

23

Varicella-Zoster

VARICELLA HOSPITALISATION NOTIFIABLE
OUTBREAK NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

Introduction

Infection with the varicella-zoster virus (VZV) causes two distinct clinical syndromes, varicella (chickenpox) and zoster (shingles). Primary infection results in varicella, an acute exanthematous disease. The virus becomes latent in the cells of the dorsal root or cranial nerve ganglia and may reactivate after a period, which may be several decades. Reactivation results in zoster.

Epidemiology

The virus is very infectious, 1 case potentially infecting 10-12 susceptible people (R_0 10-12).

In Ireland, the incidence of varicella is seasonal, reaching a peak from January to April. Transmission is by inhalation of respiratory droplets, by direct contact with vesicular fluid, or by contact with fomites. The incubation period is from 14 to 16 days (range 10-21). This may be prolonged up to 28 days in immunocompromised patients and in individuals who have received specific varicella-zoster immunoglobulin (VZIG).

Cases of varicella are infectious from 2 days before the appearance of the rash until all of the lesions have crusted, typically a total of 7 days. This

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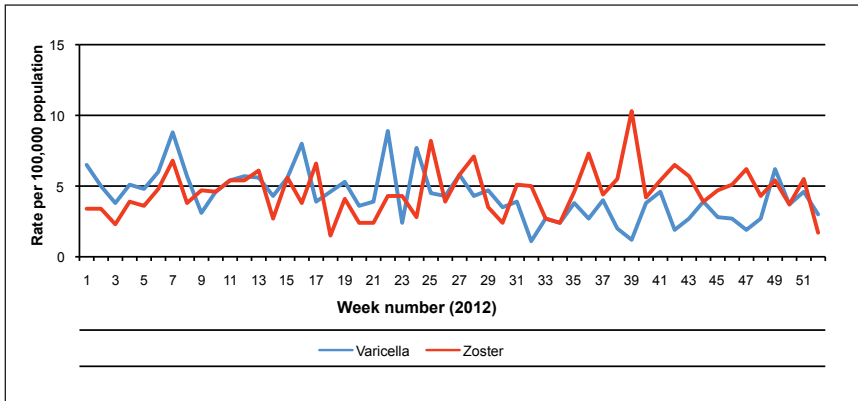
period may be prolonged in immunosuppressed individuals. In the family setting the secondary attack rate ranges from 60-90% for susceptible persons.

VZV can be transmitted from individuals with zoster to non-immune contacts and causes varicella. Such transmission is infrequent and is dependent on direct or indirect contact, including inhalation, from non-intact vesicles. The period of infectivity of zoster is typically 5 days, from the appearance of the lesions until all lesions have crusted. Viral load and/or viral shedding may be increased with increased risk of transmission if the zoster lesions are exposed or disseminated, or in immunosuppressed patients with localised zoster on any part of the body.

In Ireland hospitalised cases of varicella became notifiable in late 2011. Between January – December 2012 there were 81 notifications and one death. This data significantly underestimates the true burden of disease. Varicella and zoster incidence in the community is estimated from data obtained from the sentinel surveillance system of the ICGP/HPSC. This data demonstrates the increased incidence of disease in the winter/ spring period (Figure 23.1).

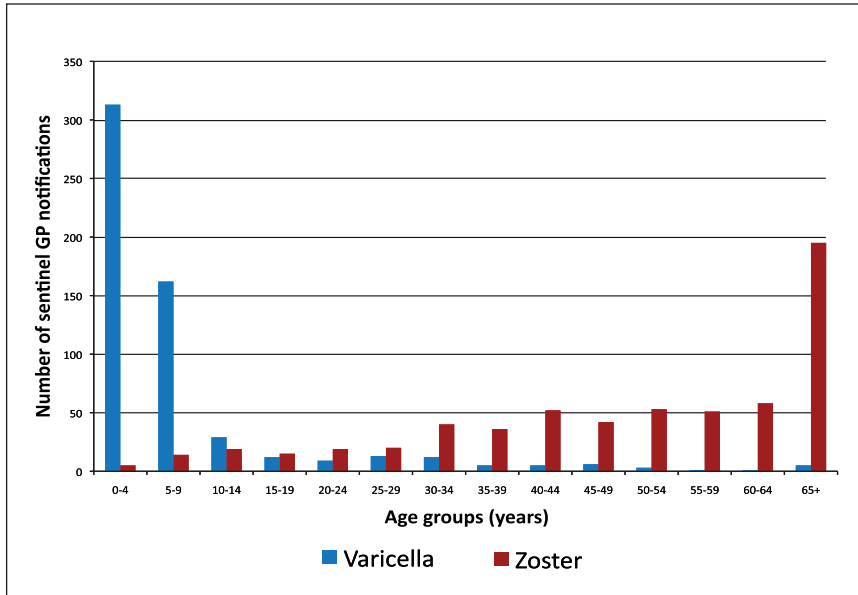
Figure 23.1 Varicella and zoster rates per 100,000 population by week for 2012

