Guidance on Viral Rash in Pregnancy

Investigation, Diagnosis and Management of Viral Rash Illness, or Exposure to Viral Rash Illness, in Pregnancy.
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Summary of changes

This document updates and consolidates previous guidance, specifically the 2000 report of
the Public Health Laboratory Service (PHLS - now the Health Protection Agency) Working
Group [1-3]. A specialist HPA working group was established to review all currently available
scientific evidence and consult with experts where required. The revised guidelines have
been circulated within the HPA for comment and signed off by the HPA Vaccine Programme
Board.

In addition to covering rubella, parvovirus B19, and chickenpox infection and exposure in
pregnancy, it has been extended to cover measles infection. It also considers other infective
causes of rash illness in the UK with reference to relevant established guidance where this
exists and now including non-varicella vesicular rash. The document has been extensively
restructured to improve ease of reference.

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Introduction

This guidance aims to help decision-making in the investigation, diagnosis and management of the pregnant woman who has, or is exposed to, rash illness. A rash illness is defined as “a rash compatible with a systemic viral illness”.

The information presented by this guidance is intended to supplement, not substitute for, the expertise and judgement of healthcare professionals.

This guidance is in four parts: the first part sets out the scope of the document and presents background information; the second focuses on women who present with viral rash illness in pregnancy; and the third section focuses on pregnant women who have had contact with a viral rash illness. The fourth part provides advice on the management of susceptible women in the first 20 weeks of pregnancy who are working in occupational settings that may suggest increased risk of exposure, highlights current antibody screening recommendations in pregnancy and discusses inadvertent immunisation in pregnancy.
PART ONE: Scope and background

This guidance focuses on the investigation and diagnosis of maculopapular rashes caused by rubella, parvovirus and measles and vesicular rash caused by chickenpox in pregnant women or pregnant women in contact with such rashes.

Pregnant women may present with a generalised rash, or after contact with a person who has a generalised rash, the cause of which is not always clinically apparent. Therefore, the guidance includes a section on management from the first presentation. Sometimes the clinical and/or epidemiological features may be sufficient to directly implement disease specific investigation and management, for example with chickenpox infection.

This guidance is largely aimed at the management of healthy pregnant women. For guidance on measles and chickenpox infection or contact in immunosuppressed individuals the HPA Immunoglobulin Handbook should be referred to http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Immunoglobulin/. For the management of parvovirus B19 infection in immunosuppressed individuals, specialist advice should be sought.

1.1 Background and epidemiology of viral infections associated with a rash

Table 1 shows the characteristic features and incidence of those infections in the UK of particular significance for the fetus and where intervention can prevent or reduce the potential for adverse outcomes – rubella, parvovirus B19, measles and chickenpox. Any febrile illness, including those that can present with a rash, may be associated with an increased risk of foetal loss in the first trimester. The specific risk associated with each individual viral infection is therefore difficult to ascertain.

Streptococcal\(^1\), meningococcal disease\(^2\), syphilis\(^3\), and imported infections are not considered further as clinical and epidemiological information would focus appropriate investigation and diagnosis in the field.

Viral infections that commonly present with a generalised rash illness in the UK include:

- varicella
- cytomegalovirus
- enterovirus
- human herpes virus 6 & 7
- Epstein-Barr virus
- measles
- parvovirus B19
- rubella

The background and epidemiology of a range of viral rash illnesses is presented in Section 1.1, but where management is already well established, relevant guidance and sources of further information are cited. As with the previous report, this guidance does not attempt to embrace all aspects of management and focuses on the investigation and diagnosis of viral rashes where medical intervention can prevent or reduce the potential for adverse outcomes.

\(^1\) http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/StreptococcalInfections/Guidelines/,
\(^2\) http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ScarletFever/GuidelinesScarletFever/
\(^3\) http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Syphilis/Guidelines/
in the pregnant woman or the fetus or neonate. HIV and HSV infection in pregnancy are not covered by this guidance and other established guidelines should be consulted.\textsuperscript{3,4}

1.1.1 Rubella

The clinical features and consequences for the fetus of primary rubella in pregnancy are well established \textsuperscript{[4]}. The unreliability of a clinical diagnosis of rubella is accepted \textsuperscript{[5]}. The risk to the fetus of primary rubella in the first 16 weeks gestation is substantial (Table 1), with major and varied congenital abnormalities being associated with infection in the first trimester \textsuperscript{[4]}. Rubella infection between 16 and 20 weeks gestation is associated with a minimal risk of deafness only \textsuperscript{[6]} and rubella prior to the estimated date of conception or after 20 weeks carries no documented risk \textsuperscript{[4,7]}.

A rubella reinfection is defined as rubella infection in someone who has previously had either documented natural rubella virus infection or successful rubella immunisation \textsuperscript{[8]}. Maternal reinfection is usually subclinical and diagnosed by changes in antibody concentration (IgG and/or IgM) only. The risk to the fetus of subclinical maternal reinfection in the first 16 weeks gestation has not been precisely determined, but an overview would suggest the risk of congenital damage is less than 10\%, and probably less than 5\% \textsuperscript{[9]}. Maternal rubella reinfection with fetal infection and damage made a substantial contribution to the incidence of congenital rubella in the UK in the late 1980s and early 1990s \textsuperscript{[9]}, but has declined as the incidence of rubella has fallen. Maternal reinfection with a rash is very rare; it can be presumed to present a significant, but not quantified, risk to the fetus as viraemia will have occurred.

In the UK, rubella immunisation was introduced in 1970 for pre-pubertal girls and non-immune women of child-bearing age. The epidemiology of rubella changed substantially with the introduction of measles, mumps and rubella (MMR) vaccine in 1988 for males and females in the second year of life, which included a “catch-up” programme for children up to five years of age at that time. An increase in cases of measles in 1993 was followed by a measles/rubella vaccine campaign of school-aged children in 1994. This campaign also allowed the cessation of the selective vaccination of young teenage girls against rubella when a two-dose MMR schedule was introduced in 1996.

Since the early 1990s, rubella has largely affected young adult males with only a few cases confirmed in pregnant women and a significant proportion of all cases being imported \textsuperscript{[9,10]}. Between 2005 and 2009 there have been 13 reported cases of rubella infection in pregnancy of which eight were known to have been in women born outside the UK. In that time, six cases of congenital rubella infection were confirmed, five of whom had mothers who were born outside the UK (Institute of Child Health and Health Protection Agency data).

1.1.2 Parvovirus B19 (B19V)

There is a wide range of potential consequences of parvovirus B19 infection. These extend from minor febrile illness to erythema infectiosum (fifth disease, slapped cheek syndrome), a generalised rash illness clinically indistinguishable from rubella, aplastic crises in patients with increased red cell turnover, arthropathy, and persistent infection in the immunocompromised. Infection in the first 20 weeks of pregnancy can lead to intrauterine death (risk 15\% c.f. 5\% in control group; excess risk 9\%) and hydrops fetalis (risk 3\% if infection between 9–20 weeks gestation of which about half die \textsuperscript{[11]}. These consequences usually occur some 3–5 weeks after the onset of maternal infection, but can be later. Permanent congenital abnormality and/or congenital anaemia have rarely been identified as a consequence of intrauterine infection \textsuperscript{[12]}.

