Royal College of Obstetricians & Gynaecologists

# Chickenpox in Pregnancy

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# Chickenpox in Pregnancy

This is the fourth edition of this guideline, originally published in 1997 and reviewed in 2001 and 2007 under the same title.

## Executive summary of recommendations

*Varicella prevention*

Can the non-immune woman be immunised prior to pregnancy or postnatally?

**Varicella vaccination prepregnancy or postpartum is an option that should be considered for women who are found to be seronegative for varicella-zoster virus immunoglobulin G (VZV IgG).** D

**While universal serological antenatal testing is not recommended in the UK (see below), seronegative women identified in pregnancy could be offered postpartum immunisation.** D

**Women who are vaccinated postpartum can be reassured that it is safe to breastfeed.** D

Can varicella be prevented in the pregnant woman at her initial antenatal visit?

**Women booking for antenatal care should be asked about previous chickenpox/shingles infection.** D

**Women who have not had chickenpox, or are known to be seronegative for chickenpox, should be advised to avoid contact with chickenpox and shingles during pregnancy and to inform healthcare workers of a potential exposure without delay.** ✓

Can varicella infection be prevented in the pregnant woman who gives a history of contact with chickenpox or shingles?

**When contact occurs with chickenpox or shingles, a careful history must be taken to confirm the significance of the contact and the susceptibility of the patient.** ✓

**Pregnant women with an uncertain or no previous history of chickenpox, or who come from tropical or subtropical countries, who have been exposed to infection should have a blood test to determine VZV immunity or non-immunity.** ✓

**If the pregnant woman is not immune to VZV and she has had a significant exposure, she should be offered varicella-zoster immunoglobulin (VZIG) as soon as possible. VZIG is effective when given up to 10 days after contact (in the case of continuous exposures, this is defined as 10 days from the appearance of the rash in the index case).** D

**Non-immune pregnant women who have been exposed to chickenpox should be managed as potentially infectious from 8–28 days after exposure if they receive VZIG and from 8–21 days after exposure if they do not receive VZIG.** D

**When supplies are limited, issues to pregnant women may be restricted and clinicians are advised to establish the availability of VZIG before offering it to pregnant women.** D

**Women who have had exposure to chickenpox or shingles (regardless of whether or not they have received VZIG) should be asked to notify their doctor or midwife early if a rash develops.** ✓

**A pregnant woman who develops a chickenpox rash should be isolated from other pregnant women when she attends a general practice surgery or a hospital for assessment.** ✓

 

**A second dose of VZIG may be required if a further exposure is reported and 3 weeks have elapsed since the last dose.** ✓

### *The pregnant woman who develops chickenpox*

#### What are the maternal risks of varicella in pregnancy?

**Clinicians should be aware of the increased morbidity associated with varicella infection in adults, including pneumonia, hepatitis and encephalitis. Rarely, it may result in death.** C

#### How should the pregnant woman who develops chickenpox be cared for?

**Pregnant women who develop a chickenpox rash should immediately contact their general practitioner.** ✓

**Women should avoid contact with potentially susceptible individuals, e.g. other pregnant women and neonates, until the lesions have crusted over. This is usually about 5 days after the onset of the rash.** ✓

**Symptomatic treatment and hygiene is advised to prevent secondary bacterial infection of the lesions.** ✓

**Oral aciclovir should be prescribed for pregnant women with chickenpox if they present within 24 hours of the onset of the rash and if they are 20$^{+0}$ weeks of gestation or beyond. Use of aciclovir before 20$^{+0}$ weeks should also be considered.** C

**Aciclovir is not licensed for use in pregnancy and the risks and benefits of its use should be discussed with the woman.** ✓

**Intravenous aciclovir should be given to all pregnant women with severe chickenpox.** D

**VZIG has no therapeutic benefit once chickenpox has developed and should therefore not be used in pregnant women who have developed a chickenpox rash.** D

#### Should women be referred to hospital?

**The pregnant woman with chickenpox should be asked to contact her doctor immediately if she develops respiratory symptoms or any other deterioration in her condition. Women who develop the symptoms or signs of severe chickenpox should be referred immediately to hospital.** D

**A hospital assessment should be considered in a woman at high risk of severe or complicated chickenpox even in the absence of concerning symptoms or signs. This assessment needs to take place in an area where she will not come into contact with other pregnant women. Appropriate treatment should be decided in consultation with a multidisciplinary team that includes an obstetrician or fetal medicine specialist, a virologist and a neonatologist.** ✓

**Women hospitalised with varicella should be nursed in isolation from babies, potentially susceptible pregnant women or non-immune staff.** ✓

#### When and how should the woman with chickenpox be delivered?

**The timing and mode of delivery of the pregnant woman with chickenpox must be individualised.** D

**When epidural or spinal anaesthesia is undertaken in women with chickenpox, a site free of cutaneous lesions should be chosen for needle placement.** D

 

*Risks of maternal varicella infection to the fetus or baby*

What are the risks to the fetus of varicella infection in pregnancy and can they be prevented or ameliorated?

