



Public Health
England

Protecting and improving the nation's health

Guidance on the investigation, diagnosis and management of viral illness, or exposure to viral rash illness, in pregnancy

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

Public Health England, Wellington House, 133-155 Waterloo Road
London SE1 8UG Tel: 020 7654 8000

www.gov.uk/phe Twitter: [@PHE_uk](https://twitter.com/PHE_uk)

Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Nalini Iyanger, Helen Campbell, Gayatri Amirthalingam and Kevin Brown.
For queries relating to this document, please contact: Immunisation.lead@phe.gov.uk
Telephone: 0208 200 4400.

Acknowledgements: The authors gratefully acknowledge the expert review and advice received from:

- The NHS Infectious Diseases in Pregnancy Screening (IDPS) Screening Midwives and Specialist Nurses forum
- Royal College of Obstetricians and Gynaecologists
- Professor Judith Breuer, Professor of Virology, University College London



© Crown copyright 2019

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit [OGL](https://www.ogilive.gov.uk). Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

Published: March 2019

PHE publications

gateway number: GW-231

PHE supports the UN

Sustainable Development Goals



Contents

About Public Health England	2
Changes from previous guidance	5
1. Overview	6
2. Scope and background	7
2.1 Introduction	7
2.2 Background and epidemiology of viral infections associated with a rash	7
2.2.1 Parvovirus B19 (B19V)	8
2.2.2 Measles	9
2.2.3 Varicella	10
2.2.4 Rubella	11
2.2.5 Human Herpes Virus (HHV)-6/7	12
2.2.6 Enteroviruses	12
2.2.7 Epstein-Barr virus	13
2.2.8 Cytomegalovirus (CMV)	13
2.3 Advice and information on rash illness for pregnant women	14
3. A pregnant woman presenting with a rash illness	15
3.1 Laboratory investigation and management	15
3.2 Maculopapular rashes in pregnancy	16
3.2.1 Parvovirus	17
Laboratory investigation of suspected parvovirus B19	17
Management of confirmed parvovirus B19	17
Laboratory investigation of hydrops fetalis	18
Management of hydrops fetalis following confirmed parvovirus B19	18
3.2.2 Measles	18
Laboratory investigation of suspected measles	18
Management of confirmed measles	19
Neonates born to measles infected mothers	19
3.2.3 Rubella	19
Laboratory investigation of suspected rubella	19
Management of confirmed rubella – primary and reinfection	20
Management of the neonate born to mother infected during pregnancy	21
3.3 Generalised vesicular rash illness in pregnancy	21
3.3.1 Chickenpox	22
Laboratory investigation of suspected chickenpox	22
Management of confirmed chickenpox infection in a pregnant woman	22
Management of proven chickenpox exposure in utero	23
Management of the neonate exposed to chickenpox	24
4. A pregnant woman in contact with a rash illness	26
4.1 Contact with a maculopapular rash illness	26
4.1.1 Contact with suspected parvovirus B19 (Figure One)	26
4.1.2 Contact with suspected measles (Figure One)	27
4.1.3 Contact with suspected rubella (Figure One)	27
4.2 Contact with a vesicular rash illness	28
4.2.1 Contact with confirmed chickenpox (Figure One)	28

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

4.2.2	VZIG restrictions for pregnant women during times of shortage	30
5.	Other considerations for pregnant women	32
5.1	Occupational exposure	32
	Parvovirus B19	32
	Measles	32
	Chickenpox	32
	Rubella	32
5.2	Antibody screening	33
	Parvovirus B19	33
	Measles	33
	Varicella	33
	Rubella	33
5.3	Inadvertent immunisation during pregnancy	33
Table 1		35
References		37

Changes from previous guidance

1. Updates have been made to the epidemiology of rash illnesses in pregnancy and their sequelae.
2. Advice on post exposure prophylaxis for chickenpox and measles has been updated to reflect current guidance.
3. Advice on assessing immunity to rubella has been updated and the 10 IU/ml threshold for IgG antibody levels has been removed. The presence of antibodies at any level is sufficient to confirm immunity.
4. The section on antibody screening for rubella has been updated to note that universal antenatal screening is no longer offered.
5. A section has been added on the potential for restrictions to the use of varicella zoster immunoglobulin (VZIG) for pregnant women during times of VZIG shortage.
6. A section has been added on the management of a neonate born to a mother with rubella infection during pregnancy.
7. A section has been added on the management of inadvertent shingles immunisation in pregnancy. Unlike inadvertent immunisation in pregnancy with other live vaccinations, for which only reporting is encouraged, inadvertent vaccination with the live shingles vaccination should be treated as an exposure and assessed according to guidance on exposure to shingles.

1. Overview

This document updates and consolidates previous guidance, specifically the 2000 report of the Public Health Laboratory Service (PHLS) Working Group [1-3], and the Health Protection Agency (HPA), now Public Health England (PHE), guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness in pregnancy, published in 2011. This revised guidance has been circulated to PHE and external experts for comment and signed off by the PHE Vaccine Science and Surveillance Group.

This guidance aims to help decision making in the investigation, diagnosis and management of a pregnant woman who has, or is exposed to, rash illness. A rash illness is defined as “a rash compatible with a systemic viral illness”. This guidance should be read in conjunction with more detailed PHE guidance on prophylaxis for pregnant women exposed to measles and chickenpox.

This guidance is in 4 parts: the first part sets out the scope of the document and presents background information; the second part focuses on women who present with viral rash illness in pregnancy; and the third part 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.

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

2. Scope and background

2.1 Introduction

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 PHE Immunoglobulin guidance should be referred to: www.gov.uk/government/publications/immunoglobulin-when-to-use. For the management of parvovirus B19 infection in immunosuppressed individuals, specialist advice should be sought.

2.2 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 – parvovirus B19, measles, rubella and chickenpox. Any febrile illness, including those that can present with a rash, may be associated with an increased risk of fetal loss in the first trimester. The specific risk associated with each individual viral infection is therefore difficult to ascertain.

Streptococcal¹, meningococcal disease², syphilis³, and imported rash causing infections such as Zika and dengue virus⁴ are not considered further as clinical and epidemiological information would focus appropriate investigation and diagnosis in the field.