Source: ICGP/HPSC sentinel surveillance



Fifty four per cent of varicella cases in 2012 occurred in children <5 years of age. Sixty four per cent of zoster cases reported in 2012 were aged >45 years (Figure 23.2).

Figure 23.2. Varicella and zoster notifications in sentinel GP sites, 2012
Source: ICGP/HPSC sentinel surveillance



Effects of varicella

Varicella is typically a benign infection of childhood characterised by a generalised, pruritic vesicular rash. A mild prodrome of fever and malaise may occur, more commonly in adults. The rash usually starts on the head and progresses to the trunk and extremities. The rash may involve mucous membranes (mouth, respiratory tract, vagina, conjunctiva and cornea). The rash progresses from macules to papules to vesicular lesions that crust over as they dry. Successive crops appear over several days. The number of lesions ranges from a few to hundreds.

In children the clinical course is generally mild with malaise, pruritus and fever for 2-3 days. Complications of varicella are uncommon in childhood and include superinfection (usually with Group A streptococcus), skin scarring, encephalitis, pneumonia, glomerulonephritis, myocarditis, hepatitis and coagulopathy. The risk of complications is higher in infants under 1 year and in persons over 15 years of age, particularly pregnant women, smokers, and the immunocompromised.

In the USA prior to the introduction of routine childhood varicella vaccination, adults had a risk 25 times greater and infants had a risk 4 times greater of dying from varicella than did children 1-4 years old, Since the introduction

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of the vaccine in the U.S. the number of hospitalisations and fatalities from varicella has decreased markedly.

Recovery from primary varicella infection usually results in lifelong immunity. Recurrent disease is rare, but is more likely in immunocompromised individuals.

Infection in pregnancy carries an increased risk of severe varicella pneumonia in the mother, especially late in the second trimester and early in the third trimester. Risks to the foetus and neonate are related to the time of infection in the mother.

In the first 20 weeks of pregnancy maternal infection can result in the congenital (foetal) varicella syndrome, which includes limb hypoplasia, microcephaly, cataracts, growth retardation and skin scarring. The mortality rate in the foetus is high. A large prospective study showed an incidence of <1% in the first 12 weeks, around 2% between 13 and 20 weeks of pregnancy, and no cases of congenital varicella syndrome after 20 weeks gestation.

In the second and third trimester, infection can cause zoster in the foetus. Case reports of chorioretinal damage, microcephaly and skin scarring following maternal varicella between 20 and 28 weeks gestation have been published.

In the week before to a week after delivery, infection in the mother is associated with risk of neonatal infection. The highest risk is associated with maternal infection from 5 days before to 2 days after delivery.

Other groups at increased risk of severe complications include immunocompromised patients, especially those who have leukaemia or other disorders in which there is depressed cell mediated immunity, and transplant recipients.

Effects of zoster

Zoster (Herpes zoster, shingles) occurs as a result of reactivation of VZV which remains latent in the sensory ganglia following varicella. This reactivation occurs when VZV-specific cellular-mediated immunity decreases, mainly due to age-related immunosenescence and immunosuppressive conditions. The individual lifetime risk of developing HZ is between 23.8% and 30%. Two-thirds of HZ cases occur in individuals aged 50 years or over. The risk of zoster in those aged 85 and over is 50%.

