34

Varicella

NOTIFIABLE IN SCOTLAND AND NORTHERN IRELAND

The disease

Varicella (chickenpox) is an acute, highly infectious disease caused by the varicella zoster (VZ) virus.

The illness usually starts with one to two days of fever and malaise although this may be absent, particularly in young children. Vesicles begin to appear on the face and scalp, spreading to the trunk and abdomen and eventually to the limbs. After three or four days, the vesicles dry with a granular scab and are usually followed by further crops. Vesicles may be so few as to be missed or so numerous that they become confluent, covering most of the body. Virus is plentiful in the nasopharynx in the first few days and in the vesicles before they dry up; the infectious period is from one to two days before the rash appears until the vesicles are dry. This may be prolonged in immunosuppressed patients. Early treatment with high-dose oral aciclovir and analogues or systemic aciclovir shortens the duration and number of vesicles (Balfour *et al.*, 1992; Dunkle *et al.*, 1991).

Herpes zoster (shingles) is caused by the reactivation of the patient's varicella virus. Virus from lesions can be transmitted to susceptible individuals to cause chickenpox but there is no evidence that herpes zoster can be acquired from another individual with chickenpox. Although more common in the elderly, it can occur in children and is especially common in immunosuppressed individuals of any age. Vesicles appear in the dermatome, representing cranial or spinal ganglia where the virus has been dormant. The affected area may be intensely painful with associated paraesthesia.

Varicella is transmitted directly by personal contact or droplet spread. The incubation period is between one and three weeks. The secondary infection rate from household contact with a case of chickenpox can be as high as 90%. The infection is most common in children below the age of ten, in whom it usually causes mild disease.

The disease can be more serious in adults, particularly pregnant women and those who smoke, as they are at greater risk of fulminating varicella pneumonia. Pregnant women appear to be at greatest risk late in the second or early in the third trimester; of the nine deaths due to varicella in pregnancy in England and Wales between 1985 and 1998, seven occurred between 27 and 32 weeks' gestation (Enders and Miller, 2000). For neonates and immunosuppressed individuals, the risk of disseminated or haemorrhagic varicella is greatly increased.

Risks to the fetus and neonate from maternal chickenpox are related to the time of infection in the mother (Enders *et al*., 1994; Miller *et al*., 1990):

- **in the first 20 weeks of pregnancy** – congenital (fetal) varicella syndrome, which includes limb hypoplasia, microcephaly, cataracts, growth retardation and skin scarring. The mortality rate is high. From the largest available prospective study, the incidence has been estimated to be less than 1% in the first 12 weeks and around 2% between 13 and 20 weeks of pregnancy (Enders *et al*., 1994). In this study, no cases of congenital varicella syndrome occurred among the 477 pregnancies in which maternal varicella occurred after 20 weeks' gestation.
- **in the second and third trimesters of pregnancy** – herpes zoster in an otherwise healthy infant. Occasional cases of fetal damage comprising chorioretinal damage, microcephaly and skin scarring following maternal varicella between 20 and 28 weeks' gestation have been reported (Tan and Koren, 2005), but the risk is likely to be substantially lower than that of the typical congenital varicella syndrome which occurs after maternal varicella in the first 20 weeks' gestation.
- **a week before, to a week after delivery** – severe and even fatal disease in the neonate. Before the introduction of human varicella zoster immunoglobulin (VZIG) in the UK, half the deaths in infants under one year old occurred in those aged less than three weeks in whom infection would have been contracted either before or during birth or in the first week of life.

History and epidemiology of the disease

The incidence of varicella is seasonal and classically reaches a peak from March to May, although in recent years seasonality has been less marked. Since chickenpox is so common in childhood, 90% of adults raised in the UK are immune.

Herpes zoster is less common than chickenpox and the incidence is highest in older people. The incidence of shingles increases with age and around one in four adults will experience an attack in their lifetime (Miller *et al*., 1993).

The varicella vaccination

Varicella vaccines are lyophilised preparations containing live, attenuated virus derived from the Oka strain of varicella zoster virus. Two vaccines are currently available: Varilrix® (Oka-RIT) and Varivax® (Oka/Merck). On reconstitution, both preparations should be given as a 0.5ml dose. Although there are no data on interchangeability, it is likely that a course can be completed effectively with a different vaccine.

Varicella vaccines do not contain thiomersal. They contain live organisms which have been attenuated.

Transmission of vaccine virus from immunocompetent vaccinees to susceptible close contacts has occasionally been documented but the risk is very low. Transmission in the absence of a post-vaccination rash has not been documented (Annunziato and Gershon, 2000).

The two-dose vaccination schedule provides about 98% protection in children (Shapiro *et al.,* 2011) and about 75% protection in adolescents and adults (Annunziato and Gershon, 2000). In both age groups, most of the breakthrough infections are modified and vaccinated individuals who contract varicella have fewer lesions and less systemic upset than unvaccinated individuals.

Human varicella zoster immunoglobulin

Two licensed VZIG preparations are available in the UK: VZIG distributed in England and Wales is made by the Bio Products Laboratory (BPL), Elstree; and in Scotland and Northern Ireland, it is provided by the Protein Fractionation Centre (PFC), Edinburgh.

VZIG is prepared from pooled plasma of non-UK donors with suitably high titres of VZ antibody. The supply of VZIG is limited by the availability of suitable donors and its use is restricted to those at greatest risk and for whom there is evidence that it is likely to be effective.