¹ <https://www.gov.uk/government/collections/scarlet-fever-guidance-and-data>

² <https://www.gov.uk/government/collections/meningococcal-disease-guidance-data-and-analysis>

³ <https://www.gov.uk/government/collections/syphilis-surveillance-data-and-management>

⁴ <https://www.gov.uk/government/publications/zika-virus-interim-algorithm-for-assessing-pregnant-women-with-a-history-of-travel>

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

- parvovirus B19
- measles
- rubella
- varicella
- human herpes virus 6 and 7 (HHV-6 and HHV-7)
- enterovirus

Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) rarely present as a rash illness but should be included as differential diagnoses.

The background and epidemiology of a range of viral rash illnesses is presented in this part but where management is already well established, relevant guidance, sources of further and background information are cited. 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 in a pregnant woman, the fetus or neonate. Human immunodeficiency virus (HIV) and herpes simplex virus (HSV) infection in pregnancy are not covered by this guidance and other established guidelines should be consulted.^{5,6}

2.2.1 Parvovirus B19 (B19V)

There are a wide range of potential consequences of parvovirus B19 infection. These range 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 (average excess risk of 9%) [4]. Hydrops fetalis occurs in 3% of cases if infection is between 9-20 weeks gestation, about half of which die [4]. A more recent study reported fetal hydrops in 11% of pregnancies where infection occurred between 9 and 20 weeks gestation, 40% of whom died [5]. Fetal loss was seen in 7% of pregnancies, if maternal infection occurred at under 20 weeks gestation. Maternal infection after 20 weeks is rarely associated with developmental hydrops or fetal loss (<1%) [5]. These consequences usually occur some 3-5 weeks after the onset of maternal infection, but can be later. Permanent congenital abnormality and/or

⁵ British HIV Association. BHIVA guidelines for the management of HIV infection in pregnant women 2012 (2014 interim review). <http://www.bhiva.org/pregnancy-guidelines.aspx>

⁶ Royal College of Obstetricians and Gynaecologists. Management of Genital Herpes in Pregnancy (October 2014). <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/genital-herpes/>

congenital anaemia have rarely been identified as a consequence of intrauterine infection [4;6;7;8].

In studies, parvovirus B19 reinfection has been shown after administration of high dose virus [9] 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 [10]. An increased incidence occurs every 3-4 years, largely in schoolchildren [11]. In 2013 and 2017/18, there was a particular increase in laboratory reported confirmed cases in women aged 15-44 years [11]. 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 Public Health England) after consultation with a range of authorities [1]. However, a number of areas in relation to management in pregnancy are outside the scope of that guidance.

2.2.2 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 and encephalitis [12]. The incubation period is 7-21 days and the patient is considered infectious from 4 days before to 4 days after the rash appears.

Measles in pregnancy is relatively uncommon but can be associated with severe maternal morbidity, as well as fetal loss and preterm delivery [13]. Maternal morbidity due to pneumonitis has been variously reported as 10% to 52% in case series [14]. There is no evidence to support an association with congenital infection and damage [14]. 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 [15].

Although indigenous measles was rare in the UK following introduction of MMR vaccine in 1988 and the MR vaccine campaign of 1994, fall in vaccine coverage in the late nineties and early 2000s contributed to a rise in the cohort of susceptible individuals, and an increase in the incidence of measles [16]. By 2007, the annual incidence of measles exceeded 1,000 cases for the first time in a decade and large outbreaks continued, leading to national catch up campaigns. In the last few years, coverage for the first and second dose of MMR has increased annually and the number of cases annually has remained below 1,000 since 2014. In 2016, the UK was certified as having

eliminated endemic measles transmission, which means that even though the UK continues to have measles cases, transmission is limited [17;18].

The UK SSPE register is co-ordinated by PHE and all cases are confirmed by the virology reference department. The reference laboratory receives samples from about 20 patients being investigated for SSPE annually. Between 2006 to 2017, only 2 cases of SSPE were identified with presumed UK measles acquisition [18].

2.2.3 Varicella

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 [19], although there are variations in different ethnic groups [20]. The incubation period is 7-21 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 all the 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 1000 pregnancies and more recent data based on retrospective reviews of hospital admissions suggest an incidence between 5-6 per 10,000 deliveries [3;21;22]. 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 [23].

Historic estimates of pneumonitis in varicella cases in pregnancy have been between 10% to 14%, reported in small case series [24]. In a more recent US based study of almost 1,000 pregnant women with chickenpox admitted to hospital between 2003 and 2010, the proportion with pneumonitis was 2.5% and no maternal deaths were reported, probably reflecting improved medical care and use of aciclovir treatment [25]. Studies show that the risk of pneumonitis in pregnant women with chickenpox is increased towards term [26;27]. The highest risk of maternal pneumonitis appears to be associated with maternal 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 [28;29].

The risk of fetal 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 [30]. Isolated case reports have indicated that fetal abnormality consistent with fetal varicella syndrome may occur following infections as late as 28 weeks in pregnancy [31] but the risk is likely to be substantially lower than that of the typical fetal varicella syndrome which occurs after maternal varicella in the first 20 weeks' gestation. The rare clinical manifestations of fetal varicella syndrome include low birth weight, severe multi-system involvement with neurological involvement, eye lesions, and skeletal anomalies, skin scarring and limb hypoplasia [32;33].

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 2 years of life) [33]. This is thought to be due to reactivation of virus after a primary infection in utero.

Fetuses exposed to maternal chickenpox 7 to 20 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 7 days before and 7 days after delivery, the neonate may develop a severe disseminated haemorrhagic neonatal chickenpox known as purpura fulminans [21]. Death may occur in the neonatal period.

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 [34], although it is uncertain whether dissemination of shingles, as may occur in the immunocompromised, carries a fetal/neonatal risk.

2.2.4 Rubella

Rubella is extremely rare in the UK. Over the last 5 years (April 2013 - March 2018), of the nearly 1,500 oral fluid samples tested for rubella by the national reference laboratory as part of the enhanced surveillance programme, 7 cases have been confirmed [35]. Between 2003 and 2016, 31 rubella infections in pregnancy were diagnosed across the UK (0.23 infections per 100,000 pregnancies). Of these, 5 were considered to have been reinfections and 26 primary infections. Of those with primary infections, all women for whom a country of birth was available (n=20) were born outside the UK. Of the 22 women with known place of acquisition, 14 acquired their infection abroad. A total of 12 infants were born with congenital rubella syndrome (CRS) between 2003 and 2016. Five infants were born to women diagnosed with infection during pregnancy. A further 7 infants were diagnosed with CRS at birth but with no laboratory confirmation of maternal infection in pregnancy [36].