**Women should be advised that the risk of spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester.** C

**If the pregnant woman develops varicella or shows serological conversion in the first 28 weeks of pregnancy, she has a small risk of fetal varicella syndrome (FVS) and she should be informed of the implications.** C

Can varicella infection of the fetus be diagnosed prenatally?

**Women who develop chickenpox in pregnancy should be referred to a fetal medicine specialist, at 16–20 weeks or 5 weeks after infection, for discussion and detailed ultrasound examination.** ✓

**Given that amniocentesis has a strong negative predictive value but a poor positive predictive value in detecting fetal damage that cannot be detected by non-invasive methods, women who develop varicella infection during pregnancy should be counselled about the risks versus benefits of amniocentesis to detect varicella DNA by polymerase chain reaction (PCR).** ✓

**Amniocentesis should not be performed before the skin lesions have completely healed.** ✓

What are the neonatal risks of varicella infection in pregnancy and can they be prevented or ameliorated?

**If maternal infection occurs in the last 4 weeks of a woman's pregnancy, there is a significant risk of varicella infection of the newborn. A planned delivery should normally be avoided for at least 7 days after the onset of the maternal rash to allow for the passive transfer of antibodies from mother to child, provided that continuing the pregnancy does not pose any additional risks to the mother or baby.** D

**A neonatologist should be informed of the birth of all babies born to women who have developed chickenpox at any gestation during pregnancy.** ✓

**Women with chickenpox should breastfeed if they wish to and are well enough to do so.** ✓

## 1. Purpose and scope

Varicella, the primary infection with varicella-zoster virus (VZV; human herpesvirus 3), in pregnancy may cause maternal mortality or serious morbidity. It may also cause fetal varicella syndrome (FVS) and varicella infection of the newborn, which includes congenital varicella syndrome (CVS) and neonatal varicella. This guideline addresses the role of varicella vaccination in susceptible women of reproductive age. The guideline also assesses the evidence regarding the maternal and fetal risks of VZV infection in pregnancy and whether or not these complications can be prevented or modified beneficially by the administration of varicella-zoster immunoglobulin (VZIG) or by treatment of infected individuals with aciclovir. This information should guide the prudent use of VZIG, which is manufactured from the plasma of human blood donors and hence is a limited and expensive resource. The management of neonates is outside the scope of this guideline. Guidance on neonatal exposure and disease is available from other sources.[1,2]

## 2. Introduction and background epidemiology

VZV is a DNA virus of the herpes family that is highly contagious and transmitted by respiratory droplets and by direct personal contact with vesicle fluid or indirectly via fomites (e.g. skin cells, hair, clothing and bedding). The primary infection is characterised by fever, malaise and a pruritic rash that develops into crops of maculopapules, which become vesicular and crust over before healing. The incubation

 

period is between 1 and 3 weeks and the disease is infectious 48 hours before the rash appears and continues to be infectious until the vesicles crust over. The vesicles usually crust over within 5 days.

Chickenpox (or primary VZV infection) is a common childhood disease that usually causes a mild infection. Over 90% of individuals over 15 years of age in England and Wales are seropositive for VZV immunoglobulin G (IgG) antibody.[3] Studies of pregnant women in Spain and France found that 96.1% and 98.8% respectively were immune to varicella.[4,5] For this reason, although contact with chickenpox is common in pregnancy, especially in women with young children, primary VZV infection in pregnancy is uncommon; it is estimated to complicate 3 in every 1000 pregnancies.[6] Women from tropical and subtropical areas are more likely to be seronegative for VZV IgG and are therefore more susceptible to the development of chickenpox in pregnancy.[7]

Following the primary infection, the virus remains dormant in sensory nerve root ganglia but can be reactivated to cause a vesicular erythematous skin rash in a dermatomal distribution known as herpes zoster, also called 'zoster' or 'shingles'. The risk of acquiring infection from an immunocompetent individual with herpes zoster in non-exposed sites (e.g. thoracolumbar) is remote but can occur.[8] However, disseminated zoster or exposed zoster (e.g. ophthalmic) in any individual or localised zoster in an immunosuppressed patient should be considered to be infectious as the viral shedding may be greater.[1]

## 3. Identification and assessment of evidence

The Cochrane Library, including the Cochrane Central Register of Controlled Trials, was searched for relevant randomised controlled trials, systematic reviews and meta-analyses. A search of MEDLINE and PubMed (electronic databases) from 1966 to January 2013 was also carried out. The databases were searched using the relevant Medical Subject Headings (MeSH) terms, including all subheadings, and this was combined with a keyword search using the terms 'chickenpox', 'varicella zoster' and 'pregnancy'.