In studies, parvovirus B19 reinfection has been shown after administration of high dose virus [13] and reactivation has been documented in the immunocompromised, but there is no evidence to suggest reinfection is a risk to the fetus.

Parvovirus B19 infection is common with some 50–60% of adults having been infected [14]. An increased incidence occurs every 3–4 years, largely in schoolchildren. There is currently no licensed vaccine for parvovirus B19 and preventive measures are not available.

In 1998, guidance on the management of parvovirus B19 infection was issued by the PHLS (now the Health Protection Agency) after consultation with a range of authorities [1]. A number of areas in relation to management in pregnancy are outside the scope of that guidance, however.

1.1.3 Measles
The clinical features and complications of measles in the child and adult are well established and include disseminated rash, coryza, conjunctivitis, pneumonia, otitis media, encephalitis etc [15]. Measles in pregnancy is relatively uncommon but can be associated with severe maternal morbidity as well as fetal loss and preterm delivery [16]. There is no evidence to support an association with congenital infection and damage [17]. Although rare, neonatal measles has been associated with subacute sclerosing panencephalitis (SSPE) with a short onset latency and fulminant course and acquiring measles infection before one year of age is associated with an increased risk of SSPE [18].

Although indigenous measles was rare in the UK following introduction of MMR vaccine in 1988 and the MR vaccine campaign of 1994, recent falls in vaccine coverage have contributed to a rise in susceptible individuals, and an increase in the incidence of measles [19]. Human normal immunoglobulin (HNIG) may not prevent measles, but has been shown to attenuate the illness. There is no evidence that it prevents intrauterine death or pre-term delivery [17].

Given changes in measles epidemiology, age-related susceptibility of the population and HNIG preparations in current use, revised HPA guidance on post exposure prophylaxis for measles has been published in May 2009 (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587).

1.1.4 Epstein-Barr virus
Infectious mononucleosis (IM) is a common presentation of primary Epstein-Barr virus (EBV) in young adults. IM is characterised by generalised lymphadenopathy, fever, sore throat and typical haematological and serological findings, including the detection of heterophil antibody. A generalised maculopapular rash may be an associated accompanying feature [20], particularly if ampicillin, or a similar antibiotic, has been taken.

Primary EBV infection in pregnancy (whether clinically-apparent as IM or asymptomatic) carries no specific risk to the fetus [21]. EBV infection results in a latent infection with persistent excretion in the throat of a proportion (c. 20%) of individuals. Hence exposure to EBV can occur irrespective of whether the contact patient has IM, and exposure to IM does not require investigation and the patient can be reassured.

Some 50% of young adults are susceptible to EBV, with higher rates in more affluent social groups, and some 2% or more of those susceptible become infected annually. About 50% of these infections will present with IM.
1.1.5 **Cytomegalovirus (CMV)**

CMV can be another cause of infectious mononucleosis, although primary infections are generally mild or even asymptomatic. Rarely patients may present with a generalised maculopapular rash. Following primary infection the virus remains latent and can periodically reactivate throughout life, and especially in pregnancy. The fetus can be infected either during primary or reactivation, and CMV infection is now the commonest cause of viral congenital infection [22]. It is estimated that the overall birth prevalence of congenital CMV infection in the UK is around 3/1000 [23]. However, there is no treatment currently recommended to prevent or reduce mother-to-child transmission, and as presentation with a rash, or contact of a rash is rarely implicated, CMV infection is not considered further in this guidance. If primary infection or re-infection is suspected it should be appropriately investigated with CMV-specific assays and, if indicated, referral to an appropriate specialist unit.

1.1.6 **HHV-6/7**

HHV-6 and 7 are closely related to CMV. Primary infection with HHV-6 and 7 during infancy and early childhood is universal and characterised by a high fever with a subset of children developing roseola infantum [24]. After infection the virus remains latent with periodic asymptomatic reactivation. In approximately 1% of the population HHV6 is integrated into the human genome. However no clinical implications have been identified and any long-term consequences of congenital infection with HHV-6 are yet to be defined.

1.1.7 **Enteroviruses**

Enterovirus infection (Coxsackie virus groups A and B; echovirus; enterovirus 68-71) may have a wide range of manifestations such as meningitis; rash; febrile illness; myocarditis; and Bornholm disease. Sporadic enterovirus infection is not uncommon, but major summer epidemics have not been seen in the UK for some years. Except for poliovirus, no vaccines are available.

Vertical transmission has been documented in pregnancy. Whilst infection with coxsackie virus during pregnancy has been associated with early onset neonatal hepatitis [25-28], congenital myocarditis [25;29-33], early onset childhood insulin dependent diabetes mellitus [31], and abortion or intrauterine death [34], there is no clear causal relationship. There are no known treatments or preventative methods and these infections are not considered further in this guidance. Infection may be problematic in vulnerable infants, for example those in SCBU. Immunoglobulin has been used as a therapeutic agent for neonates with enterovirus disease; however, clinical efficacy has not been proven [35;36] and specialist advice should be sought from the HPA Centre for Infections, Virus Reference Department (Immunisation and Diagnosis Unit).

Hand, foot and mouth disease is an enteroviral infection characterised by vesicular lesions of hands, feet, and mouth; the latter soon break down to ulcers. Pregnant women presenting with the characteristic features of hand, foot and mouth, or who have been in contact with the infection may be reassured that there is no adverse consequence for the fetus.

1.1.8 **Varicella**

Disseminated primary chickenpox (varicella-zoster virus infection) presents as an illness characterised by vesicular rash, and clinical diagnosis is highly specific although not very sensitive as sub-clinical and mild cases occur. Chickenpox is endemic within the UK, with more than 85% of young adults having been infected [37], although there are variations in different ethnic groups [38]. The incubation period is 7–24 days. This can be prolonged if the patient is on steroids, immunosuppressed or has received VZIG (varicella zoster immunoglobulin). For investigation and consideration of VZIG, and contact management, the
patient is considered infectious 48 hours before the rash appears and until vesicles crust over.

Reliable data on the incidence of chickenpox in pregnancy are not available but projecting from GP consultation rates for chickenpox in adults in 1996, Miller suggested an infection risk of approximately 2–3 per 1,000 pregnancies and more recent data based on retrospective reviews of hospital admissions suggest an incidence between 5–6 per 10,000 deliveries [3;39;40]. In theory, as for rubella and parvovirus B19, the risk of chickenpox infection for susceptible women in a second or subsequent pregnancy may be higher due to exposure to their own young children or their peers. Non immune pregnant women should be advised to avoid exposure to chickenpox and shingles where practical. Chickenpox reinfection has been described, but is rare [41].