Because of a theoretical risk of transmission of vCJD from plasma products, VZIG used in the UK is now prepared from plasma sourced from outside the UK, and supplies are scarce. All donors are screened for HIV, hepatitis B and C, and all plasma pools are tested for the presence of RNA from these viruses. A solvent detergent inactivation step for envelope viruses is included in the production process.

Storage

The unreconstituted vaccine and its diluent should be stored in the original packaging at +2˚C to +8˚C and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Effectiveness cannot be guaranteed for vaccines unless they have been stored at the correct temperature. Freezing may cause increased reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents.

VZIG should be stored in a refrigerator between +2˚C and +8˚C. These products are tolerant to ambient temperatures for up to one week. They can be distributed in sturdy packaging outside the cold chain if needed.

Presentation

Varicella vaccines are available as lyophilised preparations for reconstitution with a diluent.

- Varilrix is a pink-coloured pellet, which on reconstitution may vary from a pink to a red solution.
- Varivax is an off-white powder, which on reconstitution produces a clear, colourless to pale yellow liquid.

After reconstitution of the lyophilised suspension, the vaccines must be used within one hour. Discard any unused vaccine one hour following reconstitution.

VZIG is a clear, pale yellow or light brown solution dispensed in vials containing 250mg protein in approximately 2–3ml of fluid (minimum potency 100IU of VZ antibody per ml) with added sodium chloride.

Dosage and schedules

Varicella vaccination

Children from one year of age or older and adults

Children from one year of age or older and adults should receive two doses of varicella vaccine, four to eight weeks apart (and certainly not less than four weeks apart).

Varicella zoster immunoglobulin

The dosage for both the BPL and PFC products are:

- 0–5 years, 250mg (one vial)
- 6–10 years, 500mg (two vials)
- 11–14 years, 750mg (three vials)
- 15 years or over, 1000mg (four vials).

If a second exposure occurs after three weeks, a further dose is required.

Contacts with bleeding disorders who cannot be given an intramusc ular injection should be given intravenous normal immunoglobulin at a dose of 0.2g per kg body weight (i.e. 4ml/kg for a 5% solution) instead. This will produce serum VZ antibody levels equivalent to those achieved with VZIG (Paryani *et al*., 1984).

Administration

Varilrix should only be administered by deep subcutaneous injection.

Varivax can be administered by either intramuscular or deep subcutaneous injection.

Varicella vaccine can, and ideally should (see below), be given at the same time as other live vaccines such as MMR. The vaccines should be given at a separate site, preferably in a different limb. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2003). The site at which each vaccine was given should be noted in the individual's records.

If live vaccines are given simultaneously, then each vaccine virus will begin to replicate and an appropriate immune response is made to each vaccine. After a live vaccine is given, natural interferon is produced in response to that vaccine. If a second live vaccine is given during this response, the interferon may prevent replication of the second vaccine virus. This may attenuate the response to the second vaccine. Based on evidence that MMR vaccine can lead to an attenuation of the varicella vaccine response (Mullooly and Black, 2001), the recommended interval between live vaccines is currently four weeks. For this reason, if live vaccines cannot be administered simultaneously, a four-week interval is recommended.

VZIG is given by intramuscular injection in the upper outer quadrant of the buttock or the anterolateral thigh.

When VZIG is being used for prevention of varicella, it must be remembered that it may interfere with the subsequent development of active immunity from live virus vaccines. If immunoglobulin has been administered first, then an interval of three months should be observed before administering a live virus vaccine. If immunoglobulin has been given within three weeks of administering a live vaccine, then the vaccine should be repeated three months later. This does not apply to yellow fever vaccine since VZIG does not contain significant amounts of antibody to this virus.

Disposal

Equipment used for vaccination, including used vials, ampoules, or partially discharged vaccines should be disposed of at the end of a session by sealing in a proper, puncture-resistant 'sharps' box according to local authority regulations and guidance in the technical memorandum 07-01 (Department of Health, 2006).

Recommendations for the use of the vaccine

Pre-exposure vaccination

The aim of varicella immunisation is to protect from exposure those who are at most risk of serious illness. This is done by immunising specific individuals who are in regular or close contact with those at risk. Since 2003, this recommendation includes vaccinating non-immune healthcare workers who themselves will derive benefit as they will be protected from contact with infectious patients. Varicella vaccine is also recommended for healthy susceptible close household contacts of immunocompromised patients.

Non-immune groups recommended to receive pre-exposure vaccination

Healthcare workers (see Figure 34.1)

The definition of a healthcare worker includes those working in general practice and hospitals who have patient contact, e.g. cleaners on wards, catering staff, ambulance staff, receptionists in general practice, as well as medical and nursing staff, whether employed directly or through contract.

Those with a definite history of chickenpox or herpes zoster can be considered protected. Healthcare workers with a negative or uncertain history of chickenpox or herpes zoster should be serologically tested and vaccine offered only to those without VZ antibody. A recent survey showed that a history of chickenpox is a less reliable predictor of immunity in individuals born and raised overseas (MacMahon *et al*., 2004) and routine testing should be considered.