Zoster is characterized by a vesicular skin rash localized in the sensory region of the affected ganglia, and is often preceded, or accompanied by acute pain or itching. Headache, photophobia, and malaise may occur in the prodromal phase.

The rash most commonly appears on the trunk along a thoracic dermatome. The rash does not usually cross the midline. Less commonly, the rash can be more widespread and affect three or more dermatomes (disseminated zoster). This generally occurs only in people with compromised immune systems.

New vesicles continue to form over three to five days and progressively dry and crust over. They usually heal in two to four weeks. They may leave permanent pigmentation changes and scarring on the skin.

Post herpetic neuralgia (PHN) is a persistent pain in the area of the rash. PHN can last for weeks or months and occasionally for years. The risk of PHN increases with age. Older adults are more likely to have PHN and to have longer lasting and more severe pain. Approximately 13% (and possibly more) of people 60 years of age and older with herpes zoster will get PHN.

Diagnosis

Diagnosis is primarily clinical. If necessary, diagnosis can be confirmed from swab of vesicle fluid for culture or biopsy for electron microscopy. Serology is also available and can be used to demonstrate immunity.

Varicella vaccine

Varicella zoster vaccine is a live attenuated viral vaccine, derived from the Oka strain of VZV. The vaccine is available as lyophilised preparation for reconstitution with a diluent.

Vaccine efficacy is estimated to be 70-90% against infection, and 90-100% against moderate or severe disease. Vaccine efficacy is lower (~75%) in those aged >13 years. Immunity in most appears to be long lasting, probably lifelong. However, approximately 1% of vaccinees per year have developed mild breakthrough infections.

An up to date list of licensed vaccines can be accessed on the HPRAs website www.hpra.ie

As the vaccine is less stable than other live virus vaccines the storage temperature requirements are critical. The unreconstituted vaccine and its diluent should be stored in the original packaging at +2°C to +8°C and protected from light. After reconstitution the vaccine should be used immediately. Discard any vaccine unused after 30 minutes.

Dose and route of administration

The dose is 0.5 ml given by I.M. or subcutaneous injection into the anterolateral thigh or deltoid region.

Indications

Varicella vaccination is not included as part of the routine childhood immunisation schedule.

However parents may choose to have their child immunised.

PRE-EXPOSURE PROPHYLAXIS

Two doses, at least 4 weeks apart, are recommended for non immune children from 12 months of age and adults in the following risk groups:

1. Health-care workers (HCWs) without a definite history of varicella, proof of immunity or vaccination status, particularly those working with haematology, oncology, obstetric, paediatric or neonatal patients.

A history of varicella is a less reliable predictor of immunity in individuals born and raised overseas, and therefore routine testing should be considered in this group of HCWs. In addition, HCWs from outside Ireland and Western Europe are less likely to be immune.

2. Laboratory staff who may be exposed to varicella virus in the course of their work.
3. Immunocompromised patients. Some immunocompromised patients may be vaccinated, e.g. those with lymphocytic leukaemia in remission, and transplant recipients (see Chapter 3).
4. Close household contacts of immunocompromised patients.
5. HIV infected children (see Chapter 3).
6. Children in residential units for physical and intellectual disability.
7. All women of childbearing age without a history of varicella infection should have their immunity checked.

Women with negative serology should be vaccinated prior to or after pregnancy. Pregnancy should be avoided for 1 month following varicella vaccination

Contraindications

1. Anaphylaxis to any of the vaccine constituents.
2. Immunosuppression (see Chapter 3).

3. Pregnancy should be avoided for 1 month following varicella vaccination.

Precautions

1. Acute severe febrile illness, defer until recovery.
2. Recent (3-11months) receipt of an antibody product (see Chapter 2 Table 2.4).
3. Salicylates should be avoided for 6 weeks after vaccination in children less than 16 years of age (theoretical risk of Reye's syndrome).
4. Persons with active untreated tuberculosis (although there is no evidence that varicella exacerbates tuberculosis).
5. Receipt of some antivirals (e.g. acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination.