Studies show that the risk of pneumonia in pregnant women with chickenpox is increased towards term [42;43] and the fatality increases to 20—40% if untreated. The highest risk of maternal pneumonia appears to be associated with infection after 18 to 20 weeks of pregnancy. Encephalitis is a rare complication with mortality of 5-10%.

There is little evidence to suggest that pregnancies complicated by chickenpox in the first trimester are more likely to result in fetal loss [44;45].

Chickenpox infection during the first two trimesters of pregnancy can lead to intrauterine infection in up to a quarter of cases but only a small proportion of these will develop congenital varicella syndrome. The risk of congenital varicella syndrome is estimated to be 0.4% when maternal infection occurs between conception and week 12 of pregnancy and nearly 2% when infection occurs between weeks 12 and 20 [46]. Isolated case reports have indicated that fetal abnormality consistent with congenital varicella syndrome may occur following infections as late as 28 weeks in pregnancy [47] 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. The rare clinical manifestations of congenital varicella syndrome include low birth weight, severe multi system involvement with neurological involvement, eye lesions, skeletal anomalies, skin scarring and limb hypoplasia [48;49].

Babies born to those infected with chickenpox late in pregnancy (20–37 weeks) may develop shingles of infancy or early childhood (0.8 – 1.7% risk in first two years of life) [49]. This is thought to be due to reactivation of virus after a primary infection in utero.

Fetuses exposed to chickenpox between 20 and seven days before delivery may develop neonatal chickenpox but this is usually less severe as transplacentally transmitted antibodies partially protect the fetus by this stage. If the mother develops a chickenpox rash between day seven before and day seven after delivery, the neonate may develop a severe disseminated haemorrhagic neonatal chickenpox known as purpura fulminans [39]. Death in the neonatal period may occur.

Localised shingles (herpes zoster) reflects reactivation of latent virus, and is usually dermatome restricted. There is a theoretical risk of postnatal transmission to the baby from maternal shingles on the chest, abdomen or in exposed areas. There is no other observed risk to the fetus or neonate of localised maternal shingles [50], although it is uncertain whether dissemination of shingles, as may occur in the immunocompromised, carries a fetal/neonatal risk.
1.2 Advice and information on rash illness for pregnant women

Information and advice to pregnant women should reflect the guidance set out in this document. At booking, midwives should:

- Enquire if women have had a rash illness or had contact with a rash illness during the current pregnancy. Those with a recent rash should be investigated according to this guidance (Part 2).

- Advise women to inform their midwife, GP or obstetrician urgently if they develop a rash at any time in pregnancy. They should be advised to avoid any antenatal clinic or maternity setting until clinically assessed, to avoid exposing other pregnant women.

- Advise women that they should inform their midwife, GP or obstetrician urgently if they have contact at any time in pregnancy with someone who has a rash.
  - If a woman can give a history of chickenpox or shingles and has had contact with either of these during pregnancy she can be offered reassurance that she is not at any risk. Appropriate referral and investigation should be initiated for women with uncertain or no known history of chickenpox (Section 3.2).

All pregnant women with rash illness, or contact with rash illness, should be referred for medical management and laboratory investigation in line with this guidance (Part 2 and Part 3) should be initiated.

Before any testing or screening is undertaken women should be provided with information regarding screening and diagnostic tests, the meaning and consequences of both, what to expect in terms of results and further options for management.
2 PART TWO: The pregnant woman presenting with a rash illness

A full clinical history and examination should be undertaken for all pregnant women presenting with a rash. The appearance of the rash should be determined as vesicular or non-vesicular in order to direct laboratory investigation and management of the patient. Care must be taken in assessing the rash in a patient with a dark skin as the appearance may not be typical of that seen in those with a lighter skin. Those whose natural language is not English may not be familiar with common terms, such as “German measles”, and hence relevant history obtained must be interpreted with care. Patients who have spent their childhood years in other countries may not have had the same exposure to natural infection or vaccination opportunities as those brought up in the UK; consequently, the risk estimates presented here may not apply to these groups as they may have a higher or lower level of susceptibility. If the nature of the rash is unclear they should be investigated for both vesicular and non-vesicular rash.

2.1 Laboratory investigation and management

All requests for laboratory investigation must clearly state that the patient is pregnant and give the following information to enable the results to be reported with the correct interpretation:

- Full demographic details
- Gestation of pregnancy (date of last menstrual period)
- Date of onset, clinical features, type and distribution of any rash illness
- Past relevant history of infection
- Past relevant history of antibody testing
- Past relevant history of vaccine administration (and dates/places)
- Any known contacts with rash illness, and dates of contact

Booking sera or previous serum samples may be helpful and should be obtained if possible from the relevant laboratory. Antenatal screening sera should be retained for at least two years to assist diagnosis/exposure in later pregnancy and investigation of the neonate (UK National Screening Committee, Infectious Diseases in Pregnancy Screening Programme: Handbook for Laboratories 2010 http://infectiousdiseases.screening.nhs.uk/standards). This may include exposure to chickenpox and parvovirus B19, when the availability of such sera for testing can be invaluable in rapidly assessing susceptibility. Although testing of amniotic fluid may be helpful where this has been taken for other purposes it is not advocated specifically for investigation of these infections.

When any diagnostic testing is undertaken it should be made clear to the woman that:

- Tests to establish the initial diagnosis will usually be on samples of blood.
- The requirement for more invasive tests such as amniocentesis, is uncommon, and is only required in rare situations as advised by a specialist.
- Further testing may be necessary in order to confirm the diagnosis, which may prolong the time to result.
- If investigation is commenced some weeks after rash or contact, it may not be possible to confirm or refute a particular diagnosis.

In addition, minimum standards of information prior to any screening or diagnostic tests done to differentiate the origin of rash in pregnancy should include:

- How long the results will take (consult local laboratory).
• Who will give the test results?
• Who will discuss future management of the pregnancy?
• Who they can contact if they have any unanswered queries or concerns.

Written information should be provided to back up verbal advice or information given. The use of a competent adult interpreter for women who do not speak English and the use of translations and/or different media to reiterate verbal discussions are considered good practice. All discussions, advice and care management plans should be documented.

Decisions on management of the pregnant woman diagnosed with any of the infections potentially causing congenital pathology in her first 20 weeks of pregnancy are best made in a specialist fetal medicine unit to enable patient access to counselling, serial ultrasound scanning and further follow up, investigations and treatment, where appropriate, should ultrasound be abnormal.

2.2 Maculopapular rashes in pregnancy
Although parvovirus B19 and rubella infections predominantly have a specific impact on the fetus if infection occurs in the first 20 weeks gestation, investigation after 20 weeks is also strongly advised for the following reasons:

• Specific diagnosis would help in managing potential risk to contacts (e.g. in healthcare situations such as GP surgeries, ANC clinics).
• It would confirm the date of infection related to gestational age.
• Estimate of the gestation may be wrong.
• The mother may be reassured that a specific diagnosis has been reached or excluded, and may be helpful in the management of subsequent exposure.
• Measles infection can affect the pregnancy at any stage.