The clinical features and consequences for the fetus of primary rubella in pregnancy are well established [37]. The unreliability of a clinical diagnosis of rubella is accepted [38]. The risk to the fetus of primary rubella in the first 16 weeks gestation is substantial, with major and varied congenital abnormalities being associated with infection in the first trimester [37]. Rubella infection between 16 and 20 weeks gestation is associated with a minimal risk of deafness only [39] and rubella prior to the estimated date of conception or after 20 weeks carries no documented risk [37;40].

A rubella reinfection is defined as rubella infection in someone who has previously had either documented natural rubella virus infection or successful rubella immunisation [41]. 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% [42]. 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 5 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.

2.2.5 Human Herpes Virus (HHV)-6/7

HHV-6 and 7 are closely related to Cytomegalovirus (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 [43]. After infection, the virus remains latent with periodic asymptomatic reactivation. HHV6 is integrated into the human genome in approximately 1% of the population. However no clinical implications have been identified and any long-term consequences of congenital infection with HHV-6 are yet to be defined.

2.2.6 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 [44-46], congenital myocarditis [44;48-52], early onset childhood insulin dependent diabetes mellitus [47], abortion or intrauterine death [53], 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 special care baby units (SCBU). Specialist advice should be sought from the PHE Virus Reference Department.

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.

2.2.7 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 [54], 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 [55]. 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.

2.2.8 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 [56]. It is estimated that the overall birth prevalence of congenital CMV infection in the UK is around 3/1000 [57]. 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.

2.3 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:

1. Check and document MMR vaccination status in the maternity records and offer postpartum doses to those with no, incomplete or uncertain vaccination history.
2. Check and document history of chickenpox and shingles, or vaccination against chickenpox and shingles, in the maternity records.
3. 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.
4. 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.
5. 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.

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 (Parts 2 and 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.

3. A 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 first 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.

3.1 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 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)
- recent travel history and relevant dates
- any known contacts with rash illness or recent travel, 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 2 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:

www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-programme-laboratory-handbook. 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 a 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, in consultation with the patient. This will enable patient access to counselling, serial ultrasound scanning and further follow up including investigations, treatment and referral to paediatrics, where appropriate.

3.2 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 (eg in health care situations such as GP surgeries, antenatal clinics)
- It would confirm the date of infection related to gestational age
- estimate of the gestation may be wrong

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

- 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.

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 Team (www.gov.uk/health-protection-team).

3.2.1 Parvovirus

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 from the day after rash onset. 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 4 weeks prior to collection of the serum. Hence infection cannot be excluded if investigation commences more than 4 weeks after onset of rash illness (*vide supra*, rubella).

If parvovirus B19 IgM is detected in the first 20 weeks of pregnancy, confirmation is recommended by alternative assay, eg detection of high levels of B19V DNA or IgG seroconversion using an antenatal booking blood [58]. Testing a second sample may demonstrate a change in IgM reactivity and provide an additional confirmation method.

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 [59;60;8]. On diagnosis of parvovirus B19 infection, specialist advice should be sought including

the need for serial ultrasound scanning and Doppler assessment to prevent the progression of hydrops fetalis.

Laboratory investigation of hydrops fetalis

In a pregnant woman presenting with hydrops fetalis without a rash history, the diagnosis of recent parvovirus B19 infection may be achieved by testing an acute sample for B19V-specific IgM or B19V viral load [58], or 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.

Management of hydrops fetalis following confirmed parvovirus B19

Following confirmation of parvovirus B19 in a pregnant woman presenting with hydrops fetalis, referral to a fetal medicine specialist 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.

3.2.2 Measles

Measles is a notifiable disease, therefore, all suspected cases of measles should be reported to the local **Health Protection Team**.

Laboratory investigation of suspected measles

The serological diagnosis of measles is well established. A serum sample should be collected at first presentation and sent for laboratory testing for measles-specific IgM and IgG. Oral fluid should be collected at the same time, via the local Health Protection Team, 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 4 days but within one month after the onset of rash.

Management of confirmed measles

When measles has been confirmed the management of the pregnancy should continue as normal. Given the risk of maternal pneumonitis, pregnant women must be closely monitored and asked to seek urgent advice if they develop respiratory symptoms.

Neonates born to measles infected mothers

Human normal immunoglobulin (HNIG) is recommended for neonates born to mothers who develop a measles rash 6 days before to 6 days after delivery. For neonates and infants exposed to measles, HNIG is recommended for up to and including 8 months of age.

The dosage for infants is described in the detailed guidance on post exposure prophylaxis for measles (www.gov.uk/government/publications/measles-post-exposure-prophylaxis).

3.2.3 Rubella

Rubella is a notifiable disease, therefore, all suspected cases of rubella should be reported to the local **Health Protection Team**.

Laboratory investigation of suspected rubella

If investigation for rubella is required, the request form must clearly state that:

- the woman is pregnant
- recent rubella is a possibility
- whether or not she has a rash and, if rash is present, date of rash onset
- and provide the other full clinical and epidemiological details given above (see 3.1)

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 [61]. 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.

Although positive rubella IgM results which 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. All rubella IgM-positive cases should be followed up by requesting a second sample and forwarding all samples to the PHE Virus Reference Department for confirmation. Confirmatory testing includes testing for rubella IgM with 2 different formats of assay, PCR testing for rubella RNA and/or rubella IgG avidity testing.

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) is advised [61]. 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.

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, eg "No evidence of recent primary rubella".

Current methods developed for use on oral fluid must not be used alone for confirming or excluding rubella infection in pregnancy. Diagnosis must be made on serum sample(s).

Problems arise when investigation commences 4 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.

Management of confirmed rubella – primary and reinfection

There is no specific treatment for rubella. Management depends on the gestation of pregnancy, the individual circumstances of the woman and the likelihood of congenital abnormalities (Table 1). Decisions on the management of a pregnant woman diagnosed with rubella in the first 20 weeks of pregnancy are best made in a specialist fetal medicine unit.

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 PHE Virus Reference Department 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.

Management of the neonate born to mother infected during pregnancy

Neonates born to women with confirmed rubella infection in pregnancy or where rubella infection could not be ruled out during pregnancy, should be investigated at birth for congenital infection. Samples of cord blood, placenta, urine and an oral fluid should be taken from the infant soon after delivery and sent to the PHE Virus Reference Department. Congenital rubella infection (CRI) is confirmed by detection of rubella IgM in serum or oral fluid and/or detection of rubella RNA in body fluids [36].