The definitions of the types of evidence used in this guideline originate from the Scottish Intercollegiate Guidelines Network (SIGN) Grading Review Group.[9] Where possible, recommendations are based on and explicitly linked to the evidence that supports them. Recommendations lacking evidence are highlighted and annotated as 'Good Practice Points'.

## 4. Varicella prevention

### *4.1 Can the non-immune woman be immunised prior to pregnancy or postnatally?*

**Varicella vaccination prepregnancy or postpartum is an option that should be considered for women who are found to be seronegative for VZV IgG.** **D**

**While universal serological antenatal testing is not recommended in the UK (see below), seronegative women identified in pregnancy could be offered postpartum immunisation.** **D**

**Women who are vaccinated postpartum can be reassured that it is safe to breastfeed.** **D**

Varicella vaccine contains live attenuated virus derived from the Oka strain of VZV and has been licensed for use in the USA since March 1995. Following its introduction, the incidence of primary infection (chickenpox) in the general population has fallen by over 80% and the mortality related to the condition has decreased by two-thirds.[10] Immunity from the vaccine persists for up to 20 years.[11,12] Two varicella vaccines are licensed for use in the UK for the prevention of chickenpox: Varivax® (Oka/Merck; Sanofi Pasteur MSD Limited, Maidenhead, Berkshire, UK) and Varilrix® (Oka-RIT; GlaxoSmithKline UK, Uxbridge, Middlesex, UK). Both are live attenuated vaccines administered in two separate doses 4–8 weeks apart.

Evidence level 2+

 

The varicella immune status of women planning a pregnancy or receiving treatment for infertility can be determined by obtaining a past history of chickenpox and by testing the serum for varicella antibodies in those who have no history or an uncertain history of previous infection. In 2009, the UK National Screening Committee reviewed the evidence for antenatal screening for susceptibility to varicella-zoster infection. The committee concluded that there was insufficient evidence to support antenatal screening because of a lack of reliable information on the true incidence of VZV infection in pregnancy and on the outcomes following treatment.[13]

Evidence level 4

An economic model of postpartum vaccination of women who are seronegative for chickenpox indicates that it is cost-effective.[15] However, this is currently not listed as an indication for varicella immunisation in the National Health Service and women in this category may have to discuss the provision of free vaccination with their general practitioners.[1]

If a woman of reproductive age is vaccinated, she should be advised to avoid pregnancy for 4 weeks after completing the two-dose vaccine schedule and to avoid contact with susceptible pregnant women should a post-vaccination rash occur. Transmission of vaccine virus is rare, despite it being a live attenuated virus. Inadvertent exposures to the vaccine in pregnancy have been reported to a register. There have been no cases of FVS and no increase in the risk of fetal abnormality above the background risk.[14]

Evidence level 2–

Small studies have not detected the varicella vaccine in the breast milk of women who have been vaccinated postpartum.[16,17]

Evidence level 3

### *4.2 Can varicella be prevented in the pregnant woman at her initial antenatal visit?*

**Women booking for antenatal care should be asked about previous chickenpox/shingles infection.** D

**Women who have not had chickenpox, or are known to be seronegative for chickenpox, should be advised to avoid contact with chickenpox and shingles during pregnancy and to inform healthcare workers of a potential exposure without delay.** ✓

A previous history of chickenpox infection had a 97.9–99.7% positive predictive value for the presence of serum varicella antibodies in women booking for antenatal care in the USA.[18] In a study of British healthcare workers, 95% of those who reported previous chickenpox infection had antibodies.[19] Individuals born and raised in tropical climates are less likely to be immune to varicella[7,20] and a history of chickenpox can be a less reliable predictor of immunity in this population.[19] It may be appropriate to undertake serum screening routinely in this group of women. If seronegativity is identified, postpartum vaccination could be considered.

Evidence level 3

### *4.3 Can varicella infection be prevented in the pregnant woman who gives a history of contact with chickenpox or shingles?*

**When contact occurs with chickenpox or shingles, a careful history must be taken to confirm the significance of the contact and the susceptibility of the patient.** ✓

**Pregnant women with an uncertain or no previous history of chickenpox, or who come from tropical or subtropical countries, who have been exposed to infection should have a blood test to determine VZV immunity or non-immunity.** ✓

**If the pregnant woman is not immune to VZV and she has had a significant exposure, she should be offered VZIG as soon as possible. VZIG is effective when given up to 10 days after contact (in the case of continuous exposures, this is defined as 10 days from the appearance of the rash in the index case).** D

 

**Non-immune pregnant women who have been exposed to chickenpox should be managed as potentially infectious from 8–28 days after exposure if they receive VZIG and from 8–21 days after exposure if they do not receive VZIG.** D

**When supplies are limited, issues to pregnant women may be restricted and clinicians are advised to establish the availability of VZIG before offering it to pregnant women.** D

**Women who have had exposure to chickenpox or shingles (regardless of whether or not they have received VZIG) should be asked to notify their doctor or midwife early if a rash develops.** ✓

**A pregnant woman who develops a chickenpox rash should be isolated from other pregnant women when she attends a general practice surgery or a hospital for assessment.** ✓

**A second dose of VZIG may be required if a further exposure is reported and 3 weeks have elapsed since the last dose.** ✓

The history must be confirmed with particular respect to:

- the type of VZV infection
- the timing of the exposure
- the closeness and duration of contact.

