Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

CLINICAL PRACTICE GUIDELINE

CHICKENPOX IN PREGNANCY

Institute of Obstetricians and Gynaecologists,
Royal College of Physicians of Ireland
and the
Clinical Strategy and Programmes Division,
Health Service Executive

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Contents

1. Revision History

Version No.	Date	Modified By	Description
1.0			

2. Key Recommendations

2.1 Varicella vaccination should be offered to women who are not immune to chickenpox and are planning a pregnancy or receiving infertility treatment.

2.2 If a woman is identified as being non-immune to chickenpox during pregnancy she can be offered vaccination following delivery.

2.3 All women should be asked if they have ever had varicella at the time of booking. For women who give a definite history of varicella infection or 2 doses of varicella vaccine, it is not necessary to test for varicella IgG and she can be considered to be immune. Laboratories may choose to test all patients for convenience but this should be determined at a local level with respect to cost effectiveness and clinical impact.

2.4 Women who are immunosuppressed should be discussed individually with the local microbiologist or infectious disease physician as they may have impaired immunity and require VZIG irrespective of a previous history of varicella infection or vaccine.

2.5 Many maternity units test for immunity to VZV at booking. If varicella IgG is detected in the booking serum, the woman can be reassured that should contact with the disease occur, her antibodies should protect her and the baby from infection. If varicella IgG is not detected in the booking serum, the woman should be advised to avoid contact with chickenpox and shingles during pregnancy and should inform healthcare workers of potential exposure without delay.

2.6 If immunity to VZV has not been checked at booking, or the woman has not booked for antenatal care, her susceptibility to infection can be determined from her history (see below). If a woman reports that she has had chickenpox before, she can be considered as immune.

2.7 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. If the contact is significant and the pregnant woman is not immune to VZV, she should be offered VZIG as soon as possible. VZIG is

effective when given up to 10 days after contact, but ideally within 96 hours.

2.8 A pregnant woman who develops the rash of chickenpox should immediately contact her GP or maternity hospital and should be isolated from other pregnant women when she attends a general practice surgery or a hospital for assessment.

2.9 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 more than 20 weeks of gestation. Aciclovir should be used with caution in early pregnancy and the risks and benefits should be discussed with the woman.

2.10 Intravenous aciclovir should be given to all pregnant women with severe chickenpox, irrespective of when the rash developed.

2.11 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. A hospital assessment should be considered in woman at high risk of severe or complicated chickenpox even in the absence of concerning symptoms or signs.

2.12 Women hospitalised with varicella should be nursed in isolation, under airborne precautions, away from other babies or potentially susceptible pregnant women or nonimmune staff.

2.13 The timing and mode of delivery of the pregnant woman with chickenpox must be individualised. Appropriate treatment should be decided in consultation with a multidisciplinary team i.e. an obstetrician or fetal medicine specialist, a clinical microbiologist/ Infectious Disease specialist and a neonatologist.

2.14 Women should be advised that the risk of spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester. 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 and she will need to be informed of the implications.

2.15 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. 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.

2.16 The neonatology team should be informed of the birth of all babies born to women who have had chickenpox at any gestation during pregnancy.

3. Purpose and Scope

The purpose of this guideline is to assist all health care professionals in the management of chickenpox in pregnancy.

The following questions will be addressed:

1. Can chickenpox be prevented in the woman of reproductive age?
2. Can chickenpox be prevented in the pregnant woman at her first antenatal visit?
3. How should a pregnant woman who has contact with chickenpox be managed?
4. What are the maternal implications of chickenpox in pregnancy?
5. How should a pregnant woman with chickenpox be managed?
6. What are the fetal implications of chickenpox in pregnancy?
7. Can the fetal complications of chickenpox be diagnosed prenatally?
8. Can the fetal complications of chickenpox be prevented?
9. What are the neonatal implications of chickenpox in pregnancy?
10. Can neonatal chickenpox be prevented?
11. Staff and contacts at home

These guidelines are intended for healthcare professionals, particularly those in training, who are working in HSE-funded obstetric and gynaecological services. They are designed to guide clinical judgement but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the woman.

4. Background and Introduction

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 to 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 will usually have crusted over within 5 days.

Chickenpox (or primary VZV infection) is a common childhood disease that usually causes a mild infection. Over 90% of the antenatal population in the UK and Ireland are seropositive for VZV IgG antibody. 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 three in every 1000 pregnancies. 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.