Infants with congenital rubella infection are infectious. They excrete virus at birth and some may continue to excrete for more than a year. During the ante-natal period the health protection team should liaise with the hospital infection control team where the mother is booked and ensure there is an appropriate isolation plan for the neonate during and after birth. For infants diagnosed with CRI, isolation should be put in place for any subsequent healthcare attendance until the infant is no longer considered infectious. Samples to monitor duration of virus excretion as a marker of infectiousness should be arranged in discussion with the health protection team. Susceptible individuals should avoid contact with the infant and offered vaccination.

All suspected and confirmed cases of congenital rubella infection/syndrome should be reported to the local health protection team and to the [National Congenital Rubella Surveillance Programme](#).

3.3 Generalised vesicular rash illness in pregnancy

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

3.3.1 Chickenpox

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 should be 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 fetal 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.

Management of confirmed chickenpox infection in a 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.

All women require an urgent clinical assessment on presentation. If the woman 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, offered acyclovir if appropriate and sent home with arrangements for daily review and for outpatient follow up for the fetus. The woman 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.

If there is deterioration, or the fever persists, or the cropping of the rash continues after 6 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

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

- 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

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 7 days (eg aciclovir 5x800mg per day) [24]. Aciclovir should be used cautiously before 20 weeks of gestation. It is reassuring that neither the US nor Danish studies found an increase in major congenital malformations following exposure to antiviral agents in pregnancy. The US based study was a prospective registry of over 1200 pregnancies that received either oral or IV aciclovir across all stages of pregnancy [62]. The Danish national cohort study reviewed 1804 pregnancies exposed to antiviral agents (aciclovir, valaciclovir, famciclovir) during the first trimester of pregnancy and found no evidence for an increased risk of major birth defects compared to an unexposed cohort [63].

If the woman presents more than 24 hours from the onset of rash and there are no indications of complications, antivirals are not routinely advised. There is no evidence that antivirals alter the natural history of uncomplicated chickenpox when given more than 24 hours after rash onset; however, this is a clinical decision [64;65]. VZIG has no place in treatment once the rash appears.

Intravenous treatment with aciclovir is indicated if the chickenpox is severe or there are any complications [66]. Treatment of pneumonia associated with chickenpox in hospital is with intravenous aciclovir 3x10mg/kg/day for 5-10 days [67]. 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 [24].

Management of proven chickenpox exposure in utero

There is a lack of evidence to support immunoglobulin and aciclovir treatment to prevent vertical transmission or fetal varicella syndrome [21].

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

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 abortion care following an early sonographic diagnosis of fetal varicella syndrome.

Management of the neonate exposed to chickenpox

PHE guidance on use of immunoglobulins

(www.gov.uk/government/collections/chickenpox-public-health-management-and-guidance) recommends VZIG for neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery. VZIG can be given without VZV IgG antibody testing of the neonate or mother.

Prophylactic, intravenous aciclovir should also be considered in addition to VZIG for neonates whose mothers develop chickenpox in the period 4 days before to 2 days after delivery, as they are at the highest risk of a fatal outcome despite VZIG prophylaxis.

VZIG is not usually required for neonates born more than 7 days after the onset of maternal chickenpox, or in those whose mothers develop shingles before or after delivery as these neonates will have maternal antibody.

VZIG is not indicated for neonates (< 7 days old) whose mothers have been exposed during pregnancy and have been found to be VZV IgG negative, unless the mother develops chickenpox. VZIG is only indicated for the neonate if they are directly exposed postnatally. Any exposed pregnant women found to be IgG negative should be urgently assessed for post-exposure prophylaxis (PEP) as soon as exposure has occurred (see part 4).

If a neonate has possible exposure to chickenpox from someone other than their mother, refer to the VZIG guidance for risk assessment

(www.gov.uk/government/collections/chickenpox-public-health-management-and-guidance).

If severe chickenpox develops in the neonate despite VZIG, high dose intravenous aciclovir treatment of 20mg/kg every 8 hours for at least 7 days should be started as soon as possible [68].

If other children in the family have chickenpox, and the mother has had chickenpox prior to this pregnancy 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 7 days of age. This is to prevent disease in the first month of life which carries a greater risk of severe disease [34]. If a new baby returns to a home where siblings are still in

the infectious phase of chickenpox, 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 can breast feed safely. 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.

4. A pregnant woman in contact with a rash illness

Contact is defined as being in the same room (eg 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.

4.1 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 which warrant consideration include measles, rubella and parvovirus B19. Other possible infective causes in the contact should await development of illness in a 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 HPT (www.gov.uk/health-protection-team). Through liaison with the local HPT, 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 this section.

4.1.1 Contact with suspected parvovirus B19 (Figure One)

The pregnant woman should be investigated for asymptomatic parvovirus B19 infection. 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 [4]
- active management of the infected fetus may reduce the risk of adverse outcome [59] (part 3)

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

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 part 3).

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 part 3 on suspected B19V infection in pregnancy.

4.1.2 Contact with suspected measles (Figure One)

Clinical features suggestive of measles are described in part 2. 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

PHE guidance on human normal immunoglobulin (HNIG) for pregnant women should be consulted to determine if prophylaxis is warranted. The guidance is available here: www.gov.uk/government/publications/measles-post-exposure-prophylaxis.

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. If there is another exposure to measles 3 weeks or more after the first use of HNIG, the need for HNIG should be reassessed using the above guidance.

HNIG may not prevent measles, but has been shown to attenuate illness. There is no evidence that it prevents intrauterine death or pre-term delivery. [14]

4.1.3 Contact with suspected rubella (Figure One)

From 1 April 2016, antenatal rubella susceptibility screening ceased in England. 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 she must return if a rash develops:

- at least 2 documented doses of rubella containing vaccine
- at least one rubella antibody test (before or at the time of exposure) in which IgG antibody was detected

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 4 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 to the PHE Virus Reference Department for confirmatory testing. Refer to part 3 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.

4.2 Contact with a vesicular rash illness

4.2.1 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. PHE guidance on post-exposure prophylaxis (PEP) for pregnant women should be consulted to determine if prophylaxis is warranted. The guidance is available here:

www.gov.uk/government/publications/varicella-zoster-immunoglobulin.

If a woman has a past history of chickenpox or shingles or 2 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 (2 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 [69]. Those with a negative or equivocal result from a qualitative assay require confirmatory testing with a quantitative assay. For immunocompetent pregnant women, a result of 100mIU/ml or less suggests susceptibility to infection.