Chickenpox is infectious for 2 days before the appearance of the rash and for the duration of the illness while the skin lesions are active. It ceases to be infectious when the lesions have crusted over. Herpes zoster (shingles) also poses a risk if it is disseminated or it occurs in an exposed area of the body (e.g. ophthalmic shingles) or in an immunocompromised individual where viral shedding may be greater. The risk of infection following contact with herpes zoster that is not in an exposed area (e.g. thoracolumbar shingles) is remote but can occur.[8] Evidence level 4

Significant contact is defined as contact in the same room for 15 minutes or more, face-to-face contact or contact in the setting of a large open ward.[1] The susceptibility of the woman should then be determined by eliciting a past history of chickenpox or shingles. If there is a definite past history of chickenpox, it is reasonable to assume that she is immune to varicella infection. If the woman's immunity to chickenpox is unknown and if there is any doubt about previous infection, or if there is no previous history of chickenpox or shingles, serum should be tested for VZV IgG. This can usually be performed within 24–48 hours and often within a few hours if the laboratory can access serum stored from an antenatal booking blood sample. At least 80% of women tested will have VZV IgG and can be reassured.[21]

If the pregnant woman is not immune to VZV and she has had a significant exposure to chickenpox or shingles, she should be offered VZIG as soon as possible or at the very latest within 10 days of the exposure (in the case of continuous household exposures, within 10 days of appearance of the rash in the index case).[22] VZIG is indicated after significant exposure to VZV at any stage of pregnancy, and postnatally if birth occurs within 10 days of exposure.[22] If the immune status of the woman is unknown, the administration of VZIG can be delayed until serology results are available (if the laboratory turnaround time is 24–48 hours). The rationale for administration of VZIG is that it may prevent or attenuate chickenpox in non-immune individuals[1] and it may reduce the risk of development of FVS.[23] In an observational study of 212 seronegative women who received an appropriate dose of VZIG, either intramuscular or intravenous, within 10 days of significant exposure to chickenpox, half of the women developed either a normal or an attenuated form of chickenpox and a further 5% had a subclinical infection.[24] A recent meta-analysis of three case series has shown that 0/142 babies of women who developed varicella during pregnancy despite receiving VZIG suffered from FVS, compared with 14/498 (2.8%) among those who did not receive VZIG.[23] However, a case Evidence level 3

 

series of 106 women who developed chickenpox in the first 20 weeks of pregnancy included five women who had been treated with VZIG, one of whom delivered a baby with congenital varicella syndrome.[25] This evidence supports the use of VZIG to prevent FVS but is based on observational data and may be subject to reporting bias.

Evidence level 3

VZIG is a human immunoglobulin product manufactured from the plasma of non-UK donors with high VZV antibody titres. Issues to pregnant women may be restricted when supplies are limited and hence clinicians are advised to establish the availability of VZIG before offering it to pregnant women.[1]

Evidence level 4

Adverse effects of VZIG include pain and erythema at the injection site. The risk of anaphylaxis is cited as less than 0.1% by the US Centers for Disease Control and Prevention[26] and 'very rare' by Public Health England.[1] Patients with hypogammaglobinaemia with immunoglobulin A antibodies who are already receiving replacement therapy with immunoglobulin do not require VZIG and are at increased risk of anaphylactic reactions. No case of blood-borne infection has been reported with the use of VZIG.[1]

Evidence level 3

Susceptible women who have had contact with chickenpox or shingles (regardless of whether or not they have received VZIG) should be asked to notify their doctor or midwife early if a rash develops. Despite the benefits of VZIG in preventing or attenuating the disease, pregnant women may still become seriously ill.

## 5. The pregnant woman who develops chickenpox

### *5.1 What are the maternal risks of varicella in pregnancy?*

**Clinicians should be aware of the increased morbidity associated with varicella infection in adults, including pneumonia, hepatitis and encephalitis. Rarely, it may result in death.**

C

Although varicella infection is much less common in adults than in children, it is associated with a greater morbidity, namely pneumonia, hepatitis and encephalitis. As recently as the 1990s, chickenpox resulted in the deaths of 25 people per year in England and Wales; 80% of these deaths occurred in adults.[27]