The following are NOT contraindications

1. Pregnancy of recipient's mother or other close or household contact*.
2. Immunodeficient family member or household contact.*
3. Treatment with low dose (less than 2 mg/kg/day) alternate-day, topical, replacement, or aerosolised steroid preparations.
4. Asymptomatic or mildly symptomatic HIV infection.
5. Humoral immunodeficiency (e.g. agammaglobulinaemia).
6. Breast feeding.

*If a vaccinee experiences a presumed vaccine-related rash 7-25 days after vaccination, avoid direct contact with immunocompromised persons, non-immune pregnant women and their newborn in the first week of life and non-immune babies in Special Care Baby Units, for the duration of the rash, if possible.

Adverse reactions

Local: pain, redness and swelling are common.

General: Fever over 39°C is common. A localised or generalised maculopapular or papulovesicular rash may develop. Transmission of vaccine virus can occur but the risk is very low and primarily occurs in the presence of a post-vaccination rash (see * above).

Zoster vaccine

Zoster vaccine (Zostavax) is a live attenuated viral vaccine indicated for prevention of zoster and zoster-related post-herpetic neuralgia in those aged ≥ 50 years.

The safety and efficacy of zoster vaccine has not been established in adults who are known to be infected with HIV with or without evidence of immunosuppression.

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An up to date list of licensed vaccines can be accessed on the HPRA website www.hpra.ie

The vaccine should be stored at +2°C to +8°C and protected from light. After reconstitution the vaccine should be used immediately. Discard any vaccine unused after 30 minutes.

Dose and route of administration

One dose (0.65 ml) **subcutaneously**, preferably in the deltoid region.

Indications

Zoster vaccination is not included as part of the routine immunisation schedule. However anyone aged 50 or older may choose to be immunised.

It may be given to those who have had zoster. It is prudent to defer vaccination for 12 months after the zoster has resolved so that the vaccine can produce a more effective immune response.

Contraindications

1. Anaphylaxis to any of the vaccine constituents.
2. Immunosuppression due to disease or treatment (see Chapter 3).
3. Active untreated tuberculosis.
4. Pregnancy. Furthermore, pregnancy should be avoided for 1 month following vaccination.

Precautions

Acute severe febrile illness – defer until recovery.

Concomitant administration with PPV may result in reduced immunogenicity of Zostavax. However, the effectiveness of Zostavax is likely to be similar whether given with or at a different time to PPV.

Note: Zoster vaccine may be given to a recent receipt of an antibody containing blood product. The amount of antigen in zoster vaccine is high enough to offset any effect of circulating antibody. Also, studies of zoster vaccine were performed on patients receiving antibody-containing blood products with no appreciable effect on efficacy.

Adverse reactions:

Local: Pain, erythema and induration are very common.

General: Headache is common. Transmission of vaccine virus may occur rarely between vaccinees and susceptible contacts (for example, VZV-susceptible infant grandchildren).

POST EXPOSURE PROPHYLAXIS

Protection of contacts with varicella zoster immunoglobulin (VZIG)

The aim of post exposure prophylaxis is to protect individuals at high risk of developing severe varicella disease and those who may transmit infection to those at high risk (such as health care workers or household contacts). Antiviral agents may be indicated in those at high risk of complications, e.g. immunocompromised.

Indications

VZIG prophylaxis is recommended for individuals who fulfill all of the following three criteria:

1. Have had significant exposure to varicella or zoster (see Table 23.1)
and
2. Have a clinical condition that increases the risk of severe varicella (e.g. immunocompromised, pregnant women, neonates in the first week of life born to non immune women, babies in Special Care Baby Units)
and
3. Are non-immune (no antibodies to VZ virus).

Significant exposure is defined based on the following:

1. Type of VZV infection in the index case.
2. Timing of exposure in relation to the onset of rash in the index case.
3. Proximity and duration of contact.