Usually, VZIG is recommended for VZ antibody-negative pregnant contacts exposed at any stage of pregnancy, providing it can be given within 10 days of contact. However, when supplies of VZIG are short, issues to pregnant women may be restricted and revised guidance issued. Clinicians are advised to consult current guidance before offering VZIG to pregnant women (www.gov.uk/government/publications/varicella-zoster-immunoglobulin).

Where VZIG is indicated, it should be offered to eligible, susceptible women within 10 days of the exposure [70]. 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 NHS or PHE lab.

The clinical attack rates are similar whether VZIG is given within 72 hours or 4-10 days after contact [33]. 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 she has since delivered, VZIG should be administered within the 10 day period.⁷

The majority of adults will be VZV antibody positive. Lack of varicella-specific IgG antibody in a woman without a history of chickenpox is highly suggestive of susceptibility. If susceptibility in a pregnant woman has been confirmed using a quantitative assay then post-partum vaccination may be considered [24].

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

- a) VZV IgG positive - reassure as PEP is not indicated.
- b) VZV IgG equivocal or negative with a qualitative assay - retest using a quantitative assay. If time does not permit additional testing within 10 days of contact and the individual is VZV IgG negative then recommend appropriate PEP. If time does not permit additional testing within 10 days of contact and the individual is VZV IgG equivocal, then PEP is not recommended.
- c) If less than 100mIU/ml with a quantitative assay then recommend PEP.

Pregnant women who have previously received VZIG or IVIG as VZV post-exposure prophylaxis require a new risk assessment if a second exposure occurs. If the second exposure occurs:

⁷ 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.

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

- within 3 weeks of administration of VZIG or IVIG, a further dose of VZIG is not required
- between 3 and 6 weeks following administration of VZIG or IVIG, further post-exposure prophylaxis should be administered without further testing
- more than 6 weeks following administration of VZIG or IVIG, retesting of a new sample is required

As post exposure prophylaxis does not always prevent chickenpox the woman should be managed as being possibly infectious 8-28 days after exposure 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 pneumonitis associated with chickenpox infection has been reported in spite of timely VZIG administration.

The live chickenpox vaccine is contraindicated in pregnancy [72]. 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 Public Health England: www.gov.uk/guidance/vaccination-in-pregnancy-vip

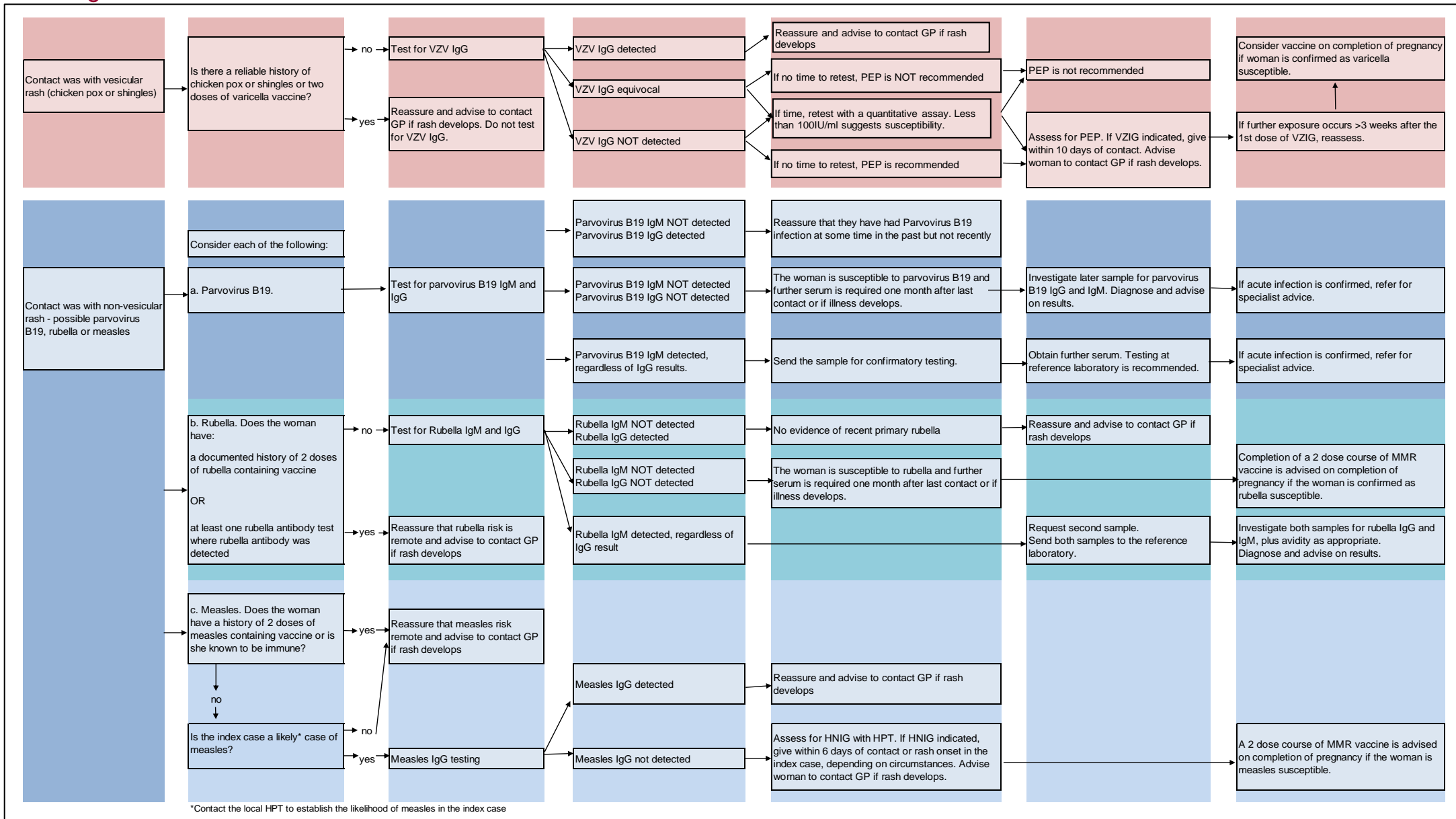
4.2.2 VZIG restrictions for pregnant women during times of shortage

During times of severe shortage of VZIG, the issue of VZIG for pregnant women exposed to chickenpox may be restricted. In such circumstances, VZIG has normally been limited to susceptible pregnant women who have had significant exposure in the first 20 weeks (20+0) of pregnancy. For women exposed after 20 weeks who are found to be susceptible to chickenpox, prophylaxis with the oral anti-viral drug, aciclovir, is recommended. Valaciclovir may also be used. Clinicians are advised to consult current guidance before offering VZIG to pregnant women:

www.gov.uk/government/publications/varicella-zoster-immunoglobulin

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

Figure One



*Contact the local HPT to establish the likelihood of measles in the index case

5. Other considerations for pregnant women

5.1 Occupational exposure

Parvovirus B19

Guidance on the management of pregnant women susceptible to parvovirus B19 has previously been published [1]. Exclusion is not routinely recommended of pregnant women susceptible to B19V from settings which may suggest a higher rate of exposure (eg nurseries and schools). Exposure to B19V is as likely to occur in the wider community, and more likely within the household setting. However, if there is a laboratory confirmed outbreak of B19V in a school or nursery, then an individual risk assessment should be undertaken, taking into account contact with other children outside the working environment.