The incidence of pneumonia complicating varicella in pregnancy has been quoted at 10–14%,[28] but these rates are based on small case series. In a series of 347 cases of varicella infection in pregnancy, prospectively documented, 5% of women developed pneumonia.[29] The overall mortality rate in case series of varicella pneumonia in pregnancy published in the English language literature in the pre-antiviral era was 10/28 (36%), which may reflect publication bias.[30] More recent case series report mortality rates of 0–14%, with improvements attributed to antiviral therapy and improved intensive care.[29,31,32] Between 1985 and 1999 there were nine indirect maternal deaths and one late maternal death reported in the UK from complications of maternal varicella infection,[33–37] suggesting a low case fatality rate. There has been no maternal death from varicella reported in the subsequent confidential enquiries.[38–40] Pneumonia may be more severe at later gestational ages due to the effects of the gravid uterus on respiratory function.[28]

Evidence level 2+

### *5.2 How should the pregnant woman who develops chickenpox be cared for?*

**Pregnant women who develop a chickenpox rash should immediately contact their general practitioner.**

✓

 

**Women should avoid contact with potentially susceptible individuals, e.g. other pregnant women and neonates, until the lesions have crusted over. This is usually about 5 days after the onset of the rash.** ✓

**Symptomatic treatment and hygiene is advised to prevent secondary bacterial infection of the lesions.** ✓

**Oral aciclovir should be prescribed for pregnant women with chickenpox if they present within 24 hours of the onset of the rash and if they are 20$^{+0}$ weeks of gestation or beyond. Use of aciclovir before 20$^{+0}$ weeks should also be considered.** C

**Aciclovir is not licensed for use in pregnancy and the risks and benefits of its use should be discussed with the woman.** ✓

**Intravenous aciclovir should be given to all pregnant women with severe chickenpox.** D

**VZIG has no therapeutic benefit once chickenpox has developed and should therefore not be used in pregnant women who have developed a chickenpox rash.** D

Aciclovir is a synthetic nucleoside analogue that inhibits replication of the varicella-zoster virus. A randomised controlled trial has shown that aciclovir administered orally (800 mg five times a day for 7 days) reduces the duration of fever and symptomatology of varicella infection in immunocompetent adults if commenced within 24 hours of developing the rash when compared to placebo. This randomised controlled trial did not have sufficient power to comment on the impact of early oral aciclovir on the serious complications of chickenpox.[41]

Evidence level 1–

Data are accumulating to suggest that there is no increase in the risk of major fetal malformation with aciclovir exposure in pregnancy.[42–44] A Danish registry-based cohort study of 837 795 live births between 1996 and 2008[43] reported the pregnancy outcome in 1804 pregnancies exposed to aciclovir, valciclovir or famciclovir in the first trimester. The rate of major birth defects in the exposed group was 2.2% compared to 2.4% in the unexposed (adjusted prevalence odds ratio 0.89, 95% CI 0.65–1.22). The most common antiviral drug used was aciclovir. Among 1561 pregnancies exposed to aciclovir, 32 babies (2.0%) had a major anomaly compared with 2.4% of controls. The study is limited in that it is based on records of prescriptions that were filled and this is indirect evidence of exposure. In addition, the study did not have the power to exclude an increased risk of any individual defect.[44]

Evidence level 2–

While some multidisciplinary publications[45–47] recommend the use of antiviral agents in all pregnant women with chickenpox, the Swiss and Canadian national guidelines dissent.[48,49] The UK Advisory Group on Chickenpox recommends oral aciclovir for pregnant women with chickenpox if they present within 24 hours of the onset of the rash and if they are more than 20 weeks of gestation.[50] Use of aciclovir before 20 weeks should also be considered.[51] Guidelines are unanimous, however, in recommending that intravenous aciclovir be administered in cases of severe maternal infection.[45–50]

Evidence level 4

VZIG is recommended for post-exposure prophylaxis and is not appropriate treatment for patients with clinical chickenpox.[1] This recommendation is based on the opinion of experts and reflects the accepted understanding of how VZIG works.

### *5.3 Should women be referred to hospital?*

**The pregnant woman with chickenpox should be asked to contact her doctor immediately if she develops respiratory symptoms or any other deterioration in her condition. Women who develop the symptoms or signs of severe chickenpox should be referred immediately to hospital.** D

 

**A hospital assessment should be considered in a woman at high risk of severe or complicated chickenpox even in the absence of concerning symptoms or signs. This assessment needs to take place in an area where she will not come into contact with other pregnant women. Appropriate treatment should be decided in consultation with a multidisciplinary team that includes an obstetrician or fetal medicine specialist, a virologist and a neonatologist.** ✓

**Women hospitalised with varicella should be nursed in isolation from babies, potentially susceptible pregnant women or non-immune staff.** ✓

Respiratory symptoms, neurological symptoms such as photophobia, seizures or drowsiness, a haemorrhagic rash or bleeding, or a dense rash with or without mucosal lesions are indicative of potentially life-threatening chickenpox and are indications for referral to a hospital with intensive care access. If the woman smokes cigarettes, has chronic lung disease, is immunosuppressed (including those who have taken systemic corticosteroids in the preceding 3 months) or is in the second half of pregnancy, a hospital assessment should be considered even in the absence of complications.[50] Evidence level 4