Table 23.1. Defining significant exposure

Criteria for defining significant exposure		
Type of VZV infection in index case	Timing of exposure in relation to onset of rash in index case	Proximity and duration of contact (any of the following)
Varicella	From 48 hours before onset of rash until crusting of lesions	Household contact
Disseminated zoster or extensive exposed lesions in an immunocompetent individual	From 48 hours before onset of rash until crusting of lesions. For zoster, from appearance of vesicles until crusting	
Localised exposed zoster	Day of onset of rash until crusting of lesions	Contact in same room* for significant period (usually 1 hour or more)
Localised or disseminated zoster in an immunosuppressed person		Face to face contact such as when having conversation (usually > 5 minutes)

**An example of 'same room' is a classroom or 2-4 bedded hospital bay. However, because airborne transmission at a distance has been reported in large open wards, the need of giving VZIG to all susceptible high-risk contacts should be considered, particularly in paediatric wards where the degree of contact may be difficult to define.*

VZIG is indicated in the following clinical situations:

1. Neonates or infants (see Figure 23.3)

- Neonates who are exposed to varicella
 - in mother from 7 days before to 7 days after delivery.
- VZ antibody-negative infants
 - exposed to varicella or zoster (other than in the mother) in the first 7 days of life.
 - of any age, exposed to varicella or zoster while requiring intensive or prolonged special care nursing.

The risk of severe varicella is greatest for neonates whose mothers develop varicella 5 days before delivery or 2 days after delivery, but VZIG may be beneficial if a mother developed varicella from 7 days before to 7 days after delivery. Approximately half of these infants may develop varicella despite immunoprophylaxis, but the disease is usually modified. IV acyclovir treatment may occasionally be required.

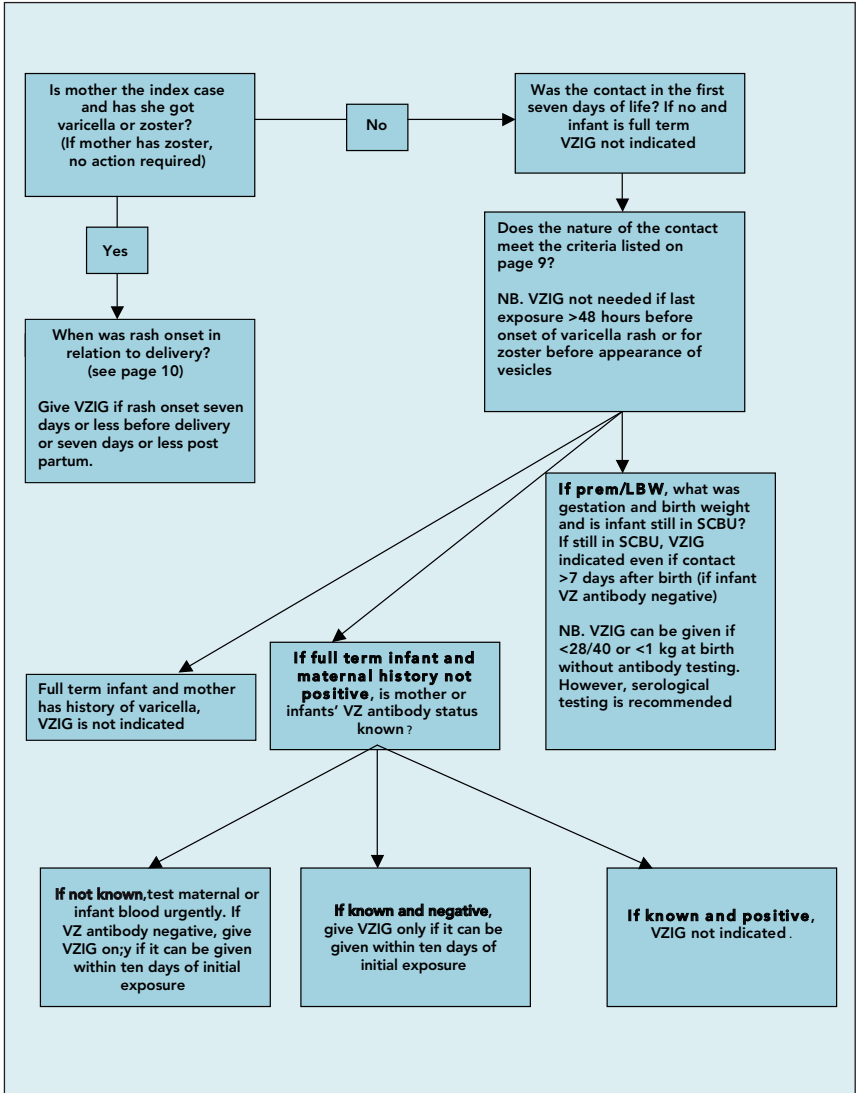
The following infants may not have maternal antibodies despite a positive maternal history of varicella and should be tested to determine their VZ antibody status in the event of a contact:

- born before 28 weeks gestation
- weighed less than 1000g at birth
- more than 60 days old
- have had packed red cell infusion

Other infants whose mothers have a positive history of varicella and/or a positive VZ antibody result will usually have maternal antibody and do not require VZIG.

VZIG is **not** indicated for full-term infants exposed to VZV (either varicella or zoster) more than 7 days after delivery or if exposure was more than 48 hours before onset of rash (varicella) or onset of vesicles (zoster) in index case.

Figure 23.3 Use of VZIG in neonates exposed to VZV

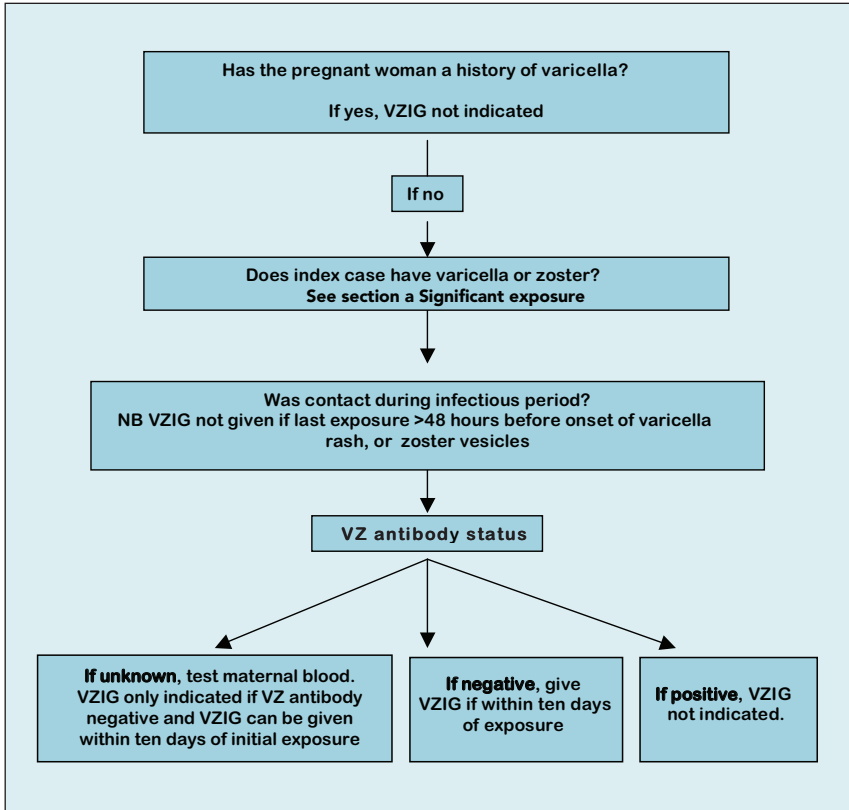


2. Pregnant women (see Figure 23.4)

Non-immune women significantly exposed to varicella **at any stage of pregnancy** should be offered VZIG as soon as possible and ideally within 96 hours of the contact. VZIG BPL product for IM administration can be administered up to 10 days post exposure.

The primary aim of VZIG immunoprophylaxis is to modify the illness in the mother, but severe maternal varicella may still occur despite prophylaxis. There is little evidence that VZIG will prevent the congenital varicella syndrome following significant exposure of a non-immune mother in the first 20 weeks of pregnancy. Management of varicella in pregnancy should be discussed urgently with an obstetrician/microbiologist/ID consultant and consideration given to the use of acyclovir.

Figure 23.4 Use of VZIG if pregnant women exposed to VZV



3. Immunosuppressed patients (see Figure 23.5)

Immunosuppressed patients who are VZ non immune and who have significant exposure to varicella or zoster may require VZIG (see Chapter 3).