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 (HZ), or simply zoster or

shingles. The risk of acquiring infection from an immunocompetent individual with herpes zoster in nonexposed sites (e.g. thoracolumbar) is remote. 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.

5. Methodology

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

Guidelines reviewed include those developed in the United Kingdom (6), Switzerland (7), United States of America (8), Canada (9), Australia and New Zealand (10).

The principal guideline developers were Dr. Bridgette Byrne (CWIUH) and Dr. Richard Drew (Rotunda).

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6. Clinical Guideline on Chickenpox in Pregnancy

6.1 Can chickenpox be prevented in the woman of reproductive age?

Varicella vaccine contains live attenuated virus derived from the Oka strain of VZV and has been licensed for use in the US since March 1995. Following its introduction, the incidence of primary infection (chickenpox) in the general population has fallen by 90% and the mortality related to the condition has decreased by two thirds. (Nguyen HQ et al 2005). Immunity from the vaccine may persist for up to 20 years. (Johnson et al 1997., Asano Y et al., 1994). The varicella vaccine licensed for use in Ireland for the prevention of chickenpox is Varivax® (Oka/Merck; Sanofi Pasteur MSD Limited, Maidenhead, Berkshire, UK). It is a live attenuated vaccine administered in two separate doses 4–8 weeks apart.

The varicella immune status of women planning a pregnancy or receiving treatment for infertility can be determined by obtaining a past history of chickenpox or by testing the serum for varicella antibodies in those who have no history or an uncertain history of previous infection. If the woman is seronegative for chickenpox she can be offered vaccination.

If a woman of reproductive age is vaccinated, she should be advised to avoid pregnancy for 1 month after the last dose (NIAC, 2013) and to avoid contact with other susceptible pregnant women should a postvaccination rash occur. Transmission of vaccine virus in the absence of a rash 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 an increase from the background risk of fetal abnormality has not been detected. (Merck/CDC Pregnancy Registry, 2009).

Postpartum vaccination of women that are seronegative for chickenpox has been shown to be cost effective (Pinot de Moira A et al., 2006).

The vaccine should be administered in the postnatal period. Every effort should be made to ensure that the process is user-friendly, so as to increase chances of the woman receiving the vaccine. Where possible clear local arrangements should be in place between the maternity hospital service and local GPs to ensure high vaccination rates.

Small studies have not detected the varicella vaccine in the breast milk of women who have been vaccinated postpartum (Dolbear GL et al., 2003, Bohlke K et al, 2003), and therefore, women who receive vaccination postnatally can be reassured that it is safe to breast feed.

Varicella vaccination should be offered to women who are not immune to chickenpox and are planning a pregnancy or receiving infertility treatment.
If a woman is identified as being non-immune to chickenpox during pregnancy she can be offered vaccination following delivery.

6.2 Can chickenpox be prevented in the pregnant woman at her first antenatal visit?

A previous history of chickenpox infection is 95–99% predictive of the presence of serum varicella antibodies. (MacMahon E et al., 2004, Watson B et al., 2007). A history of chickenpox can be a less reliable predictor of immunity in individuals born and raised in tropical climates. (Lee BW et al., 1998, Pattanasuttinont S et al., 2007).

Many maternity units currently test for immunity to VZV at booking. If varicella IgG is detected in the booking serum, the woman can be reassured that should contact with the disease occur, her antibodies should protect her and the baby from infection.

If VZIG is not detected in the booking serum, the woman should be advised to avoid contact with chickenpox and shingles during pregnancy and should inform health care workers of potential exposure without delay.

Currently the UK National Screening Committee do not recommend that there is systematic population screening for varicella IgG in pregnancy. It is recommended that only women who do not have a history of varicella, should be tested. Some Irish laboratories may choose to test all patients for convenience but this should be determined at a local level with respect to cost effectiveness and patient impact.

6.3 How should a pregnant woman who has contact with chickenpox be managed?

The following must be clarified from the history: (a) the type of VZV infection; (b) the timing of the exposure, and (c) 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.

Significant contact is determined by 1) the type of varicella infection i.e. chickenpox or zoster; 2) the timing of exposure in relation to the onset of the rash in the index case and 3) the proximity of contact i.e. defined as contact in the same room (e.g. a classroom or hospital ward) for a significant period (usually >15 minutes) or face-to-face contact (usually > 5 minutes). (NIAC, 2013).

When contact occurs with chickenpox or shingles, a careful history must be taken to confirm the significance of the contact (as above) and the susceptibility of the patient.