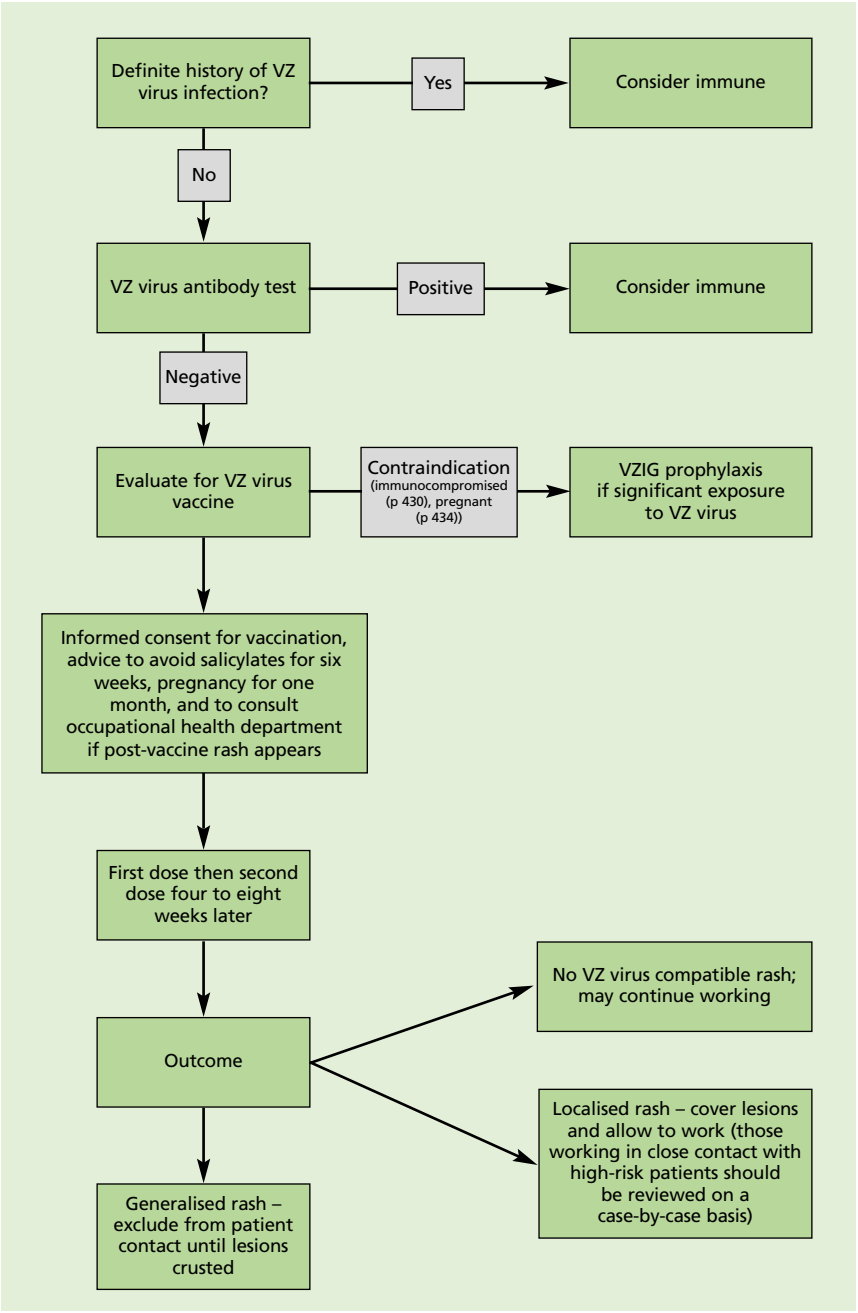

Figure 34.1 Procedure for vaccinating healthcare workers

Healthcare workers should be told at the time of vaccination that they may experience a local rash around the site of injection or a more generalised rash in the month after vaccination. In either case, they should report to their occupational health department for assessment before commencing work. If the rash is generalised and consistent with a vaccine-associated rash (papular or vesicular), the healthcare worker should avoid patient contact until all the lesions have crusted. Healthcare workers with localised vaccine rashes that can be covered with a bandage and/or clothing should be allowed to continue working unless in contact with immunocompromised or pregnant patients. In the latter situation, an individual risk assessment should be made.

Post-vaccination serological testing is not routinely recommended but is advisable in for healthcare workers in units dealing with highly vulnerable patients (e.g. transplant units) (Breuer, 2003).

Occupational health departments should visit the website of the Health Protection Agency (HPA), Varicella Zoster Reference Service, Barts and The London NHS Trust (www.clinical-virology.org/pages/vzrl/vzrl_summary.html) for advice about healthcare workers working with vulnerable patients who fail to seroconvert. Occupational health departments may also obtain advice on the management of vaccine rashes from the reference laboratory at Barts and The London NHS Trust (samples from rashes following vaccine can be sent for analysis to the HPA,Varicella Zoster Reference Service). Instructions and forms for samples are available at www.clinical-virology.org/pages/vzrl/vzrl _summary.html

Laboratory staff

Vaccination should be offered to individuals who may be exposed to varicella virus in the course of their work, in virology laboratories and clinical infectious disease units.

Contacts of immunocompromised patients

Varicella vaccine is not currently recommended for routine use in children. However, it is recommended for healthy susceptible contacts of immunocompromised patients where continuing close contact is unavoidable (e.g. siblings of a leukaemic child, or a child whose parent is undergoing chemotherapy).

Management of at-risk individuals following significant exposure to chickenpox or herpes zoster

The aim of post-exposure management is to protect individuals at high risk of suffering from severe varicella (see below) and those who may transmit infection to those at high risk (e.g. healthcare workers).

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

- significant exposure to chickenpox or herpes zoster
- a clinical condition that increases the risk of severe varicella; this includes immunosuppressed patients, neonates and pregnant women (see below)
- no antibodies to VZ virus (see below).