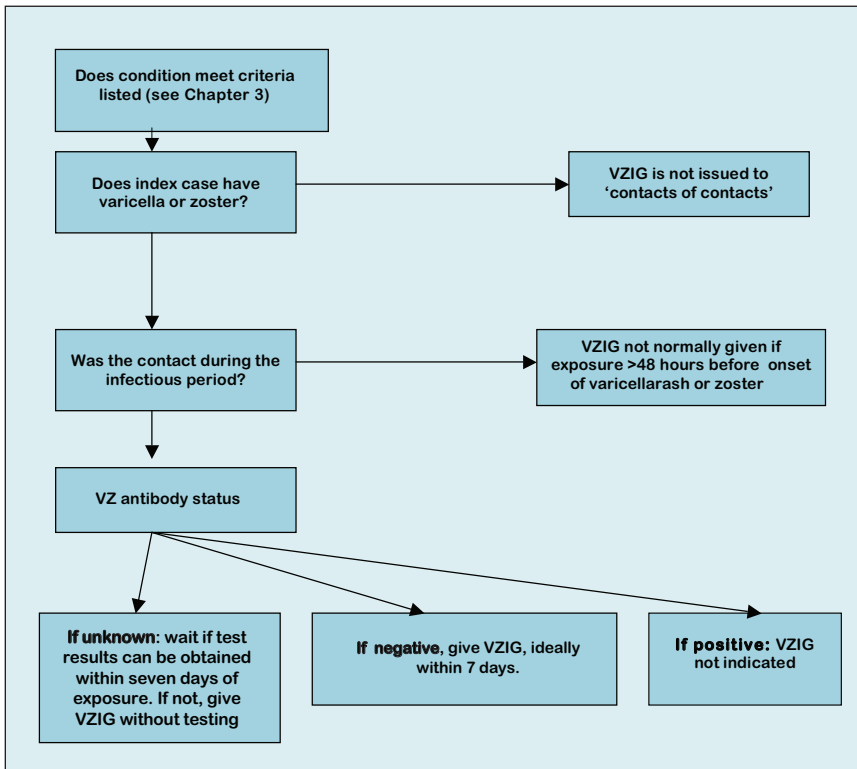
Immunosuppressed contacts should be tested for VZ antibody regardless of history of chickenpox. When antibody is not detected, VZIG is indicated. Testing will rarely be required outside normal working hours. VZIG

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administration should not be delayed >7 days after initial contact. If an immunosuppressed contact is antibody-positive, VZIG is not indicated. Patients with immunoglobulin deficiencies who are receiving replacement therapy with immunoglobulin do not require VZIG.

Immunocompetent contacts with a definite history of varicella are immune; serology or immunoprophylaxis are not necessary. The majority of adults and a substantial proportion of children without a definite history of varicella are VZ antibody positive. Those without a definite history, who are being considered for VZIG, should be tested for VZ antibody; VZ antibody detected in patients who have received blood or blood products in the previous 3 months may have been passively acquired. Re-testing in the event of subsequent exposure is required, as the patient may have become antibody negative.

Figure 23.5 Guidance on use of VZIG if immunocompromised persons exposed to VZV



Two VZIG products are licensed. Either product should be given as soon as possible after exposure, ideally within 96 hours.

1. VZIG (Bio Products Laboratory, BPL) available from Allphar Services Ltd
Contact details Tel: 01 4688451 or email: info@promedicare.ie

This product is dispensed in vials of 250mg (approximately 2–3ml with minimum potency 100 IU of VZ antibody per ml) **It is not suitable for use in infants and younger children due to the volume required.**

Dose and administration

Children and adults 15-25 IU/kg body weight, maximum 625IU by IM injection. If a large volume is required (> 1 ml for young children or > 5 ml for older children and adults) administer in divided doses at different sites.

If intramuscular administration is contra-indicated (significant bleeding disorders) the intravenous VZIG (Varitect) is preferred.

Alternative dose calculation:

0 – 5 Years	250mg (1 vial)
6 – 10 Years	500mg (2 vials)
11 – 14 Years	750mg (3 vials)
15 years and older	1000mg (4 vials)

Give a second dose if further exposure occurs and three weeks have elapsed since the first dose.