### *5.4 When and how should the woman with chickenpox be delivered?*

**The timing and mode of delivery of the pregnant woman with chickenpox must be individualised.** D

**When epidural or spinal anaesthesia is undertaken in women with chickenpox, a site free of cutaneous lesions should be chosen for needle placement.** D

Depending on the severity of the maternal condition, a respiratory physician and intensive care specialist may be involved in peripartum care. Delivery during the viraemic period, while the chickenpox vesicles are active, may be extremely hazardous. Delivery may precipitate maternal haemorrhage and/or coagulopathy due to thrombocytopenia or hepatitis. There is also a high risk of varicella infection of the newborn with significant morbidity and mortality.[52,53] Supportive treatment and intravenous aciclovir are therefore desirable, allowing resolution of the rash, immune recovery and transfer of protective antibodies from the mother to the fetus. Ideally, a minimum of 7 days should elapse between onset of the rash and delivery. However, delivery may be required to facilitate assisted ventilation in cases where varicella pneumonia is complicated by respiratory failure. Evidence level 3

There is no evidence available to inform decisions about the optimum method of anaesthesia for women requiring delivery by caesarean section. General anaesthesia may exacerbate the respiratory compromise associated with varicella pneumonia. There is a theoretical risk of transmitting the varicella-zoster virus from skin lesions to the central nervous system via spinal anaesthesia. As the dura is not penetrated, epidural anaesthesia may be safer than spinal anaesthesia, however the larger needle required for epidural anaesthesia carries the theoretical risk of transferring a greater viral load from the skin to the epidural space. A site free of cutaneous lesions should be chosen for needle placement.[54]

## 6. Risks of maternal varicella infection to the fetus or baby

### *6.1 What are the risks to the fetus of varicella infection in pregnancy and can they be prevented or ameliorated?*

**Women should be advised that the risk of spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester.** C

**If the pregnant woman develops varicella or shows serological conversion in the first 28 weeks of pregnancy, she has a small risk of FVS and she should be informed of the implications.** C

 

Spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester.[25]

Evidence level 2–

FVS is characterised by one or more of the following: skin scarring in a dermatomal distribution; eye defects (microphthalmia, chorioretinitis or cataracts); hypoplasia of the limbs; and neurological abnormalities (microcephaly, cortical atrophy, mental retardation or dysfunction of bowel and bladder sphincters).[25,55] It does not occur at the time of initial fetal infection but results from a subsequent herpes zoster reactivation in utero and only occurs in a minority of infected fetuses.

Evidence level 2+

FVS has been reported to complicate maternal chickenpox occurring as early as 3 weeks[55] and as late as 28 weeks[56] of gestation. Pooled data from nine cohort studies detected 13 cases of FVS following 1423 cases of maternal chickenpox occurring before 20 weeks of gestation: an incidence of 0.91%.[28] The risk appears to be lower in the first trimester (0.55%).[28] These cohort studies identified one case of FVS occurring among approximately 180 women who developed chickenpox between 20 and 28 weeks of gestation.[28] In addition, this review identified seven case reports of FVS following maternal infection from 20–28 weeks and one where maternal infection occurred at 28 weeks.[28,56] These case reports provide no denominators, so an incidence rate for FVS following late second trimester infection cannot be quoted, but they make the point that FVS is not confined to cases of maternal infection before 20 weeks. The observational evidence presented in section 4.3 suggests that post-exposure prophylaxis in susceptible pregnant women reduces the risk of developing FVS.

Evidence level 2–

### *6.2 Can varicella infection of the fetus be diagnosed prenatally?*

**Women who develop chickenpox in pregnancy should be referred to a fetal medicine specialist, at 16–20 weeks or 5 weeks after infection, for discussion and detailed ultrasound examination.** ✓

**Given that amniocentesis has a strong negative predictive value but a poor positive predictive value in detecting fetal damage that cannot be detected by non-invasive methods, women who develop varicella infection during pregnancy should be counselled about the risks versus benefits of amniocentesis to detect varicella DNA by polymerase chain reaction (PCR).** ✓

**Amniocentesis should not be performed before the skin lesions have completely healed.** ✓

Prenatal diagnosis of FVS is possible by ultrasound when findings such as limb deformity, microcephaly, hydrocephalus, soft tissue calcification and fetal growth restriction can be detected. A time lag of at least 5 weeks after the primary maternal infection is advised because ultrasound performed at 4 weeks has failed to detect the abnormalities.[57] Fetal magnetic resonance imaging (MRI) may provide additional information in cases where ultrasound has identified morphological abnormalities.[58]

Evidence level 4

VZV DNA can be detected in amniotic fluid by PCR. The presence of VZV DNA has a high sensitivity but a low specificity for the development of FVS. In one observational study,[59] nine (8.4%) out of 107 women who developed chickenpox before 24 weeks of gestation had VZV DNA detected in the amniotic fluid. Amniotic fluid PCR for VZV DNA correctly identified the two cases of FVS that occurred in this series, but was positive in seven other cases, five of which ended in the birth of a normal baby, one in a termination where there was no evidence of FVS in the fetus and one where intrauterine death occurred in a baby with triploidy and no evidence of FVS.