The post-exposure management algorithms for immunosuppressed patients, neonates and pregnant women, and advice on antibody testing, are summarised below and in Figures 34.2, 34.3 and 34.4.

Definition of a significant exposure to VZ virus

Three aspects of the exposure are relevant:

- **type of VZ infection in the index case:** the risk of acquiring infection from an immunocompetent individual with non-exposed zoster lesions (e.g. thoracolumbar (the trunk)) is remote. The issue of VZIG should be restricted to those in contact with chickenpox, or those in contact with the following:
  - disseminated zoster
  - immunocompetent individuals with exposed lesions (e.g. ophthalmic zoster)
  - immunosuppressed patients with localised zoster on any part of the body (in whom viral shedding may be greater).
- **the timing of the exposure in relation to onset of rash in the index case:** VZIG should normally be restricted to patients exposed to a case of chickenpox or disseminated zoster between 48 hours before onset of rash until crusting of lesions, or day of onset of rash until crusting for those exposed to localised zoster.
- **closeness and duration of contact:** the following should be used as a guide to the type of exposure, other than maternal/neonatal and continuous home contact, that requires VZIG prophylaxis:

- contact in the same room (e.g. in a house or classroom or a two- to four-bed hospital bay) for a significant period of time (15 minutes or more).
- face-to-face contact, e.g. while having a conversation
- in the case of large open wards, airborne transmission at a distance has occasionally been reported and 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).

Management of immunosuppressed patients

Immunosuppressed patients are described in detail in Chapter 6. They include:

- patients with evidence of severe primary immunodeficiency, for example, severe combined immunodeficiency (SCID), Wiskott-Aldrich syndrome and other combined immunodeficiency syndromes
- all patients currently being treated for malignant disease with immunosuppressive chemotherapy or radiotherapy, and for at least six months after terminating such treatment
- all patients who have received a solid organ transplant and are currently on immunosuppressive treatment
- patients who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer where the patient has developed graft-versus-host disease. The decision to vaccinate should depend upon the type of transplant and immune status of the patient. Further advice can be found in current guidance produced by the European Group for Blood and Marrow Transplantation (www.ebmt.org) and the Royal College of Paediatrics and Child Health (www.rcpch.ac.uk)
- all patients receiving systemic high-dose steroids until at least three months after treatment has stopped. This would include children who receive prednisolone, orally or rectally, at a daily dose (or its equivalent) of 2mg/kg/day for at least one week, or 1mg/kg/day for one month. For adults, an equivalent dose is harder to define but immunosuppression should be considered in those who receive 40mg of prednisolone per day for more than one week. Occasionally, there may be individuals on lower doses of steroids who may be immunosuppressed, and are at increased risk from infections. Therefore, live vaccines should be considered with caution in discussion with a relevant specialist physician
- patients receiving other types of immunosuppressive drugs (e.g. azathioprine, ciclosporin, methotrexate, cyclophosphamide, leflunomide and the newer cytokine inhibitors) alone or in combination with lower

doses of steroids. The advice of the physician or immunologist in charge should be sought for at least six months after treatment
- patients with immunosuppression due to HIV infection (see section below).

Note: Patients with gammaglobulin deficiencies who are receiving replacement therapy with intravenous normal immunoglobulin do not require VZIG (see below).

Determination of VZ immune status

Whenever possible, immunosuppressed contacts should be tested irrespective of their history of chickenpox. However, VZIG administration should not be delayed past seven days after initial contact while an antibody test is done. Under these circumstances, VZIG should be given on the basis of a negative history of chickenpox. If the patient has a positive history of chickenpox, wait for the antibody results. Those with a positive history in whom VZ antibody is not detected by a sensitive assay should be given VZIG.

VZIG is not indicated in immunosuppressed contacts with detectable antibody as the amount of antibody provided by VZIG will not significantly increase VZ antibody titres in those who are already positive. Second attacks of chickenpox can occasionally occur in immunosuppressed VZ antibody positive patients, but these are likely to be related to defects in cell-mediated immunity.

Management of neonates

VZIG is recommended for infants whose mothers develop chickenpox (but not herpes zoster) in the period seven days before to seven days after delivery. VZIG can be given without antibody testing of the infant.

VZIG is not usually required for infants born more than seven days after the onset of maternal chickenpox or whose mothers develop zoster before or after delivery, as these infants will have maternal antibody.

VZIG is also recommended for:

- VZ antibody-negative infants exposed to chickenpox or herpes zoster (other than in the mother) in the first seven days of life
- VZ antibody-negative infants of any age, exposed to chickenpox or herpes zoster while still requiring intensive or prolonged special care nursing.