Measles

Exclusion is not recommended of pregnant women susceptible to measles from settings which may suggest a higher rate of exposure (eg 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.

Rubella

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

Chickenpox

Exclusion is not recommended of pregnant women susceptible to chickenpox from settings which may suggest a higher rate of exposure (eg 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.

5.2 Antibody screening

Parvovirus B19

Unselected screening of pregnant women for past infection with parvovirus B19 is not recommended as neither vaccine nor prophylaxis are available [73].

Measles

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

Satisfactory evidence of protection would include documentation of having received 2 doses of measles containing vaccine or a positive antibody test for measles. All women without such evidence who need to be protected against measles should be offered MMR vaccine post-partum.

Rubella

Universal screening of all pregnant women is no longer recommended and was stopped in April 2016 [75]. Instead, rubella immunity should be established at booking by checking for documented evidence of 2 doses of a rubella-containing vaccine. All those without such evidence should be offered MMR vaccination post-partum.

Varicella

The National Screening Committee commissioned a review of antenatal screening for VZV susceptibility in 2016 which concluded that there was insufficient evidence to recommend the introduction of routine antenatal screening in the UK [74]. At present, it is good practice to establish and record whether there is a firm history of chickenpox or shingles at booking.

5.3 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. HPV vaccine, whilst inactivated, is also not advised in pregnancy. However, if a woman has been inadvertently immunised with these vaccines during pregnancy, termination should not be recommended. The woman should be reassured that no adverse effects have been identified from MMR, chickenpox or HPV vaccination during any stage in pregnancy.

The administration of shingles vaccine (Zostavax) is not recommended during pregnancy and inadvertent administration should be treated in the same way as natural

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

exposure to chickenpox. The woman's susceptibility should be urgently assessed (see part 4). [76].

Surveillance of inadvertent administration of vaccine shortly before conception or during pregnancy is being conducted by the Immunisation Department at PHE, to whom such cases should be reported (Tel: 07824 551 803 or 020 8200 4400:

www.gov.uk/guidance/vaccination-in-pregnancy-vip

Table 1

	Parvovirus B19	Measles	Rubella	Chickenpox
Proportion seronegative in young adult females	40-50%	<5%	7% of all women screened antenatally, rising from nearly 3% in 2006 (2006-2014 NHSBT data)	1.2-14% Varies with country of origin
Incubation period	4-21 days	7-21 days	14-21 days	7-21 days
Infectivity period (days pre and post rash onset)	10 days before to day of onset of rash	4 days before onset of rash to 4 days after	7 days before to 10 days post onset of rash	2 days before onset of rash until crusting has ceased and all lesions crusted. Infectivity is prolonged by VZIG and HNIG
Infectivity – risk of transmission from close contact (household attack rate)	Medium (50%)	V high (99%)	High (90%)	High (70-90%)
Risk of adverse outcome for a pregnant woman	Arthropathy	Severe measles, including pneumonitis	Arthritis	Pneumonitis
Risk of intrauterine infection by gestational age	<4 weeks – 0% 5-16 weeks – 15% >16 weeks – 25-70%, increasing with gestation	Not known	<11 weeks – 90% 11-16 weeks – 55% >16 weeks – 45%	<28 weeks- 5-10% 28-36 weeks- 25% >36 weeks- 50%
Risk of adverse fetal outcome	<20 weeks – 9% excess fetal loss. 3% hydrops fetalis, of which about 50% die without treatment [4] >20 weeks - <1% [8]	Increased fetal loss. Premature delivery	<11 weeks- 90% 11-16 weeks - 20% 16 - 20 weeks – minimal risk of deafness only >20 weeks - no increased risk	Fetal varicella Syndrome risk: <13 weeks- 0.4% 13-20 weeks- 2%. Neonatal chickenpox risk in 4 days prior to 2 days post-delivery - 20%
Risk to the neonate	None	Risk of SSPE with a short onset latency and fulminant course	None	Risk of severe disseminated haemorrhagic chickenpox. An estimated 30 neonates at risk of severe neonatal infection per year
Interventions and benefit	Fetal hydrops – resolution of infection	HNIG to susceptible	Counselling for parents to make	PEP to exposed mother and neonate

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

	Parvovirus B19	Measles	Rubella	Chickenpox
	increased from 5% spontaneous resolution to 55% after intrauterine transfusion	women and neonates attenuates infection/illness	informed decision about whether to continue with the pregnancy	attenuates illness. Intravenous aciclovir or valcyclovir within 24 hrs of rash onset for mother. Intravenous aciclovir for infected neonates.
Number of infections in pregnancy per year	1 in 512 pregnancies [14] or seroconversion of 1.5 –13% among susceptibles	Total pregnant women for whom HNIG was requested post exposure- 30 between April 2014 and March 2018	1-2 confirmed infections in pregnancy	VZIG was issued for 580 susceptible, pregnant women in 2016/17. There are an estimated 2-3 infections per 1000 pregnancies, 6 per 10,000 deliveries or 2000 maternal infections per year.
Terminations of pregnancy	Unknown – not recommended	Unknown – not recommended	4 terminations between 2003 and 2016 [36]	Unknown
Number of babies born with congenital defects	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)	None	Approx 1 per year	Approx 10 babies born with fetal damage per year, England and Wales