Evidence level 3

Ultrasound was abnormal in two of the nine cases with positive VZV PCR: a case where FVS was confirmed following termination of pregnancy and a case where ultrasound showed

 

microcalcifications of the liver but no evidence of FVS at delivery. One of the two cases of FVS, a baby born at term with bilateral micropthalmia, was not detected by ultrasound. No case of FVS occurred when amniocentesis was negative for VZV DNA.[59] The negative predictive value of this combination of amniotic fluid PCR testing and ultrasound is good but the positive predictive value is poor.

Evidence level 3

### 6.3. *What are the neonatal risks of varicella infection in pregnancy and can they be prevented or ameliorated?*

**If maternal infection occurs in the last 4 weeks of a woman's pregnancy, there is a significant risk of varicella infection of the newborn. A planned delivery should normally be avoided for at least 7 days after the onset of the maternal rash to allow for the passive transfer of antibodies from mother to child, provided that continuing the pregnancy does not pose any additional risks to the mother or baby.**

D

**A neonatologist should be informed of the birth of all babies born to women who have developed chickenpox at any gestation during pregnancy.**

✓

**Women with chickenpox should breastfeed if they wish to and are well enough to do so.**

✓

Varicella infection of the newborn (previously called congenital varicella) refers to VZV infection in early neonatal life resulting from maternal infection near the time of delivery or immediately postpartum, or from contact with a person other than the mother with chickenpox or shingles during this time. The route of infection could be transplacental, ascending vaginal or result from direct contact with lesions during or after delivery. If maternal infection occurs 1–4 weeks before delivery, up to 50% of babies are infected and approximately 23% develop clinical varicella, despite high titres of passively acquired maternal antibody. Severe chickenpox is most likely to occur if the infant is born within 7 days of onset of the mother's rash or if the mother develops the rash up to 7 days after delivery.[52] For babies born to mothers who have had chickenpox within the period 7 days before to 7 days after delivery, it is therefore vital that the neonate receives prophylaxis as soon as possible with VZIG with or without aciclovir; there is no need to test in these circumstances.[1,2]

Evidence level 3

Women with chickenpox should breastfeed if they wish to and are well enough to do so. If there are active chickenpox lesions close to the nipple, they should express breast milk from the affected breast until the lesions have crusted over. The expressed breast milk may be fed to the baby who is receiving treatment with VZIG and/or aciclovir.[22]

Evidence level 4

## 7. Recommendations for future research

- A randomised controlled trial should be performed in a population of women who were not born in the UK, comparing a policy of serological screening at the antenatal booking visit with the current practice of testing only if a varicella contact occurs. Measurable outcomes would be use of VZIG, rates of postnatal vaccination and cost.
- Given the apparent equipoise in the literature regarding the benefit or otherwise of aciclovir, women with mild cases of chickenpox in pregnancy could be recruited to a randomised controlled trial of oral aciclovir versus placebo.

## 8. Auditable topics

- The proportion of pregnant women who are not immune to VZV who are offered VZIG following a significant exposure (100%).

 

- The proportion of women who develop chickenpox in pregnancy who are referred to a fetal medicine specialist at 16–20 weeks of gestation or 5 weeks after infection (100%).
- The proportion of pregnant women with severe chickenpox who are given intravenous aciclovir (100%).
- The proportion of cases where a neonatologist has been informed of the birth of a baby born to a woman who developed chickenpox during pregnancy (100%).

## 9. Useful links and support groups

- NHS Choices. *What are the risks of chickenpox during pregnancy?* [http://www.nhs.uk/chq/pages/1109.aspx?categoryid=54&subcategoryid=137]
- RCOG patient information leaflet. *Chickenpox in pregnancy: what you need to know* [https://www.rcog.org.uk/en/patients/patient-leaflets/chickenpox-in-pregnancy/]
- Royal College of Physicians, Faculty of Occupational Medicine, NHS Plus. *Varicella zoster virus: occupational aspects of management. A national guideline*. London: RCP; 2010 [https://www.rcplondon.ac.uk/sites/default/files/varicella-zoster-guidelines-web-navigable.pdf].