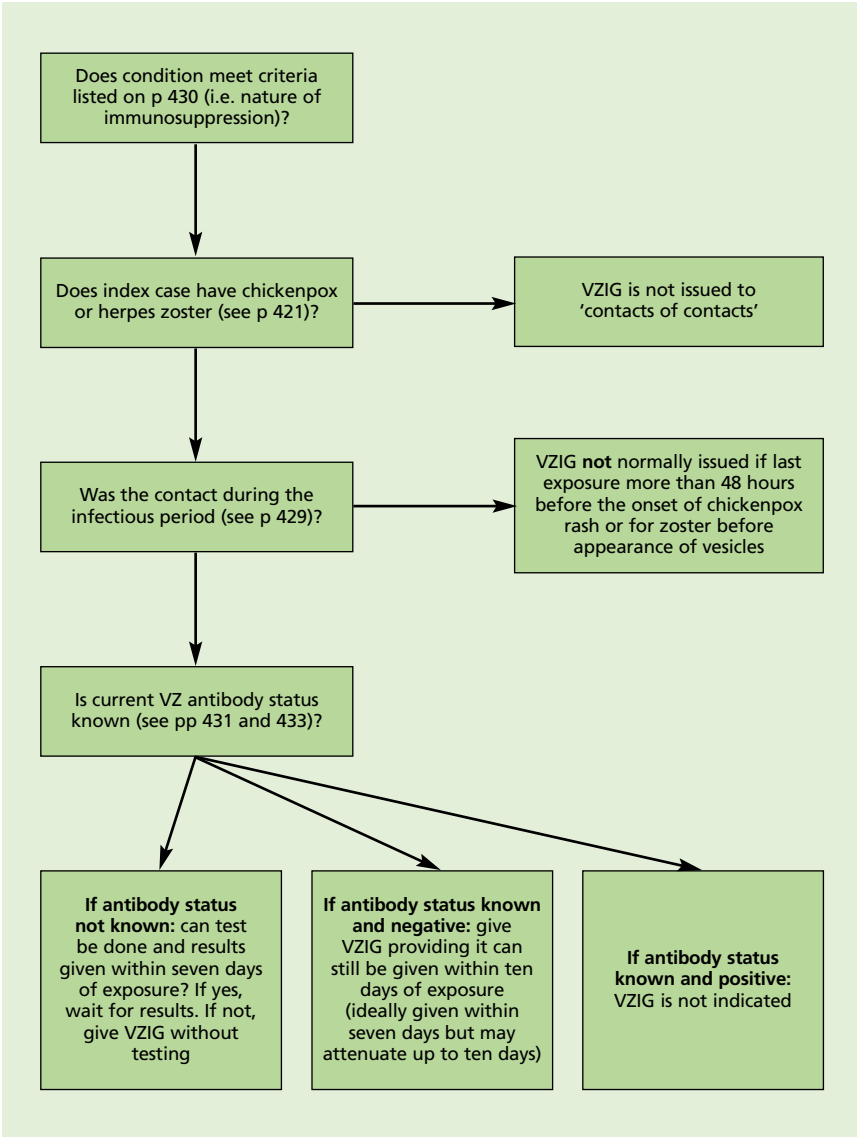

Figure 34.2 VZIG algorithm for immunocompromised patients who have been exposed to varicella zoster

For infants in these two exposure groups who were born before 28 weeks' gestation, or weighed less than 1000g at birth, or are more than 60 days old, or have had repeated blood sampling with replacement by packed red cell infusion, maternal antibodies may not be present despite a positive maternal history of chickenpox (Patou *et al*., 1990; Gold *et al*., 1993). It is recommended that, where possible, such infants are tested to determine their VZ antibody status in the event of a contact. Other infants whose mothers have a positive history of chickenpox and/or a positive VZ antibody result will usually have maternal antibody and do not require VZIG.

Management of pregnant women

VZIG is recommended for VZ antibody-negative pregnant contacts exposed at any stage of pregnancy, providing VZIG can be given within ten days of contact. However, when supplies of VZIG are short, issues to pregnant women may be restricted. Clinicians are advised to check availability of VZIG (see 'Supplies' below) before offering it to pregnant women.

Pregnant contacts with a positive history of chickenpox do not require VZIG. Those with a negative history must be tested for VZ antibody before VZIG is given (see below). The outcome in pregnant women is not adversely affected if administration of VZIG is delayed up to ten days after initial contact (Enders and Miller, 2000; Miller *et al*., 1993). There is still time to test for VZ antibody even when the woman presents relatively late after contact.

Determination of VZ immune status

The majority of adults and a substantial proportion of children without a definite history of chickenpox will be VZ antibody positive. One UK study found that 11% of children aged 1 to 5 years, 37% aged 6 to 16 years and 89% of adults given VZIG on the basis of a negative history of chickenpox were VZ antibody positive (Evans *et al*., 1980). To prevent wastage of VZIG, all individuals being considered for VZIG should have a serum sample tested for VZ antibody; only those without antibody require VZIG. If urgent VZ antibody testing is required for patients presenting late, VZIG can be ordered (see 'Supplies' below) at the same time that the blood is sent for testing and can be returned if the result is positive. VZ antibody testing should be available within 24 to 48 hours – seek advice from the local HPA or NHS laboratory.

VZ antibody detected in patients who have been transfused or who have received intravenous immunoglobulin in the previous three months may have been passively acquired. Although VZIG is not indicated if

antibody from other blood products is detectable, re-testing in the event of a subsequent exposure will be required, as the patient may have become antibody negative.

About 15% of patients given VZIG who remain symptom-free after a home contact will have had a sub-clinical infection and will seroconvert asymptomatically (Evans *et al*., 1980; Miller *et al*., 1993). Patients who have received VZIG in the past following a close exposure should be re-tested for VZ antibody in the event of another exposure.

Effectiveness of VZIG prophylaxis

Immunosuppressed patients

About half of susceptible immunosuppressed home contacts will develop clinical chickenpox despite VZIG prophylaxis, and a further 15% will be infected sub-clinically (Evans *et al*., 1980). Severe or fatal varicella can occur despite VZIG prophylaxis. Immunocompromised contacts given VZIG should still be monitored and aciclovir should be used at the first signs of illness.