Investigation will be directed by clinical/epidemiological information. For a non-vesicular rash, the probability of streptococcal and meningococcal infection, measles, enterovirus, syphilis and infectious mononucleosis (EBV or CMV) should be suggested by clinical features and would instigate appropriate specific investigation and management. Any doubt as to one of these diagnoses, or failure to confirm by laboratory investigation, must result in initiating specific investigation for rubella and parvovirus B19 (sections 2.2.1 and 2.2.3).

If features are compatible with rubella, parvovirus B19 or measles, appropriate laboratory investigation should be initiated, irrespective of past testing or immunisation. There is a remote possibility of past laboratory or documentation error, failed immunisation, or symptomatic reinfection.

Cases of measles and rubella diagnosed on the basis of clinical suspicion are notifiable diseases and should be reported to the local Health Protection Unit.

2.2.1 Laboratory investigation of suspected rubella
The routine antenatal testing for rubella antibody is for determining susceptibility and identifying those for whom vaccine is advised post delivery: it does not determine whether rubella may have occurred in the current pregnancy. If such investigation is required, the request form must clearly state that the woman is pregnant, recent rubella is a possibility and provide the other full clinical and epidemiological details given above (see section 2.1).

It is recommended that, irrespective of a request for specific rubella or parvovirus B19 testing, all sera from women with rash illness are simultaneously investigated for both infections. The serological diagnosis of rubella is well established [51]. A serum at first presentation must be collected and sent for laboratory testing. Booking sera or other earlier
serum samples may be available and may also aid in the diagnosis but the initial investigation should not be delayed. It is recommended that the laboratory investigates all cases of possible rubella by simultaneous testing for rubella-specific IgG (or total rubella antibody) and IgM. Current methods developed for use on oral fluid should not be used alone for confirming or excluding rubella infection in pregnancy.

When reporting the results of rubella serology, the laboratory must advise on any further sera/follow-up required, and give a definitive conclusion of their investigations, e.g. “no evidence of recent primary rubella”.

Problems arise when investigation commences four weeks or more after the onset of rash illness. If rubella-specific IgG is detected, and specific IgM is not detected, rubella as a cause of the rash illness cannot be excluded serologically unless past sera can be tested to determine whether seroconversion has occurred recently. An assessment of probabilities has to be made based on recent epidemiology of rubella in the community, past history of vaccine and testing, characteristics of illness, etc.

Some women present significant problems in diagnosis, particularly those who give a positive result for rubella-specific IgM. Although positive rubella IgM results that do not reflect recent rubella (primary or reinfection) (‘false positive’) are infrequent, the control of rubella in the UK means that most rubella-specific IgM positive results do not reflect recent rubella.

No pregnant woman should have rubella diagnosed on the basis of a single positive rubella-specific IgM alone. Results must be interpreted in relation to full clinical and epidemiological information. Unless seroconversion has been shown, further testing by alternative rubella-specific IgM tests, testing an acute sample and a sample taken 10–14 days later for rubella IgG, and measuring the strength of binding of specific IgG (avidity) [51] is advised. IgG avidity is low soon after a primary infection, but matures over a few weeks to become more strongly binding. If rubella-specific IgM positivity reflects a recent rubella episode (whether primary or reinfection), the degree of reactivity will usually change over the period of a few weeks, rather than persisting at a similar level.

2.2.2 Management of confirmed rubella – primary and reinfection

The management of primary rubella or symptomatic rubella reinfection would depend on the gestation of pregnancy at which rubella occurred (Table 1), and the individual circumstances of the woman.

If a case of asymptomatic rubella reinfection is identified or suspected, management would, as for primary rubella, depend on the gestation of pregnancy and the individual circumstances of the woman. Given the low but definite risk to the fetus of maternal rubella reinfection in the first 16 weeks of pregnancy, there may be occasions when consideration is given to further fetal investigation by PCR to ascertain if fetal infection has occurred.

The necessary virological techniques for fetal investigation are not widely available in the UK and the HPA Centre for Infections, Virus Reference Department (Immunisation and Diagnosis Unit) should be consulted for advice if such approaches are being considered. It is strongly advised that management is based on risk assessment. Appropriate expert advice should also be obtained for the investigation of suspected cases of congenital rubella syndrome identified post-natally.

2.2.3 Laboratory investigation of suspected parvovirus B19

In patients with a rash, recent parvovirus B19 infection can be confirmed or excluded by testing for parvovirus B19 specific IgM on the first serum obtained. Booking sera or other
earlier serum samples may be available and may also aid in the diagnosis but the initial investigation should not be delayed.

Failure to detect parvovirus B19 specific IgM excludes infection in the four weeks prior to collection of the serum. Hence infection cannot be excluded if investigation commences more than four weeks after onset of rash illness (vide supra, rubella).

If parvovirus B19 IgM is detected in the first 20 weeks of pregnancy, confirmation is required by alternative assay, e.g. detection of high titre B19V DNA or IgG seroconversion using an antenatal booking blood. Repeat testing may demonstrate a change in IgM reactivity and provide an additional confirmation method.

2.2.4 **Management of confirmed parvovirus B19**

The management of proven parvovirus B19 infection has become more active with the demonstration that intrauterine transfusion of the fetus improves the outcome [52]. On diagnosis of parvovirus B19 infection, specialist advice should be sought including the need for serial ultrasound scanning and Doppler assessment in the case of development of hydrops fetalis.

2.2.5 **Laboratory investigation of hydrops fetalis**

In a pregnant woman presenting with hydrops fetalis without a rash history, the diagnosis of recent parvovirus B19 infection can only sometimes be achieved by testing for B19V-specific IgM as the acute infection was usually some weeks prior to presentation.

Infection with parvovirus B19 as the cause of hydrops fetalis can be investigated by testing the antenatal booking sample in parallel with the sample at presentation for parvovirus-specific IgG to show seroconversion. Inability to detect B19V-specific IgG in maternal blood at the time of hydrops excludes B19V as the aetiological agent. Parvovirus B19 infection as the cause of hydrops fetalis can be confirmed by detection of B19V DNA in amniotic fluid or fetal blood if available.

2.2.6 **Management of hydrops fetalis following confirmed parvovirus B19**

Following confirmation of parvovirus B19 in a pregnant woman presenting with hydrops fetalis, referral to a Regional Unit of Fetal Medicine is recommended if this has not already occurred. If a fetal blood sample is collected then examination by quantitative PCR to confirm fetal infection should be arranged.

Proven parvovirus B19 infection in the hydropic fetus will influence the management of the patient as it is important in establishing the aetiology of the hydrops and in excluding other causes so allowing appropriate counselling of the patient.

2.2.7 **Laboratory investigation of suspected measles**

The serological diagnosis of measles is well established. A serum at first presentation should be collected and sent for laboratory testing for measles-specific IgM and IgG. Oral fluid should be collected at the same time for confirmation of the diagnosis by detection of viral RNA.