References

1. Crowcroft NS, Roth CE, Cohen BJ, Miller E. Guidance for control of parvovirus B19 infection in healthcare settings and the community. *J Public Health Med* 1999 Dec;21(4):439-46.
2. Morgan-Capner P, Crowcroft NS. Guidelines on the management of, and exposure to, rash illness in pregnancy (including consideration of relevant antibody screening programmes in pregnancy). *Commun Dis Public Health* 2002 Mar;5(1):59-71.
3. Nathwani D, Maclean A, Conway S, Carrington D. Varicella infections in pregnancy and the newborn. A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect* 1998 Jan;36 Suppl 1:59-71.
4. Miller E, Fairley CK, Cohen BJ, Seng C. Immediate and long term outcome of human parvovirus B19 infection in pregnancy. *Br J Obstet Gynaecol* 1998 Feb;105(2):174-8.
5. Enders M, Klingel K, Weidner A, Baisch C, Kandolf R, Schalasta G, Enders G. Risk of fetal hydrops and non-hydropic late intrauterine fetal death after gestational parvovirus B19 infection. *J Clin Virol* 2010 Jul; 49: 163-8.
6. Brown KE. Parvovirus B19 infection in the fetus and child. In: David TJ, editor. *Recent advances in paediatrics*. London: RSM Press; 2007. p. 209-22.
7. Jonathan Lassen J, Bager P, Wohlfahrt J, Bottiger B, Melbye M. Parvovirus B19 infection in pregnancy and subsequent morbidity and mortality in offspring. *Int J Epidemiol* 2013 Aug;42(4):1070–6.
8. Bascietto F, Liberati M, Murgano D, Buca D, Iacovelli A, Flacco ME et al. Outcomes associated with fetal Parvovirus B19 infection: A systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2018 May.
9. Doyle S, Corcoran A. The immune response to parvovirus B19 exposure in previously seronegative and seropositive individuals. *J Infect Dis* 2006 Jul 15;194(2):154-8.
10. Vyse AJ, Andrews NJ, Hesketh LM, Pebody R. The burden of parvovirus B19 infection in women of childbearing age in England and Wales. 2006.
11. Public Health England. Increased parvovirus activity in England (2018). HPR 12(20), August 2018. Retrieved from: www.gov.uk/government/publications/health-protection-report-volume-12-2018/hpr-volume-12-issue-20-news-8-june#increased-parvovirus-activity-in-england-2018
12. Katz M. Clinical spectrum of measles. *Curr Top Microbiol Immunol* 1995;191:1-12.
13. Eberhart-Phillips JE, Frederick PD, Baron RC, Mascola L. Measles in pregnancy: a descriptive study of 58 cases. *Obstet Gynecol* 1993 Nov;82(5):797-801.
14. Manikkavasagan G, Ramsay M. The rationale for the use of measles post-exposure prophylaxis in pregnant women: a review. *J Obstet Gynaecol* 2009 Oct;29(7):572-5.
15. Campbell H, Andrews N, Brown KE, Miller E. Review of the effect of measles vaccination on the epidemiology of SSPE. *Int J Epidemiol* 2007 Dec;36(6):1334-48.

16. Choi YH, Gay N, Fraser G, Ramsay M. The potential for measles transmission in England. *BMC Public Health* 2008;8:338-46.
17. Public Health England. UK measles and rubella elimination. Retrieved from: www.gov.uk/government/publications/measles-and-rubella-elimination-uk/uk-measles-and-rubella-elimination. Accessed: August 2018.
18. Public Health England. UK Measles and Rubella elimination strategy 2019. January 2019. Retrieved from: www.gov.uk/government/publications/measles-and-rubella-elimination-uk-strategy
19. Vyse AJ, Gay NJ, Hesketh LM, Morgan-Capner P, Miller E. Seroprevalence of antibody to varicella zoster virus in England and Wales in children and young adults. *Epidemiol Infect* 2004 Dec;132(6):1129-34.
20. Talukder YS, Kafatos G, Pinot dM, Aquilina J, Parker SP, Crowcroft NS, et al. The seroepidemiology of varicella zoster virus among pregnant Bangladeshi and white British women in the London Borough of Tower Hamlets, UK. *Epidemiol Infect* 2007 Nov;135(8):1344-53.
21. Miller E, Cradock-Watson JE, Ridehalgh MK. Outcome in newborn babies given anti-varicella-zoster immunoglobulin after perinatal maternal infection with varicella-zoster virus. *Lancet* 1989 Aug 12;2(8659):371-3.
22. McKendrick MW, Lau J, Alston S, Bremner J. VZV infection in pregnancy: a retrospective review over 5 years in Sheffield and discussion on the potential utilisation of varicella vaccine in prevention. *J Infect* 2007 Jul;55(1):64-7.
23. Gershon AA, Steinberg SP, Gelb L. Clinical reinfection with varicella-zoster virus. *J Infect Dis* 1984 Feb;149(2):137-42.
24. Royal College of obstetricians and gynaecologists. Chickenpox in pregnancy. Bristol; 2015 Jan. Report No.: Guide no. 13.
25. Zhang HJ, Patenaude V, and Abenheim HA. Maternal outcomes in pregnancies affected by varicella zoster virus infections: Population-based study on 7.7 million pregnancy admissions. *J Obstet Gynaecol Res* 2015 Jan;41(1): 62–68.
26. Smego RA, Jr., Asperilla MO. Use of acyclovir for varicella pneumonia during pregnancy. *Obstet Gynecol* 1991 Dec;78(6):1112-6.
27. Esmonde TF, Herdman G, Anderson G. Chickenpox pneumonia: an association with pregnancy. *Thorax* 1989 Oct;44(10):812-5.
28. Paryani SG, Arvin AM. Intrauterine infection with varicella-zoster virus after maternal varicella. *N Engl J Med* 1986 Jun 12;314(24):1542-6.
29. Balducci J, Rodis JF, Rosengren S, Vintzileos AM, Spivey G, Vosseller C. Pregnancy outcome following first-trimester varicella infection. *Obstet Gynecol* 1992 Jan;79(1):5-6.
30. Sauerbrei A, Wutzler P. Herpes simplex and varicella-zoster virus infections during pregnancy: current concepts of prevention, diagnosis and therapy. Part 2: Varicella-zoster virus infections. *Med Microbiol Immunol* 2007 Jun;196(2):95-102.
31. Alonso AM, Perrotin F, Harchaoui Y, Body G, Lansac J. [Varicella pneumonia during pregnancy after double exposure in the 2nd trimester. Value of seroprophylaxis]. *J Gynecol Obstet Biol Reprod (Paris)* 1999 Dec;28(8):838-41.