Neonates

About half of neonates exposed to maternal varicella will become infected despite VZIG prophylaxis (Miller *et al*., 1990). In up to two-thirds of these infants, infections are mild or asymptomatic but rare fatal cases have been reported despite VZIG prophylaxis in those with onset of maternal chickenpox in the period four days before to two days after delivery. Early treatment with intravenous aciclovir is recommended for infants in this exposure category who develop varicella despite VZIG prophylaxis.

Pregnant women

The rationale for the use of VZIG prophylaxis in pregnant women is twofold: reduction in severity of maternal disease and reduction of risk of fetal infection for women contracting varicella in the first 20 weeks of pregnancy. The risk of fatal varicella is estimated to be about five times higher in pregnant than non-pregnant adults with fatal cases concentrated late in the second or early in the third trimester (Enders and Miller, 2000).

One study showed a significant reduction in the risk of congenital VZ virus infection in women who developed varicella after VZIG prophylaxis compared with women who developed varicella without VZIG prophylaxis; however, the study was too small to assess whether the risk of congenital varicella syndrome was reduced (Enders *et al*.,1994). A case of congenital

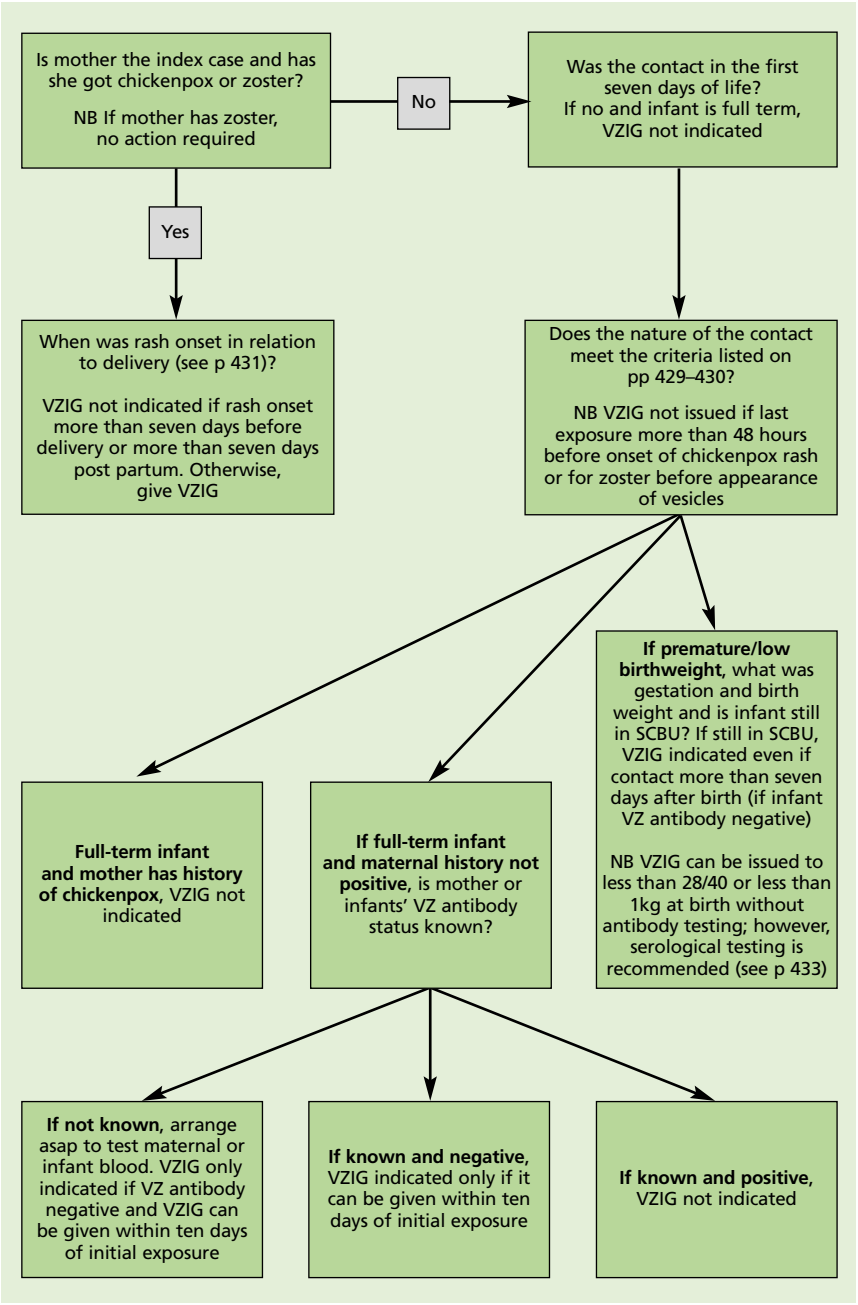

Figure 34.3 VZIG algorithm for neonates

varicella syndrome has been reported in the infant of a woman exposed at the eleventh week of gestation and who developed clinical varicella despite post-exposure prophylaxis with VZIG (Pasturszak *et al*., 1994).

About 50% of susceptible pregnant women given VZIG after a household exposure to chickenpox will develop clinical varicella, although the disease may be attenuated; the clinical attack rates are similar whether VZIG is given within 72 hours or four to ten days after contact (Enders and Miller, 2000; Miller *et al*., 1993). A further quarter will be infected sub-clinically (Miller *et al*., 1993). Severe maternal varicella may still occur despite VZIG prophylaxis. Prompt treatment with aciclovir is indicated in such cases.