The susceptibility of the woman can be determined from the results of her booking bloods. If she has not had serum tested for varicella IgG at booking, her susceptibility to infection can be determined by history. If there is a definite past history of chickenpox or shingles or 2 varicella vaccines, it is reasonable to assume that she is immune to varicella infection. If there is any doubt about previous infection, if there is no previous history of chickenpox or shingles, or if she is from a tropical country, serum should be tested for varicella IgG. This can usually be performed on stored serum from her booking or on a fresh sample within 24–48 hours. At least 80–90% of women tested will have varicella IgG and can be reassured (McGregor JA et al., 1987).

If the pregnant woman is not immune to VZV and she has had a significant exposure to chickenpox or shingles, she should be offered Varicella Zoster Immune Globulin (VZIG) as soon as possible. Ideally, it should be administered within 96 hours, but can have effect up to 10 days after exposure. 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 to 48 hours). The evidence that VZIG prevents or attenuates the disease in pregnancy comes from a study of 212 seronegative women who received an appropriate dose of VZIG either IM or IV within 10 days of significant exposure to chickenpox. Doctors and patients need to be aware that half of the women in this study developed either a usual or an attenuated form of chickenpox and a further 5% had a subclinical infection (Enders G et al., 2000).

VZIG is a human immunoglobulin product manufactured from the plasma of non-Irish donors with high VZV antibody titres. When supplies are limited, issues to pregnant women may be restricted and clinicians are advised to check the availability of VZIG before offering it to pregnant women (NIAC, 2013). VZIG can be administered intramuscularly or intravenously. The national immunization guidelines should be consulted for further detail on dosing and administration. The intramuscular preparation is preferable as it is has similar efficacy and is less costly. The IV preparation can be used in women with contraindications to IM injections. Adverse effects of VZIG include pain and erythema at the injection site. Anaphylaxis occurs in less than 1% of recipients (Paryani SG et al, 1984). Patients with gammaglobulin deficiencies who are already receiving replacement therapy with gammaglobulin do not require VZIG and are at increased risk of anaphylactic reactions.

Nonimmune pregnant women who have been exposed to chickenpox should be managed as potentially infectious from 8–21 days after exposure but this period is prolonged to 8–28 days after exposure if they receive VZIG. They should avoid contact with susceptible individuals. They should be put under airborne precautions in a single isolation room if admitted. They 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.

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

6.4 What are the maternal implications of chickenpox in pregnancy?

Although varicella infection is much less common in adults than in children, it is associated with greater morbidity, namely pneumonia, hepatitis and encephalitis. As recently as the 1990s, chickenpox resulted in the death of 25 people per year in England and Wales and three-quarters of these deaths occurred in adults (Rawson, H et al., 2001). Hospitalised cases of varicella became notifiable in the Republic of Ireland in late 2011. There were 81 cases notified in children and adults in 2012 and one death (NIAC, 2013).

Pneumonia has been reported to complicate 10 to 14% of chickenpox infections in pregnancy and the severity of the pneumonia seems to be increased in later gestation (Tan MP et al., 2005). This incidence may be overestimated, however, because pneumonia only complicated 5% of prospectively documented infections in one series (Harger JH et al., 2002). The mortality rate in case series of varicella pneumonia published in English in the pre-antiviral era was 10/28 (36%) and may reflect publication bias (Broussard RC et al., 2001, DoH report). More recent literature reports mortality of 0-14% (Harger JH et al., 2002, Smego RA et al., 1991, Schutte TJ et al., 1996), a reduction that has been attributed to antiviral therapy and improvements in intensive care medicine. Between 1985 and 1999, there were nine indirect maternal deaths and one late maternal death reported in the UK as complications of maternal varicella infection (RCOG 33-37), (DoH report, Why Mothers Die 1997-1999) suggesting a low case fatality rate. There has been no maternal death from varicella reported in the subsequent confidential enquiries (Why Mothers Die 2000-2002, Confidential Enquiry into Child and Maternal Health, Cantwell R et al., 2011, Saving Lives, Improving motherscare 2014).

6.5 How should a pregnant woman with chickenpox be managed?

Pregnant women who develop the rash of chickenpox should immediately contact their GP or maternity hospital and should be isolated from other pregnant women when she attends a general practice surgery or a hospital for assessment. The diagnosis is primarily clinical but if there is doubt, it can be confirmed by swabbing the base of the lesion or sending vesicle fluid for VZV PCR. Serology testing can also be helpful (NIAC, 2013). In practice, swabs should be sent for confirmation as this will help in ensuring that the correct diagnosis is made.