Recent measles infection can be confirmed or excluded by testing for measles-specific IgM on serum sample taken more than four days, but within one month, after the onset of rash.

2.2.8 **Management of confirmed measles**

When measles has been confirmed the management of the pregnancy should continue as normal. Although no congenital infection or damage would be anticipated, follow-up of the infant should be considered.
2.2.9 Neonates born to measles infected mothers.

Administration of Human Normal Immunoglobulin (HNIG) immediately after birth or post-natal exposure is recommended for neonates born to mothers in whom the rash appears six days before to six days after birth. The dosage (0.6ml/kg up to a maximum of 5mls) for infants is described in the revised 2009 detailed guidance on post exposure prophylaxis for measles (http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1195733810613?p=191942172795).

2.3 Generalised vesicular rash illness in pregnancy

Investigation will be directed by clinical/epidemiological information. A disseminated vesicular rash is highly suggestive of chickenpox.

2.3.1 Laboratory investigation of suspected chickenpox

The diagnosis can be made clinically in many instances, but if there is doubt confirmation of chickenpox should be sought. Laboratory diagnosis of active infection is by DNA detection, virus antigen or electron microscopy of vesicle fluid.

Detection of VZV DNA in the amniotic fluid by polymerase chain reaction (PCR) can also be used for the confirmation of chickenpox infection in the fetus. However, this is not routinely advised, the precise predictive value is unknown and the norms for viral load relating to congenital varicella syndrome are also unknown. Therefore, this should only be requested by a specialist in fetal medicine and is usually requested in tandem with serial ultrasound scanning.

2.3.2 Management of confirmed chickenpox infection in the pregnant woman

Management has to take into account the possible effect on both mother and fetus. Pregnant women should be advised to consult their general practitioner at the first sign of chickenpox. They should avoid contact with others who might be at risk, such as other pregnant women and neonates, and the immunosuppressed.

The time of onset of the rash is important for determining the likely effectiveness of antiviral treatment. Onset is timed from the first observable lesion. If the woman presents within 24 hours of the onset of the rash, and she has reached 20 weeks gestation, she should be offered oral antiviral treatment for seven days (aciclovir 5x800mg per day). Aciclovir should be used cautiously before 20 weeks of gestation. It is reassuring that the US-based aciclovir prospective pregnancy registry [55] found no increase in the risk of congenital malformations amongst 596 infants whose mothers were exposed to systemic aciclovir during the first trimester of pregnancy.

---

5 A recent review commissioned by the National Screening Committee [53] detailed that:

Aciclovir has been considered for the treatment of severe complications of chickenpox in pregnancy, such as varicella pneumonia in the second half of pregnancy and has been shown to be clinically effective in reducing mortality. Although aciclovir has not been approved for use in pregnancy by the manufacturer, the consensus of a working group of obstetricians in the UK was that oral aciclovir should be considered for women in the second half of their pregnancy because of the risk of pneumonia [3]. This is thought to be effective if administered within 24 hours of the onset of the rash, but in women with respiratory involvement, intravenous aciclovir is advised [3]. In the US, aciclovir is classified as a Category B drug in the Food and Drug Administration use-in-pregnancy rating. Although US guidance does not recommend the routine use of oral aciclovir for pregnant women, in instances of serious, viral-mediated complications (e.g., pneumonia), it does recommend that intravenous aciclovir should be considered [54].
If it is more than 24 hours from the onset of rash, then antivirals are not advised as there is no evidence that they would alter the natural history in the uncomplicated case [56]. VZIG has no place in treatment once the rash appears.

If there is deterioration, or the fever persists, or the cropping of the rash continues after six days, or the woman develops respiratory symptoms, the woman should be referred for urgent hospital assessment. The general practitioner should have a low threshold for considering hospitalisation. The criteria indicating that hospitalisation is required are [3]:

**Absolute indicators**
- Respiratory symptoms
- Neurological symptoms other than headache
- Haemorrhagic rash or bleeding
- Severe disease – dense rash/numerous mucosal lesions
- Significant immunosuppression

**Contributory factors**
- Pregnancy approaching term
- Bad obstetric history
- Smoker
- Chronic lung disease
- Poor social circumstances
- GP unable to monitor patient closely

Intravenous treatment with aciclovir is indicated if the chickenpox is severe or there are any complications [57]. Treatment of pneumonia associated with chickenpox in hospital is with intravenous aciclovir 3x10mg/kg/day for 5-10 days [58]. Delivery by caesarean section may need to be considered. Detailed recommendations, including the management of delivery, are given by the Royal College of Obstetricians and Gynaecologists [59].

The woman needs to be assessed when she presents, and if she shows evidence of severe disease at that stage or subsequently, she should be referred immediately for urgent assessment in a specialist isolation facility where she has access to the expertise of an obstetrician, infectious disease specialist and paediatrician. If the chickenpox is uncomplicated, the woman can be reassured and sent home for daily review, and for outpatient follow up for the fetus. She should be advised to seek help if the clinical picture deteriorates. Women who appear to have uncomplicated infections must be monitored closely for deterioration by an appropriate clinician.

### 2.3.3 Management of proven chickenpox exposure in utero

Neither immunoglobulin nor aciclovir treatment have not been shown to prevent vertical transmission or congenital fetal varicella syndrome [40].

Chickenpox during pregnancy does not justify termination without prior prenatal diagnosis as only a minority of fetuses will be infected and not all those infected will develop fetal varicella syndrome. The parents should be offered counselling in a specialist fetal unit and the option of termination following an early sonographic diagnosis of congenital fetal varicella syndrome.

### 2.3.4 Management of the neonate exposed to chickenpox

The HPA Immunoglobulin Handbook, ([http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947367049](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947367049)) recommends VZIG use in neonates as follows:
• Infants whose mothers develop chickenpox (but not shingles) in the period seven days before to seven days after delivery. VZIG can be given without antibody testing of the infant.

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

If a neonate has possible exposure to chickenpox in someone other than their mother, refer to the HPA Immunoglobulin Handbook (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947367049).

If severe chickenpox develops in the neonate despite VZIG, high dose intravenous aciclovir treatment of 20mg/kg every eight hours for at least seven days should be started as soon as possible [60]. Prophylactic intravenous aciclovir should also be considered for infants whose mothers develop chickenpox four days before to two days after delivery as they are at the highest risk of fatal outcome despite VZIG prophylaxis.

If other children in the family have chickenpox, and the mother has had chickenpox or is shown to have varicella-zoster virus antibody, then there is no reason to prevent a new baby going home. If the mother is susceptible, contact with siblings with chickenpox should ideally be delayed until the new baby has reached seven days of age. This is to prevent disease in the first month of life, which carries a greater risk of severe disease [61]. If a new baby returns to a home where siblings are still in the infectious phase of chicken pox, the risks must be clearly explained to the parent/s and every effort should be made to avoid significant contact with the siblings – VZIG is not a suitable alternative to avoiding such contact. The family should be advised to bring the infant back promptly if any chickenpox spots develop so that they can be treated with intravenous aciclovir at the earliest opportunity.