2. Intravenous VZIG (Varitect CP) supplied by Aquilant Pharmaceuticals
Contact details Telephone: +353 (1) 452 0388 or email contactus@aquilantpharmaceuticals.ie

This product is available as 5ml (125IU) and 20 ml (500IU) vials
Dose: 25 IU/ kg body weight IV

Patients with immunoglobulin deficiencies who are receiving replacement therapy with immunoglobulin do not require VZIG.

Adverse reactions

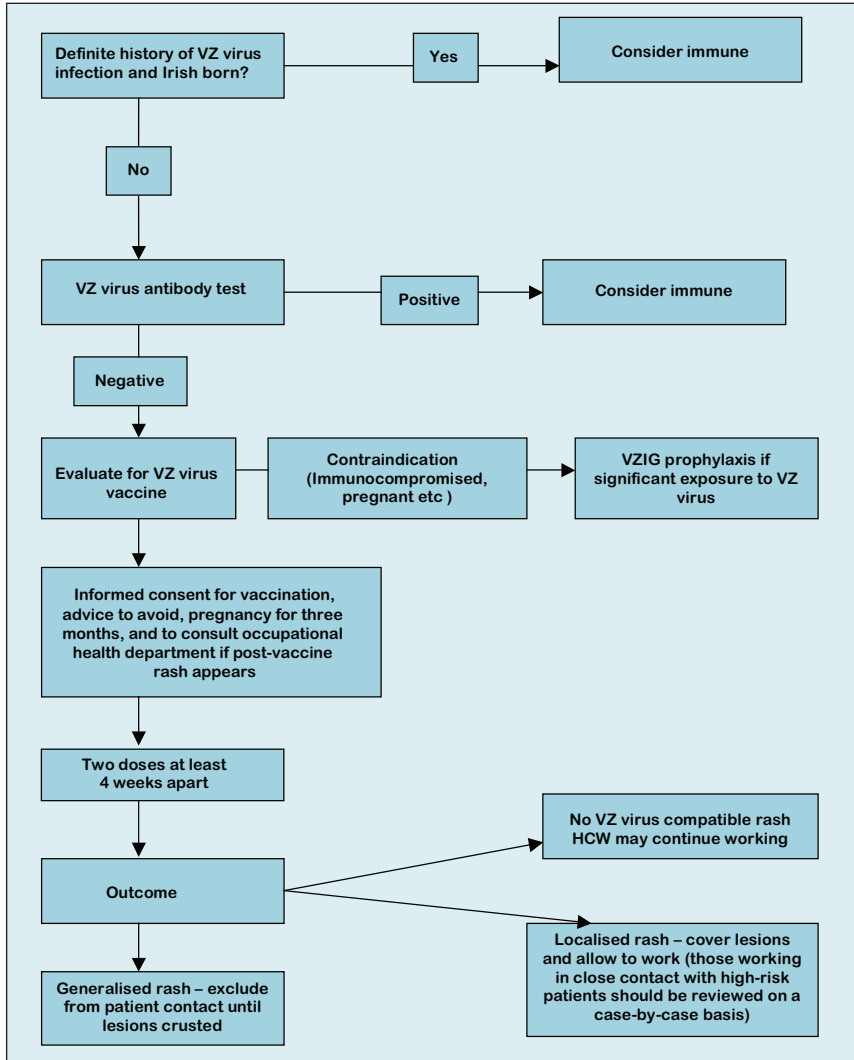
Nausea, chills, fever, headache, vomiting, allergic reactions, arthralgia and mild back pain may occasionally occur. The efficacy of live virus vaccines may be impaired for up to 5 months.

Management of HCW exposure to varicella or zoster (see Figure 23.6)

Non-immune HCWs who have had significant exposure to VZV (see Table 23.1) should be excluded from contact with high-risk patients from 8-21 days after exposure.

HCWs with localised zoster on a part of the body that can be covered with a bandage and/or clothing may be allowed to continue working unless they are in contact with high-risk patients, in which case an individual risk assessment should be carried out.

Figure 23.6 Guidance on management of HCW exposed to VZV



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