Women should avoid contact with potentially susceptible individuals, i.e. other pregnant women and neonates, until the lesions have completely 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.

Aciclovir is a synthetic nucleoside that inhibits replication of the human herpes 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 (Wallace MR et al., 1992).

Data are accumulating to suggest that there is no increase in the risk of major fetal malformation with aciclovir exposure in pregnancy (Stone KM et al., 2004, Pasternak B et al., 2010, Mills JL et al., 2010). A Danish registry-based cohort study of 837,795 live births between 1996 and 2008, (Pasternak B et al,. 2010) reported the pregnancy outcome in 1804 women who were exposed to either aciclovir (1549), valciclovir (229) or famciclovir (26) in the first trimester. The rate of major birth defect 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 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 (Mills JL et al., 2010).

The Royal Australia and New Zealand College of Obstetricians Guideline recommends oral aciclovir in all cases of chickenpox in pregnancy regardless of gestational age (Daley AJ et al., 2008). While this view is supported by other multidisciplinary publications 8 (Lamont RF et al., 2011) the Swiss and Canadian national guidelines dissent (Kempf W et al., 2007, Shrim A et al., 2012). The RCOG guidelines recommend 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 gestation (RCOG guideline 13). Guidelines are unanimous, however, in recommending that intravenous aciclovir be administered in cases of severe maternal infection (RCOG guideline 13, Kempf W et al., 2007, Gardella C., 2007, Shrim A et al., 2012, Daley AJ, 2008).

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 more than 20 weeks of gestation. Aciclovir should be used with caution in women less than 20 gestational weeks and the risks and benefits should be discussed with them. It may be prudent to prescribe aciclovir at less than 20 weeks gestation if the woman has risk factors for the development of the complications of chickenpox. Intravenous aciclovir should be given to all pregnant women with severe chickenpox irrespective of gestation or when the rash developed.

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

If a pregnant woman develops chickenpox and 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 (Nathwani D et al., 1998). Respiratory symptoms, neurological symptoms such as photophobia, seizures, or drowsiness, a haemorrhagic rash or bleeding, 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.

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. They should also be advised to attend if they have a recurrence of their fever or if they develop painful skin lesions. Women who develop the symptoms or signs of severe chickenpox should be referred immediately to hospital.

A hospital assessment should be considered in woman at high risk of severe or complicated chickenpox even in the absence of concerning symptoms or signs. Women hospitalised with varicella should be nursed in isolation from babies or potentially susceptible pregnant women or nonimmune staff.

If there is any uncertainty about the diagnosis, varicella IgM and IgG testing should be performed as well as sending vesicle fluid for VZV PCR. If severe sepsis is considered possible, then blood cultures, full blood count, liver function tests, urea and electrolytes, C-reactive protein and skin swabs for bacterial culture should also be sent.

Depending on the severity of the maternal condition, a respiratory physician and intensive care specialist may be involved inperipartum 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 (Miller E, et al., 1989, Meyers JD., 1974). Supportive treatment including antimicrobials to cover *Staphylococcus aureus*, Group A Streptococcus and *Streptococcus pneumoniae* as well as intravenous aciclovir are therefore desirable, allowing resolution of the rash, immune recovery and transfer of protective antibodies from the mother to the fetus. However, delivery may be required in women to facilitate assisted ventilation in cases where varicella pneumonia is complicated by respiratory failure. It is critical that the patient is monitored for signs of toxic shock as this may occur due to Group A Streptococcal super-infection of the vesicular lesions.

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 varicella pneumonia. There is a theoretical risk of transmitting the varicella virus from skin lesions to the central nervous system via spinal anaesthesia. This results in advice that epidural anaesthesia may be safer than spinal anaesthesia, because the dura is not penetrated. A site free of cutaneous lesions should be chosen for needle placement (Brown NW et al., 2003).

The timing and mode of delivery of the pregnant woman with chickenpox must be individualised. Appropriate treatment should be decided in consultation with a multidisciplinary team: i.e. an obstetrician or fetal medicine specialist, an

anaesthetist, a clinical microbiologist/ Infectious Disease specialist and a neonatologist.

6.6 What are the fetal implications of chickenpox in pregnancy?

Spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester (Pastuszak AL et al., 1994). Fetal varicella syndrome 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 and dysfunction of bowel and bladder sphincters). 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.