Management of healthcare workers exposed to VZ virus infection

Vaccinated healthcare workers or those with a definite history of chickenpox or zoster and having a significant exposure to VZ virus (as above and including those dressing localised zoster lesions on non-exposed areas of the body) should be considered protected and be allowed to continue working. As there is a remote risk that they may develop chickenpox, they should be advised to report to their occupational health department for assessment before having patient contact if they feel unwell or develop a fever or rash.

Unvaccinated healthcare workers without a definite history of chickenpox or zoster and having a significant exposure to VZ virus (see above) should either be excluded from contact with high-risk patients from eight to 21 days after exposure, or should be advised to report to their occupational health department before having patient contact if they feel unwell or develop a fever or rash. There is some evidence that varicella vaccine administered within three days of exposure may be effective in preventing chickenpox (Ferson, 2001). (Varivax® is licensed for post-exposure prophylaxis.) In any case, irrespective of the interval since exposure, vaccine should be offered to reduce the risk of the healthcare workers exposing patients to VZ virus in the future (see above).

Management of healthcare workers with herpes zoster

Healthcare workers with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing should 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.

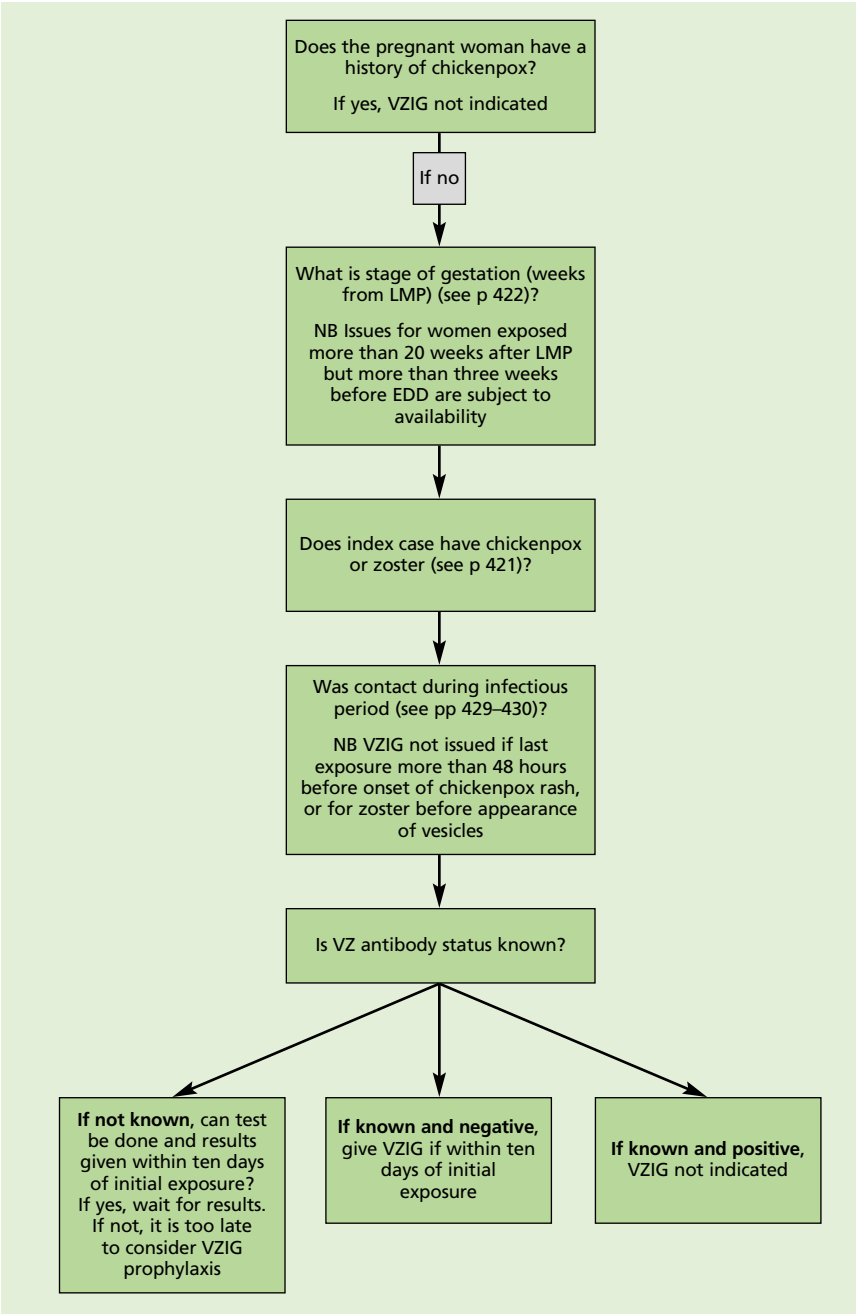

Figure 34.4 VZIG algorithm for pregnant women

Contraindications

The vaccine should not be given to:

- immunosuppressed patients. For patients who require protection against chickenpox, seek advice from a specialist
- women who are pregnant. Pregnancy should be avoided for one month following the last dose of varicella vaccine (see below)

or to those who have had:

- a confirmed anaphylactic reaction to a previous dose of the vaccine
- a confirmed anaphylactic reaction to any component of the vaccine, including neomycin or gelatin.

Precautions

Unless protection is needed urgently, immunisation should be postponed in acutely unwell individuals until they have recovered fully. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any sign or symptoms to the adverse effects of the vaccine.

Pregnancy and breast-feeding

Women who are pregnant should not receive varicella vaccine and pregnancy should be avoided for one month following the last dose.

