not recommended
At least 2 years post-HSCT, aged ≥ 12 months	1 dose (no data for 2 doses)	No data, not recommended

HSCT - hematopoietic stem cell transplant

[a] Children with varicella-like illness that occurred before 12 months of age should be vaccinated after age 1 year with age-appropriate schedule

* If rapid, complete protection against varicella is required, a minimum interval of 6 weeks between 2 doses may be used.

BOOSTER DOSES AND RE-IMMUNIZATION

Re-immunization with varicella-containing vaccine after age and risk appropriate vaccination is not necessary. Herpes zoster vaccine is recommended for persons 60 years of age and older without contraindications and may be used in persons 50 to 59 years of age without contraindications Refer to *Herpes Zoster (Shingles) Vaccine* in Part 4 for additional information.

SEROLOGICAL TESTING

PRE-IMMUNIZATION

Serologic testing is not recommended in children (12 months to 12 years of age) before receiving a varicella-containing vaccine. In adolescents and adults (13 to less than 50 years of age) who may be susceptible to varicella (refer to *Susceptibility and immunity* for a definition of susceptible) serologic testing should be performed before immunization as the majority of such individuals will be immune and will not require varicella vaccine. Individuals 50 years of age and over are presumed to be immune unless known to be varicella-susceptible based on serology previously drawn for other purposes. Routine serology is not recommended in this age group.

POST-IMMUNIZATION

Serologic testing is not recommended for healthy children. Previously vaccinated individuals who are inadvertently tested are likely to be immune to varicella even if there is no detectable antibody. Commercially available varicella antibody tests, such as the enzyme-linked immunosorbant assay (ELISA) and latex agglutination (LA), may not have sufficient sensitivity to detect antibody after vaccination, although they are useful for establishing immunity after wild-type infection.

Immunocompromised people who are vaccinated with univalent varicella vaccine may have antibody testing performed 6 to 8 weeks after the last dose (refer to *Figure 1*). However, local antibody tests may not be sensitive enough to detect antibody after immunization. The glycoprotein ELISA (gpELISA) test is more sensitive, but is not routinely available.

STORAGE REQUIREMENTS

VARILRIX®: Store the vaccine in a refrigerator at +2°C to +8°C. The diluent may be stored in the refrigerator or at ambient temperature (maximum +25°C). The freeze-dried vaccine is not affected by freezing.

VARIVAX® III: Store the vaccine at +2°C to +8°C or colder. The vaccine may be stored in a freezer; if subsequently transferred to a refrigerator, the vaccine should not be refrozen. Protect from light. The vial of diluent should be stored separately at room temperature (+20°C to +25°C) or in the refrigerator (+2°C to +8°C).

PRIORIX-TETRA™: Store the vaccine and diluent in a refrigerator at +2°C to +8°C and do not freeze. Protect the vaccine from light.

Refer to *Storage and Handling of Immunizing Agents* in Part 1 for additional general information. Refer to *Passive Immunization* Part 5 for information regarding Varig storage requirements.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Varicella-containing vaccine may be administered concomitantly with routine childhood vaccines or live intranasal influenza vaccine (LAIV). Different injection sites and separate needles and syringes must be used for concomitant parenteral injections. If not given concomitantly, a minimum interval of 4 weeks is recommended between administration of two live vaccines. These recommendations are to address the hypothetical risk of interference from the vaccine given first on the vaccine given later. Recommended intervals between varicella-containing vaccines are provided in *Table 3*. Refer to *Timing of Vaccine Administration* in Part 1 for additional general information.

VACCINE AND IMMUNE GLOBULIN SAFETY AND ADVERSE EVENTS

Refer to *Vaccine Safety and Adverse Events Following Immunization* Part 2 for additional general information.

COMMON AND LOCAL ADVERSE EVENTS

Univalent varicella vaccine

Reactions to univalent varicella vaccine are generally mild and include injection site pain, swelling and redness in 10% to 20% of recipients. A low-grade fever has been documented in 10% to 15% of vaccinees. A varicella-like rash occurs at the injection site or is generalized in 3% to 5% of vaccinees after the first dose and 1% after a second dose. The rash usually appears within 5 to 26 days after immunization. As varicella-like rashes that occur within the first two weeks after immunization may be caused by wild-type virus, health care providers should obtain specimens from the vaccinee to ensure varicella disease is not confused with a reaction to vaccination.

The safety profile of a 2-dose regimen is comparable to that of a single dose: the incidence of injection site reactions observed within 3 days after vaccination was slightly higher after dose 2 (25.4%) than after dose 1 (21.7%), while fever incidence (which can occur 7 to 21 days after receipt of vaccine) was 7% after dose 1 and 4% after dose 2, and varicella-like rash incidence after dose 1 was 3%, compared with 1% after dose 2. Febrile seizures should be reported following varicella-containing vaccines.

MMRV vaccine

Pain and redness at the injection site and/or low-grade fever occur in 10% or more of vaccinees. Rash, including measles-like, rubella-like and varicella-like rash, as well as swelling at the injection site and moderate fever (greater than 39°C), occur in 1% to less than 10% of vaccinees. As varicella-like rashes that occur within the first two weeks after immunization may be caused by wild-type virus, health care providers should obtain specimens from the vaccinee to ensure varicella disease is not confused with a reaction to vaccination.

VarIg

Reactions to VarIg are rare. The most frequent treatment related adverse events are pain at the injection site (17%), headache (7%), and rash (5%).

Rubella-containing vaccines

Acute transient arthritis or arthralgia may occur 1 to 3 weeks after immunization with rubella-containing vaccine, such as MMRV. It lasts for about 1 to 3 weeks, and rarely recurs. This is more common in post-pubertal females, among whom arthralgia develops in 25% and arthritis in 10% after immunization with rubella-containing vaccine. There is no evidence of increased risk of new onset, chronic arthropathies or neurologic conditions.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. Anaphylaxis following vaccination with varicella-containing vaccine may occur but is very rare.

Univalent varicella vaccine

Most reported serious adverse events have not been proven to be caused by the vaccine, with the exception of rare events linked to the varicella vaccine strain among immunocompromised individuals or those with other serious medical conditions.

MMR and MMRV vaccines

Immune Thrombocytopenic Purpura (ITP)

Rarely, ITP occurs within 6 weeks after immunization with MMRV vaccine. In most children, post-immunization thrombocytopenia resolves within three months without serious complications. In individuals who experienced ITP with the first dose of MMRV vaccine, serologic status may be evaluated to determine whether an additional dose of vaccine is needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases.

Encephalitis

Encephalitis has been reported in association with administration of measles vaccine in approximately 1 per million doses distributed in North America which is much lower than that observed with natural measles disease (1 per 1,000 cases).

Febrile seizures

Recent studies have found a higher risk of febrile seizures with the first dose of a MMRV vaccine (ProQuad®, Merck, not authorized for use in Canada) when compared to the concomitant administration of MMR and univalent varicella vaccine. Data from the US estimated that the risk of febrile seizures in the 5 to 12 days following the first dose of this MMRV vaccine is 1 for every 2,600 vaccinated children aged 12 to 23 months. Experience with the MMRV vaccine available in Canada is more limited; however, one study showed a statistically non-significant increased risk of febrile seizures with MMRV vaccine compared to MMR and varicella given as two separate vaccines administered concomitantly. Close surveillance and further investigation are underway.