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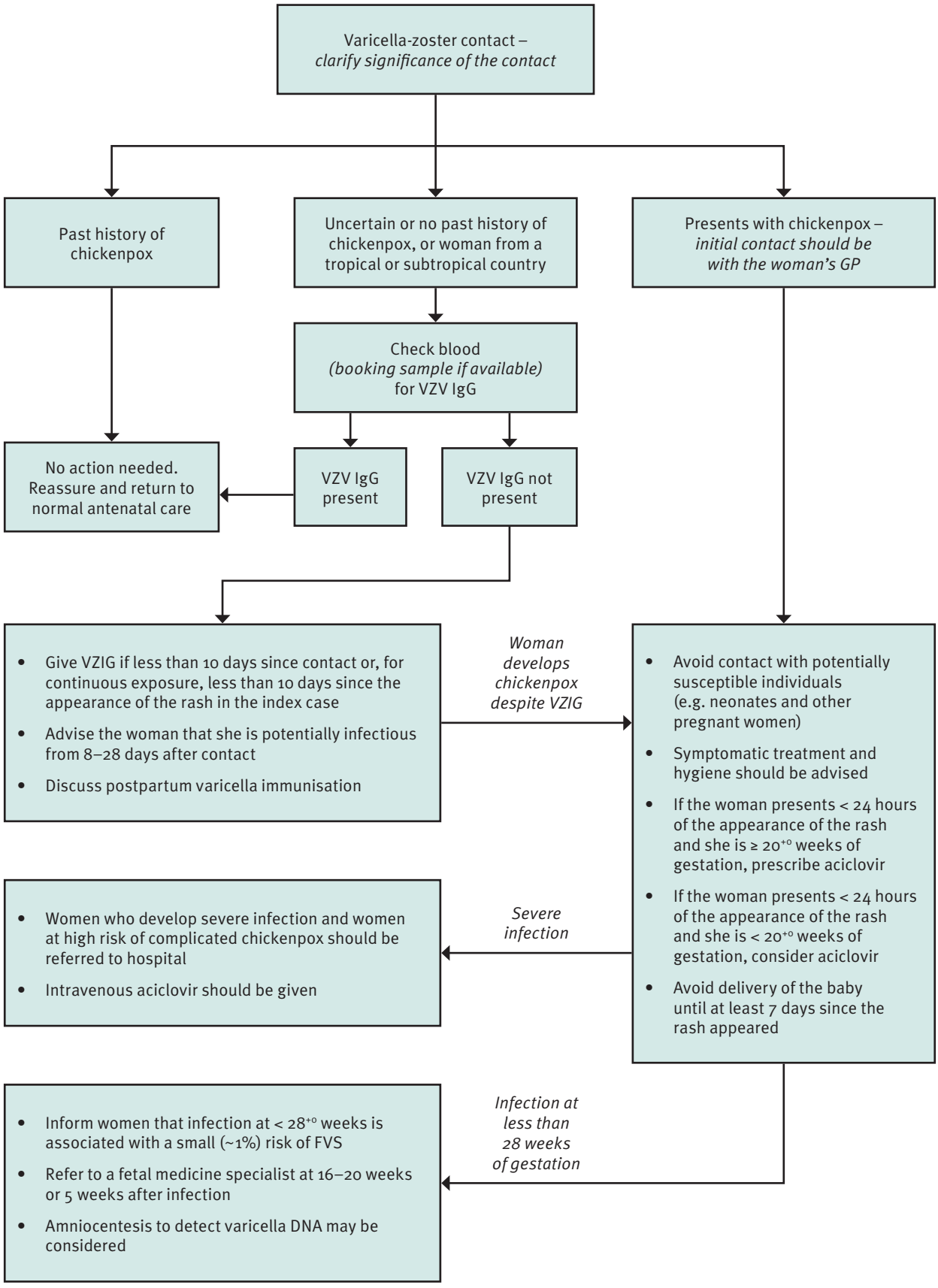
## Appendix I: Algorithm for the management of varicella-zoster contact in pregnancy




**Abbreviations:** FVS fetal varicella syndrome; GP general practitioner; IgG immunoglobulin G; VZIG varicella-zoster immunoglobulin; VZV varicella-zoster virus

## Appendix II: Explanation of guidelines and evidence levels

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1 *Development of RCOG Green-top Guidelines* (available on the RCOG website at http://www.rcog.org.uk/green-top-development). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

### Classification of evidence levels

| | |
|---|---|
| 1++ | High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias |
| 1+ | Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias |
| 1– | Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias |
| 2++ | High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+ | Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2– | Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal |
| 3 | Non-analytical studies, e.g. case reports, case series |
| 4 | Expert opinion |

### Grades of recommendations

| | |
|---|---|
| A | At least one meta-analysis, systematic reviews or randomised controlled trial rated as 1++, and directly applicable to the target population; or<br><br>A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results |
| B | A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as 1++ or 1+ |
| C | A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as 2++ |
| D | Evidence level 3 or 4; or<br>Extrapolated evidence from studies rated as 2+ |

### Good practice point

| | |
|---|---|
| ✓ | Recommended best practice based on the clinical experience of the guideline development group |

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