Fetal varicella syndrome has been reported to complicate maternal chickenpox that occurs as early as 3 weeks and up to 28 weeks 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% (Tan MP et al., 2005). The risk appears to be lower in the first trimester (0.55%) (Tan MP et al., 2005). Cases of fetal varicella syndrome have been reported following maternal infection between 20 and 28 weeks (Tan MP et al., 2005, Romero Sanchez J et al., 1997, Boumahni B et al., 2005). This is thought to be extremely rare, based on the fact that only one case has been reported in all the cohort studies of varicella in pregnancy. No case of FVS has been reported when maternal infection has occurred after 28 weeks of gestation (Tan MP et al., 2005).

Women should be advised that the risk of spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester. 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 and she will need to be informed of the implications.

6.7 Can the fetal complications of chickenpox be diagnosed prenatally?

Prenatal diagnosis is possible using detailed 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 infection is advised because ultrasound performed at 4 weeks has failed to detect the deformities (Pretorius DH et al., 1992). Fetal MRI imaging can be useful to look for morphological abnormalities (Verstralen H., 2003).

VZV DNA can be detected in amniotic fluid by polymerase chain reaction (PCR). VZV DNA has a high sensitivity but a low specificity for the development of fetal varicella syndrome. In one observational study, 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. It was positive, however, in seven other cases, five of which ended in the birth of a normal baby, one in 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.

Ultrasound was abnormal in two of the nine cases with positive amniotic fluid PCR for VZV DNA. One had features of FVS that were confirmed histologically after termination of pregnancy. The other had microcalcifications of the lungs, liver and spleen and was healthy following delivery. One of the two cases of FVS was a baby born at term with bilateral microphthalmia that was not detected by ultrasound. No case of FVS occurred when amniocentesis was negative for VZV DNA (Mouly F et al., 1997). The negative predictive value of this combination of amniotic fluid PCR testing and ultrasound is good but the positive predictive value is poor.

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. 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.

6.8 Can the fetal complications of chickenpox be prevented?

A recent analysis of published case series has shown that 0/142 babies of women, who developed varicella during pregnancy despite receiving VZIG, suffered from fetal varicella syndrome compared with a rate of 14/498 (2.8%) among those who did not receive VZIG (Cohen A et al., 2011). This evidence supports the use of VZIG to prevent Fetal Varicella syndrome but is observational and may be subject to reporting bias.

6.9 What are the neonatal implications of chickenpox in pregnancy?

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 to 4 weeks before delivery, up to 50% of babies are infected and approximately 23% of these 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 when cord blood VZV IgG is low (Enders G et al., 1994).

6.10 Can neonatal chickenpox be prevented?

If maternal infection occurs in the last 4 weeks of a woman's pregnancy, there is a significant risk of varicella of the newborn. Elective 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 (Enders G et al., 1994).

Neonatal VZIG administration is advised in babies born to mothers who develop chickenpox 7 days before and up to 7 days after delivery (NIAC, 2013). The management of the neonate with chickenpox is beyond the scope of this document. The National Immunisation Guidelines should be consulted on this topic for further detail.

Women with chickenpox should breastfeed if they wish to and are well enough to do so. If there is active chickenpox lesions close to the nipple, they should express milk from the affected breast until the lesions are crusted over.

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

6.11 Staff and contacts at home

Staff should know their immune status before starting to work in a maternity ward. Immune staff need no follow up, however, non-immune staff should be referred to occupational health and consideration given to vaccination at their pre-employment check. Non-immune Health Care Workers should avoid contact with pregnant women for 8 to 21 days after significant exposure (NIAC, 2013). For this reason it is important that all healthcare staff who work with at risk patient (e.g. pregnant women and neonates) should be immune to varicella, either from natural infection or vaccination.

The patient should inform other significant contacts of the fact that they have been diagnosed with chickenpox. Older children and immunocompetent adults do not need any testing or prophylactic aciclovir. Immunocompromised people should make contact with their GP or hospital to discuss. See National immunisation guidelines for further detail as it is beyond the scope of this document (NIAC, 2013).

7. Research Recommendations

The production of these guidelines have highlighted some areas in which further research is required:

1. How reliable is a patient reported history of varicella in determining immunity in an Irish population?
2. What is the most cost effective method for screening for varicella?
3. What are the optimal cut-off points on the different platforms for determining immunity to varicella?

Comparison of cost and clinical outcomes in the pregnant population where routine antenatal screening is performed compared to the population where immunity at booking is determined from history only.