Mothers with chickenpox or shingles should be allowed to breast-feed. If they have lesions close to the nipple, they should express milk from the affected breast until the lesions have crusted; this expressed milk can be fed to the baby if he/she is covered by VZIG and/or aciclovir.

3 PART THREE: The pregnant woman in contact with a rash illness

(Figure One)

Contact is defined as being in the same room (e.g. house or classroom or 2–4 bed hospital bay) for a significant period of time (15 minutes or more) or face-to-face contact. This definition is based on experience with VZV exposure. This definition of contact is probably practical for all nosocomial exposures in healthy pregnant women. In other settings, where exposure is less well defined, a less stringent definition of contact should be used, especially for measles. For parvovirus B19 infections household exposure is overwhelmingly the most important source of infections in pregnancy (followed by intense occupational exposure).

3.1 Contact with a maculopapular rash illness

The aetiology of a maculopapular rash in the contact may be diverse, and include non-infective causes. The possible causes that warrant consideration include measles, rubella and parvovirus B19. Other possible infective causes in the contact should await development of illness in the pregnant woman.
Suspected measles or rubella infection in contacts of a pregnant woman should be confirmed rapidly with oral fluid or serum testing. This can most readily be achieved through notification to the local HPU. Through liaison with the local HPU, the Virology Reference Department or with the Immunisation Department at Colindale it may be possible to confirm whether or not the contact is a known case.

A risk assessment should be undertaken for measles, rubella and parvovirus for all pregnant women following contact with a maculopapular rash and appropriate investigation and treatment undertaken as set out in sections 3.1.1 to 3.1.2.

3.1.1 Contact with suspected rubella (Figure One)
If a woman has had one of the following she should be reassured that the likelihood of rubella is remote and that specific rubella investigation is not required but to return if a rash develops:

- At least two documented doses of rubella vaccine;
- One documented dose of vaccine followed by at least one previous rubella antibody screening test which has detected rubella antibody ≥10 IU/ml;
- At least two previous rubella antibody screening tests which have detected antibody, in at least one of which rubella antibody is ≥10 IU/ml.

If the above criteria are not met, a serum should be obtained as soon after contact as possible and tested for IgM and IgG with a second sample four weeks later similarly tested if the patient is shown to be susceptible. Further testing may be required. Any evidence of seroconversion or IgM positivity should be referred for confirmatory testing (see section 2.2.1). Refer to section 2.2.2 for management of a patient who is subsequently confirmed as having rubella in pregnancy. Patients found to be IgG negative should be immunised with MMR vaccine after delivery in line with national guidelines.

3.1.2 Contact with suspected parvovirus B19 (Figure One)
The pregnant woman should be investigated for asymptomatic parvovirus B19 infection (Figure One); investigation should not be delayed to ascertain if symptomatic infection occurs. This is because:

- Maternal asymptomatic parvovirus B19 infection is at least as likely to infect and damage the fetus as symptomatic infection [39].
- Active management of the infected fetus may reduce the risk of adverse outcome [52] (section 2.2.6).

Serum should be collected as soon after contact as possible and submitted to the laboratory with full clinical and epidemiological details, including date of contact (see section 2.1). Serum should be tested for both B19V-specific IgG and IgM. If B19V-specific IgG is detected (c 50% probability), but IgM not detected, the woman should be reassured and a report issued, “Parvovirus B19 infection at some time, but not recently”. If specific IgG or IgM are not detected, further serum should be collected and tested one month after last contact. If, after one month testing, specific IgG and IgM are not detected, the woman should be reassured and a report issued “No evidence of recent parvovirus B19V infection, but is susceptible”. If B19V-specific IgM is detected, but B19V-specific IgG not detected, a further serum should be collected and tested immediately. If the sample is B19V-IgM positive further testing and management should be undertaken as in section 2.2.3 on suspected B19V infection in pregnancy.
3.1.3 **Contact with suspected measles (Figure One)**

Clinical features suggestive of measles are described in section 1.1.3. Additional factors that would increase the likelihood of measles are as follows:

- The contact is linked epidemiologically to a confirmed measles case.
- The rash contact took place when the woman was abroad.
- The contact had travelled abroad.
- The contact has not received measles vaccine in the past.
- The contact has been hospitalised recently.

HPA current guidance on whether HNIG is indicated should be consulted to determine if prophylaxis is warranted. The probability of measles immunity is considered in detail in this guidance on the basis of year of birth and clinical and immunisation history. This reflects changes in the epidemiology of measles and the age related susceptibility of the population determined by vaccine policy and coverage (Table 1 in [http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587)).

If there is another exposure to measles three weeks or more after the first use of HNIG, the need for HNIG needs to be reassessed using the above guidance.

3.2 **Contact with a vesicular rash illness**

3.2.1 **Contact with confirmed chickenpox (Figure One)**

Healthy pregnant women who are exposed to chickenpox or shingles in pregnancy should seek medical advice promptly. The date, duration and nature of the contact, any past history of chickenpox infection, shingles or vaccination should be clarified.

If the woman has a past history of chickenpox or shingles or two doses of a varicella-containing vaccine, and is not immunosuppressed, protection can be assumed and reassurance given. If there is no history of past chickenpox or shingles and the woman is not fully vaccinated (two doses) the woman's susceptibility should be determined urgently.

Laboratory diagnosis of past infection is by VZV IgG antibody in serum. Serological assays for varicella antibody are of variable sensitivity [62]. Local laboratory testing is recommended in the first instance. If time permits reference laboratory testing should be considered if results are equivocal or negative. If urgent antibody testing is required for patients presenting late, VZIG can be ordered at the same time that blood is sent for testing and not used if the result is positive. VZV antibody testing should be available within 24 to 48 hours; advice should be obtained from the local HPA or NHS lab.

The majority of adults will be VZV antibody positive. Lack of varicella-specific IgG antibody is highly suggestive of susceptibility. If susceptibility in a pregnant woman has been confirmed using a sensitive assay [59] then post partum vaccination may be considered.

VZIG should be offered to susceptible women within 10 days of the exposure[63]. The clinical attack rates are similar whether VZIG is given within 72 hours or 4–10 days after contact. [49, 60] For patients with continued exposure, for example in the household setting, exposure is likely to occur during the prodromal period, but for practical purposes the limit for administering prophylaxis should be timed from the onset of rash in the index case. Where a woman is exposed in pregnancy, even if they have since delivered, VZIG should be
administered within the 10-day period. For further information refer to the HPA Immunoglobulin Handbook (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947367049).

If a woman with a reliable history of chickenpox, shingles or full vaccination is inadvertently tested for antibody the following advice should be followed.