Studies have shown that the vaccine virus is not transferred to the infant through breast milk (Bohlke *et al*., 2003) and therefore breast-feeding women can be vaccinated if indicated.

Inadvertent vaccination in pregnancy

Surveillance of cases of inadvertent vaccination in pregnancy in the US has not identified any specific risk to the fetus. Follow-up to March 2002 of 697 women in the US who were vaccinated with Oka/Merck strain (Varivax®) while pregnant has identified no cases of congenital varicella in any liveborn infant. In addition, the rate of occurrence of congenital anomalies was similar to that reported in the general population (Merck Research Laboratories, 2003). However, it is nevertheless important to record such cases and to document the outcome of pregnancy. Surveillance of inadvertent vaccination in pregnancy is being established by the Immunisation Department of the HPA, Centre for Infections, to whom such cases should be reported (Tel: 020 8200 6868, ext 74405). Any such cases in Scotland should be reported to Health Protection Scotland (HPS) (Tel: 0141 300 1191) and in Wales, cases should be reported to the National Public Health Service for

Wales (Tel: 01352 700227 ext 4055). These will, in turn, contribute to the UK figures via the Immunisation Department of the HPA.

Immunosuppression and HIV infection

Varicella vaccine is contraindicated in immunosuppressed patients. For patients who require protection against chickenpox, seek advice from a specialist.

Further guidance is provided by the Royal College of Paediatrics and Child Health (www.rcpch.ac.uk), the British HIV Association (BHIVA) *Immunisation guidelines for HIV-infected adults* (BHIVA, 2006) and the Children's HIV Association of UK and Ireland (CHIVA) immunisation guidelines (www.bhiva.org/chiva).

Use of salicylates

Aspirin and systemic salicylates should not be given to children under 16 years of age, except under medical supervision. Vaccination with varicella vaccine is not contraindicated in individuals aged 16 years or over who need to take aspirin.

Adverse reactions

Varicella vaccines are well tolerated. Extensive clinical and post-marketing safety surveillance data from the US (for the Oka/Merck strain, Varivax®) shows the most commonly reported reactions are at the injection site (pain, redness and rash). Generalised symptoms, such as fever and rash, can also occur but less frequently. Management of these reactions in healthcare workers is detailed below.

Up to 10% of adults and 5% of children develop a vaccine-associated rash, either localised at the injection site or generalised, within one month of immunisation (Annunziato and Gershon, 2000). Varicella vaccine rashes may be papular or vesicular. Illness associated with the vaccine can be treated with aciclovir. It is important to determine whether the rash is due to the vaccine virus or to coincidental wild-type chickenpox. Samples from rashes following vaccine should be sent for analysis to the HPA Varicella Zoster Reference Service at Barts and The London NHS Trust (www.clinical-virology. org/pages/vzrl/vzrl_summary.html).

The vaccine virus strain can establish latent infection and reactivate to cause herpes zoster in immunocompetent individuals, but the risk is substantially lower than with wild varicella infection. Cases of zoster occurring in a vaccinee should be investigated and samples should be sent to the HPA Varicella Zoster Reference Service, as above.

Transmission of vaccine virus from immunocompetent vaccinees to susceptible close contacts has occasionally been documented but the risk is very low. Transmission in the absence of a post-vaccination rash has not been documented (Annunziato and Gershon, 2000).

All suspected reactions in children and severe suspected reactions in adults should be reported to the Commission on Human Medicines using the Yellow Card scheme.

Safety of VZIG

VZIG is well tolerated. Very rarely anaphylactoid reactions occur in individuals with hypogammaglobulinaemia who have IgA antibodies, or in those who have had an atypical reaction to blood transfusion.

No cases of blood-borne infection acquired through immunoglobulin preparations designed for intramuscular use have been documented in any country.

Treatment

VZIG has no place in the treatment of severe disease.

Supplies

Vaccines

- Varivax® – manufactured by Sanofi Pasteur MSD (Tel: 0800 085 5511).
- Varilrix® – manufactured by GlaxoSmithKline (Tel: 0808 100 9997).

VZIG

England and Wales: available from HPA Colindale (Tel: 020 8327 7471), HPA laboratories and selected NHS hospitals.

Northern Ireland: available from Specialist Medicines, Pharmacy Department, Royal Group of Hospitals Trust, Grosvenor Road, Belfast BT12 6BA (Tel: 028 9063 5872).

Scotland: available from regional transfusion centres.

Aberdeen and North East of Scotland Blood Transfusion Centre
Foresterhill Road
Foresterhill
Aberdeen AB9 2ZW
(Tel: 01224 685685)

North of Scotland Blood Transfusion Centre
Raigmore Hospital
Inverness IV2 3UJ
(Tel: 01463 704212)

Dundee and East of Scotland Blood Transfusion Centre
Ninewells Hospital
Dundee DD1 9SY
(Tel: 01382 645166)

The West of Scotland Blood Transfusion Centre
Gartnavel General Hospital
25 Shelly Road
Glasgow G12 0XB
(Tel: 0141 357 7700)

Edinburgh and South East of Scotland Blood Transfusion Centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh EH16 4SA
(Tel: 0131 242 7520 (Irene McKechnie))

VZIG is issued free of charge to patients who meet the criteria given above. Clinicians who wish to issue VZIG for patients not meeting these criteria should approach the manufacturer directly to purchase a dose.

No other licensed VZIG preparations for intramuscular use apart from the BPL and PFC products are available in the UK.

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