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9. Implementation Strategy

- Distribution of guideline to all members of the Institute and to all maternity units.
- Distribution to the Directorate of the Acute Hospitals for dissemination through line management in all acute hospitals.
- Implementation through HSE Obstetrics and Gynaecology programme local implementation boards.
- Distribution to other interested parties and professional bodies.

10. Qualifying Statement

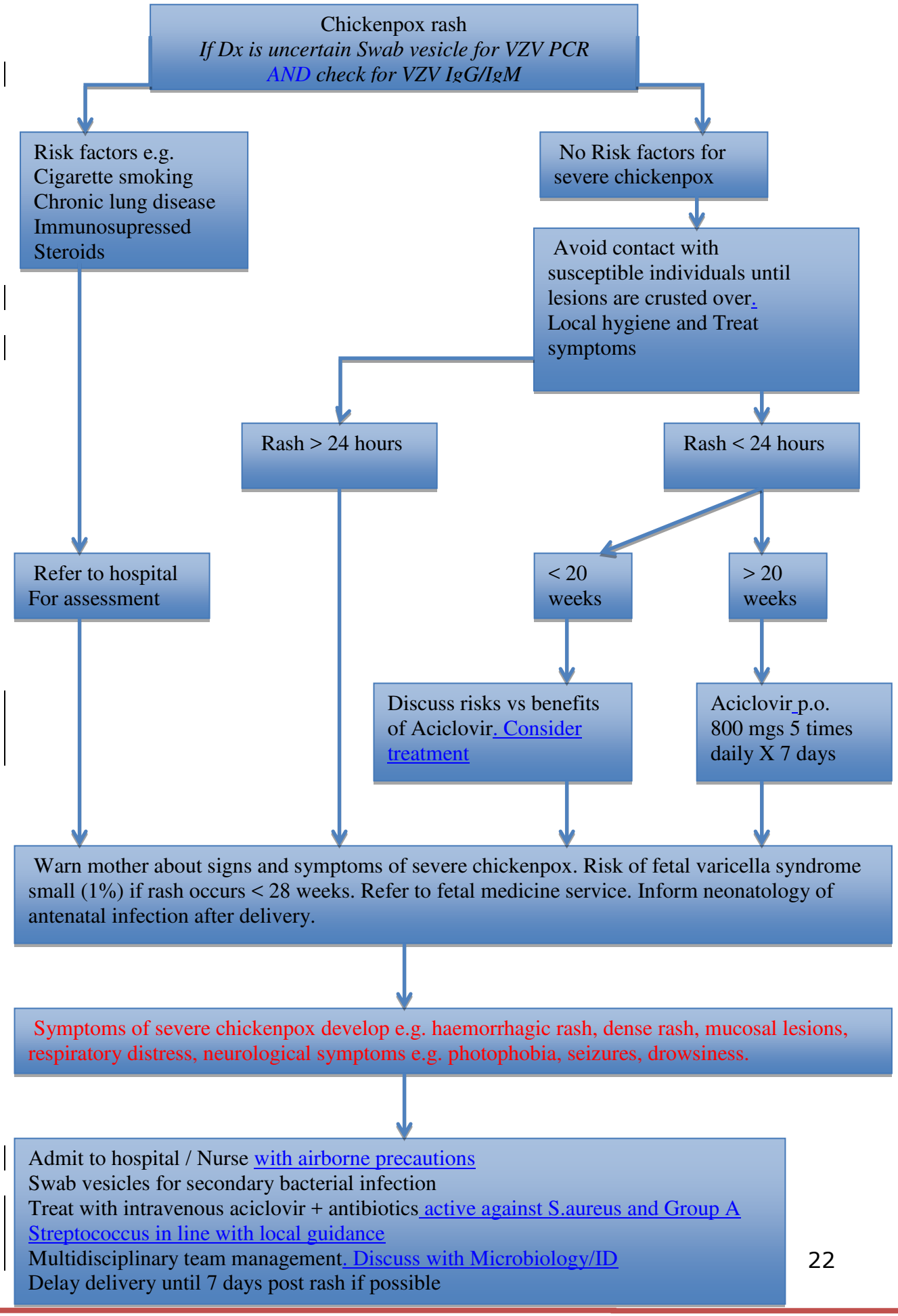
These guidelines have been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advising women of their choices and ensure informed consent is obtained.
- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.

11. Appendices

Appendix 1: MANAGEMENT OF WOMAN WITH CHICKENPOX IN PREGNANCY



Appendix 2
ALGORITHM FOR THE MANAGEMENT OF CHICKENPOX EXPOSURE IN PREGNANCY