- VZV IgG equivocal or positive—reassure as VZIG is not indicated.
- VZV IgG negative with an insensitive assay—retest using a more sensitive assay. If time does not permit additional testing within 10 days of contact, then issue VZIG. If negative with a sensitive assay, issue VZIG. If second test VZV IgG is equivocal or positive, reassure as VZIG is not indicated.

For continuous household exposure (for example when a child in the household is infected), VZIG should be offered within 10 days of the onset of rash in the index case.

If there is another exposure to chickenpox or shingles three weeks or more after the first use of VZIG, the need for VZIG needs to be reassessed using the above criteria. If more than six weeks have elapsed since first issue, antibody testing should be performed using a new (recent) sample.

As VZIG does not always prevent chickenpox the woman should be managed as being possibly infectious 8–28 days after VZIG and should be asked to contact her family doctor if she develops a rash. Up to 50% may develop a modified form of disease. Maternal pneumonia associated with chickenpox infection has been reported in spite of timely VZIG administration.

The live chickenpox vaccine is contraindicated in pregnancy. Confusion has been known to occur between the chickenpox vaccine and the varicella immunoglobulin. Staff should be trained to be aware of this known pattern of confusion and be extra careful when prescribing and administering the immunoglobulin. Inadvertent vaccination with chickenpox vaccine in pregnancy should be reported to the Health Protection Agency [64].

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6 The rationale for this is based on increased risk for severe respiratory complications in post partum women with influenza (largely experience with H1N1), suggesting that increased risk does not subside immediately on delivery.
Figure 1: Algorithm for the follow-up of women exposed to rash in pregnancy

- **Contact was with vesicular rash (chicken pox or shingles)**
  - Is there reliable history of chicken pox or shingles or two doses of varicella vaccine?
    - No: Test for VZV IgG
      - VZV IgG detected: Reassure and advise to contact GP if rash develops
      - VZV IgG NOT detected: Equivocal VZV IgG
        - If time, retest with more sensitive assay
        - If no time: Give specific VZIG within 10 days of 1st contact irrespective of gestation. Advise woman to contact GP if rash develops.
    - Yes: Reassure that measles risk remote and advise to contact GP if rash develops.
- **Contact was with non-vesicular rash - possible parvovirus B19, rubella or measles**
  - Consider each of the following:
      - Test for parvovirus B19 IgG and IgM
        - Parvovirus B19 IgG detected
          - Parvovirus B19 IgM NOT detected
          - Reassure that they have had Parvovirus B19 infection at some time in the past but not recently
          - Note on the report that: The woman is susceptible to Parvovirus B19. And further serum is required one month after last contact or if illness develops.
          - Send the sample for confirmatory testing.
        - Parvovirus B19 IgM detected regardless of IgG result
          - Reassure that they have had Parvovirus B19 infection at some time in the past but not recently
          - Note on the report that: The woman is susceptible to Parvovirus B19. And further serum is required one month after last contact or if illness develops.
          - Send the sample for confirmatory testing.
      - Parvovirus B19 IgG NOT detected
        - Parvovirus B19 IgM NOT detected
          - Reassure that they have had Parvovirus B19 infection at some time in the past but not recently
          - Note on the report that: The woman is susceptible to Parvovirus B19. And further serum is required one month after last contact or if illness develops.
          - Send the sample for confirmatory testing.
        - Parvovirus B19 IgM detected regardless of IgG result
          - Reassure that they have had Parvovirus B19 infection at some time in the past but not recently
          - Note on the report that: The woman is susceptible to Parvovirus B19. And further serum is required one month after last contact or if illness develops.
          - Send the sample for confirmatory testing.
    - b. Rubella. Does the woman have a history of:
      - rubella vaccine x1 AND at least 1 rubella antibody positive test ≥10 IU/ml;
      - OR rubella vaccine x2;
      - OR rubella antibody positive tests x2 (at least one ≥10 IU/ml)?
      - No: Test for rubella IgM and IgG
        - Rubella IgG detected
          - Rubella IgM NOT detected
            - Reassure that rubella risk remote and advise to contact GP if rash develops
        - Rubella IgG NOT detected
          - Rubella IgM NOT detected
            - Reassure that rubella risk remote and advise to contact GP if rash develops
        - Rubella IgM detected regardless of IgG result
          - Reassure that rubella risk remote and advise to contact GP if rash develops
      - Yes: Reassure that rubella risk remote and advise to contact GP if rash develops.
    - c. Measles. Does the woman have a history of 2 doses of measles containing vaccine or is she known to be immune?
      - No: Measles IgG NOT detected
        - Measles IgG testing
      - Yes: Measles IgG detected
        - Reassure and advise to contact GP if rash develops
      - No: Measles IgG NOT detected
        - Arrange HNIG via HPU

* Contact the local HPU to establish the likelihood of measles in the index case.
4 PART FOUR: other considerations for pregnant women

4.1 Occupational exposure

4.1.1 Rubella
Exclusion is not recommended of pregnant women susceptible to rubella from settings that may suggest a higher rate of exposure (e.g. nurseries and schools). Rubella is now rare in children.

4.1.2 Parvovirus B19
Guidance on the management of pregnant women susceptible to parvovirus B19 has previously been published [1].

4.1.3 Measles
Exclusion is not recommended of pregnant women susceptible to measles from settings that may suggest a higher rate of exposure (e.g. nurseries and schools). Exposure to measles is as likely to occur in the wider community. However, should there be a case or an outbreak of measles in that setting then an individual risk assessment should be undertaken.

4.1.4 Chickenpox
Exclusion is not recommended of pregnant women susceptible to chickenpox from settings that may suggest a higher rate of exposure (e.g. nurseries, schools and hospitals). Exposure to chickenpox is as likely to occur in the wider community. However, should there be a case or an outbreak of chickenpox in that setting then an individual risk assessment should be undertaken.

4.2 Rubella antibody screening

The National Screening Committee [65] most recently reviewed their advice to routinely screen pregnant women for rubella immunity in 2010 and this was published in September 2010 (http://infectiousdiseases.screening.nhs.uk/). The UK standards recommend that rubella antibody testing should be offered in each pregnancy.

Rubella-susceptible women of childbearing age who have not received two doses of rubella-containing vaccine need to be protected against rubella and should be offered MMR vaccine post delivery.

4.2.1 Laboratory guidance for rubella antibody screening

A sensitive immunoassay for rubella-specific IgG should be used, capable of providing quantitative results in IU/ml. Qualitative or semi-quantitative assays based on latex agglutination should not be used.

A result below 10 IU/ml is used to define rubella susceptibility. Laboratories should verify that the assay used is sufficiently sensitive and precise at this level to ensure accurate results. No report with a screening test result <10 IU/ml should be issued until a confirmatory test has been performed.

For screening test results below 10 IU/ml laboratories should repeat the analysis on the original specimen to confirm reproducibility and minimise the risk of laboratory error. Confirmation of an initial screening result of <10 IU/ml by an alternative analytical method is considered good laboratory practice.
All laboratories undertaking rubella screening must be able to define which specimens with low (<10 IU/ml) or borderline reactivity have rubella specific antibodies present.

A report should be issued for every screening specimen received by the laboratory. For those specimens with antibody levels $\geq$ 10 IU/ml report ‘Rubella antibody detected.’ For those specimens with antibody levels < 10 IU/ml report ‘Rubella susceptible – two doses of MMR vaccination recommended post delivery.’

For women who have already received two or more documented doses of rubella vaccine with detectable levels of rubella antibody, but less than 10 IU/ml, further doses of vaccine are unlikely to be of benefit. However, these women should be advised to seek medical advice if exposed to a rash illness during pregnancy.

4.2.2 Parvovirus B19 antibody screening
Unselected screening of pregnant women for past infection with parvovirus B19 is not recommended as neither vaccine nor prophylaxis are available.

4.2.3 Measles antibody screening
Unselected screening of pregnant women for adequate immunity to measles is not currently recommended.

All seronegative women of childbearing age who need to be protected against measles should be offered MMR vaccine post delivery. Satisfactory evidence of protection would include documentation of having received two doses of measles-containing vaccine or a positive antibody test for measles.

4.2.4 Varicella antibody screening
The National Screening Committee recently commissioned a review of antenatal screening for VZV susceptibility that concluded there was insufficient evidence to recommend the introduction of routine antenatal screening in the UK. At present it is good practice to establish and record whether there is a firm history of chickenpox or shingles at booking.

4.3 Inadvertent immunisation during pregnancy
MMR and chickenpox vaccines are live vaccines and as a matter of caution should not be given to women known to be pregnant. However, if women have been inadvertently immunised with these vaccines during pregnancy, termination should not be recommended. The woman should be given the information on the evidence on lack of risk from vaccination in pregnancy.

Surveillance of inadvertent administration of MMR and chickenpox vaccine in pregnancy is being conducted by the Immunisation, Hepatitis and Blood Safety Department of the HPA, to whom such cases should be reported (tel: 01788 540298 or 020 8200 4400, http://www.hpa.org.uk/web/HPAweb&Page&HPAwebAutoListName/Page/1221202947595).
<table>
<thead>
<tr>
<th></th>
<th>Rubella</th>
<th>Parvovirus B19</th>
<th>Measles</th>
<th>chickenpox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion seronegative in young adult females</td>
<td>3.6% of nulliparous women, rising to nearly 9% in those aged &lt;21 years (2007 NHSBT data)</td>
<td>40-50%</td>
<td>&lt;5%</td>
<td>1.2-14% varies with country of origin.</td>
</tr>
<tr>
<td>Infectivity – risk transmission from close contact (household attack rate)</td>
<td>High (90%)</td>
<td>Medium (50%)</td>
<td>V high (99%)</td>
<td>High (70-90%)</td>
</tr>
<tr>
<td>Risk of intrauterine infection by (gestational age)</td>
<td>&lt;11 weeks – 90% 11-16 weeks – 55% &gt;16 weeks – 45%</td>
<td>&lt;4 weeks – 0% 5-16 weeks – 15% &gt;16 weeks – 25-70%, increasing with gestation</td>
<td>Not known</td>
<td>&lt;28 weeks – 5-10% 28-36 weeks – 25% &gt;36 weeks – 50%</td>
</tr>
<tr>
<td>Risk of adverse fetal outcome</td>
<td>&lt;11 weeks – 90% 11-16 weeks – 20% 16 –20 weeks minimal risk of deafness only &gt;20 weeks – no increased risk</td>
<td>&lt;20 weeks – 9% excess fetal loss; 3% hydrops fetalis, of which about 50% die</td>
<td>Increased fetal loss. Premature delivery</td>
<td>Congenital varicella Syndrome risk: &lt;13 weeks 0.4% 13-20 weeks 2%. Neonatal chickenpox risk: 4 days prior to 2 days post delivery 20%</td>
</tr>
<tr>
<td>Risk of adverse outcome for the pregnant woman</td>
<td>Arthritis</td>
<td>Arthropathy</td>
<td>Severe meases, including pneumonia</td>
<td>Pneumonitis. Case fatality rate for pneumonia in mother is 10%</td>
</tr>
<tr>
<td>Interventions and benefit</td>
<td>Termination of pregnancy</td>
<td>Fetal hydrops – intrauterine transfusion reduces odds of death to 0.14</td>
<td>HNIG to susceptible women and neonate attenuates infection/illness</td>
<td>VZIG to exposed mother and neonate attenuates illness. Intravenous Aciclovir or Valyclovir within 24 hrs of rash onset for mother. Intravenous Aciclovir for infected neonates</td>
</tr>
<tr>
<td>Incubation period</td>
<td>14-21 days</td>
<td>14-21 days</td>
<td>8-14 days</td>
<td>10-21 days</td>
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<tr>
<td>Infectivity period (days pre and post rash onset)</td>
<td>7 days pre to 10 days post onset of</td>
<td>10 days pre to day of onset of rash</td>
<td>4 days before onset of rash to 4 days after</td>
<td>2 days pre onset of rash until cropping has ceased and all</td>
</tr>
<tr>
<td>Number of infections in pregnancy per year</td>
<td>2-3 confirmed infections in pregnancy</td>
<td>1 in 512 pregnancies (ref [14] or seroconversion of 1.5 –13% among susceptibles</td>
<td>Total pregnant women in whom HNIG was used post exposure 07/08 37 08/09 24</td>
<td>The number of pregnant women in whom VZIG has been used post exposure averaged around 1260 between 04/05 and 2007/08. There are an estimated 2-3 infections per 1000 pregnancies, 6 per 10,000 deliveries or 2000 maternal infections per year</td>
</tr>
<tr>
<td>------------------------------------------</td>
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<td>---------------------------------------------------------------------------------</td>
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<tr>
<td>Terminations of pregnancy</td>
<td>1997 – 2 (last year in which separate numbers were available)</td>
<td>Unknown – not recommended</td>
<td>Unknown – not recommended</td>
<td>Unknown</td>
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<tr>
<td>Number of babies born with congenital defects</td>
<td>Approx 1 per year</td>
<td>An estimated 2-8 fetal hydrops per 100,000 pregnancies (14-56 cases per year in UK) 12-48 per 100,000 spontaneous abortion (84-336 cases per year in UK)</td>
<td>None</td>
<td>Approx 10 babies born with congenital damage per year, England and Wales</td>
</tr>
<tr>
<td>Risk to the neonate</td>
<td>None</td>
<td>None</td>
<td>Risk of SSPE with a short onset latency and fulminant course</td>
<td>Risk of severe disseminated haemorrhagic chickenpox. An estimated 30 neonates at risk of severe neonatal infection per year</td>
</tr>
</tbody>
</table>
Further reading


References


53. Manikkavasagan G, Bedford H, Peckham C, Dezateux C. Antenatal Screening for Susceptibility to Varicella Zoster Virus in the UK: A Review commissioned by the National Screening Committee. National Screening Committee, UK; 2009.