32. Birthistle K, Carrington D. Fetal varicella syndrome – a reappraisal of the literature. A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect* 1998 Jan;36 Suppl 1:25-9.
33. Enders G, Miller E, Cradock-Watson J, Bolley I, Ridehalgh M. Consequences of varicella and herpes zoster in pregnancy: prospective study of 1739 cases. *Lancet* 1994 Jun 18;343(8912):1548-51.
34. Enders G, Miller E. Varicella and herpes zoster in pregnancy and the newborn. In: Arvin AM, Gershon AA, editors. *Varicella zoster virus: basic virology and clinical management*. Cambridge: Cambridge University Press; 2000.
35. Public Health England. Rubella notifications and confirmed cases by oral fluid testing 2013 to 2018. Retrieved from: www.gov.uk/government/publications/rubella-confirmed-cases/rubella-notifications-and-confirmed-cases-by-oral-fluid-testing-in-england-2013-to-2014-by-quarter. Accessed: August 2018.
36. Bukasa A, Campbell H, Brown K, Bedford H, Ramsay M, Amirthalingam G, Tookey P. Rubella infection in pregnancy and congenital rubella in United Kingdom, 2003 to 2016. *Eurosurveillance* 2018 May 23(19); 17-00381.
37. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 1982 Oct 9;2(8302):781-4.
38. Anderson MJ, Kidd IM, Morgan-Capner P. Human parvovirus and rubella-like illness. *Lancet* 1985 Sep 21;2(8456):663.
39. Grillner L, Forsgren M, Barr B, Bottiger M, Danielsson L, de Verdier C. Outcome of rubella during pregnancy with special reference to the 17th-24th weeks of gestation. *Scand J Infect Dis* 1983;15(4):321-5.
40. Enders G, Nickerl-Pacher U, Miller E, Cradock-Watson JE. Outcome of confirmed periconceptual maternal rubella. *Lancet* 1988 Jun 25;1(8600):1445-7.
41. Best JM, Banatvala JE, Morgan-Capner P, Miller E. Fetal infection after maternal reinfection with rubella: criteria for defining reinfection. *BMJ* 1989 Sep 23;299(6702):773-5.
42. Morgan-Capner P, Miller E, Vurdien JE, Ramsay ME. Outcome of pregnancy after maternal reinfection with rubella. *CDR (Lond Engl Rev)* 1991 May 24;1(6):R57-R59.
43. Ward KN. Human herpesviruses-6 and -7 infections. *Curr Opin Infect Dis* 2005 Jun;18(3):247-52.
44. Bendig JW, Franklin OM, Hebden AK, Backhouse PJ, Clewley JP, Goldman AP, et al. Coxsackievirus B3 sequences in the blood of a neonate with congenital myocarditis, plus serological evidence of maternal infection. *J Med Virol* 2003 Aug;70(4):606-9.
45. Cheng LL, Ng PC, Chan PK, Wong HL, Cheng FW, Tang JW. Probable intrafamilial transmission of coxsackievirus b3 with vertical transmission, severe early-onset neonatal hepatitis, and prolonged viral RNA shedding. *Pediatrics* 2006 Sep;118(3):e929-e933.
46. Konen O, Rathaus V, Bauer S, Dolfen T, Shapiro M. Progressive liver calcifications in neonatal coxsackievirus infection. *Pediatr Radiol* 2000 May;30(5):343-5.
47. Dahlquist GG, Ivarsson S, Lindberg B, Forsgren M. Maternal enteroviral infection during pregnancy as a risk factor for childhood IDDM. A population-based case-control study. *Diabetes* 1995 Apr;44(4):408-13.

48. Euscher E, Davis J, Holzman I, Nuovo GJ. Coxsackie virus infection of the placenta associated with neurodevelopmental delays in the newborn. *Obstet Gynecol* 2001 Dec;98(6):1019-26.
49. Konstantinidou A, Anninos H, Spanakis N, Kotsiakis X, Syridou G, Tsakris A, et al. Transplacental infection of Coxsackievirus B3 pathological findings in the fetus. *J Med Virol* 2007 Jun;79(6):754-7.
50. Molnarova A, Petrovicova A, Fedeles J, Bopegamage S, Horakova E. Coxsackie viral infection and orofacial cleft. *Bratisl Lek Listy* 2002;103(10):365-7.
51. Sauerbrei A, Gluck B, Jung K, Bittrich H, Wutzler P. Congenital skin lesions caused by intrauterine infection with coxsackievirus B3. *Infection* 2000 Sep;28(5):326-8.
52. Tang JW, Bendig JW, Ossueta I. Vertical transmission of human echovirus 11 at the time of Bornholm disease in late pregnancy. *Pediatr Infect Dis J* 2005 Jan;24(1):88-9.
53. Petersson K, Norbeck O, Westgren M, Broliden K. Detection of parvovirus B19, cytomegalovirus and enterovirus infections in cases of intrauterine fetal death. *J Perinat Med* 2004;32(6):516-21.
54. Schooley RT. Epstein-Barr virus (infectious mononucleosis). In: Mandell GL, Bennet JE, Dolin R, editors. *Principles and Practice of Infectious Diseases*. 5 ed. Philadelphia: Churchill Livingstone; 2000. p. 1599-612.
55. Arvin AM, Maldonado YA. Other viral infections of the fetus and newborn. *Infectious diseases of the fetus and newborn infant*. 4 ed. 1995.
56. Ross SA, Boppana SB. Congenital cytomegalovirus infection: outcome and diagnosis. *Semin Pediatr Infect Dis* 2005 Jan;16(1):44-9.
57. UK National Screening Committee. Newborn screening for cytomegalovirus: External review against programme appraisal criteria for the UK National Screening Committee (UK NSC). Dec 2017. Retrieved from: legacyscreening.phe.org.uk/cytomegalovirus
58. Maple PAC, Hedman L, Dhanilall P, Kantola K, Nurmi V, Soderland-Venermo M, et al. Identification of Past and Recent Parvovirus B19 Infection in Immunocompetent Individuals by Quantitative PCR and Enzyme Immunoassays: a Dual-Laboratory Study. *J Clin Microbiol*. 2014 Mar; 52(3):947-56.
59. Fairley CK, Smoleniec JS, Caul OE, Miller E. Observational study of effect of intrauterine transfusions on outcome of fetal hydrops after parvovirus B19 infection. *Lancet* 1995 Nov 18;346(8986):1335-7.
60. Simms RAA, Liebling RE, Patel RR, Denbow ML, Abdel-Fattah, Soothill PW et al. Management and Outcome of Pregnancies with Parvovirus B19 Infection over Seven Years in a Tertiary Fetal Medicine Unit. *Fetal Diagn Ther* 2009 ;25:373–378.
61. Thomas HI, Morgan-Capner P, Enders G, O'Shea S, Caldicott D, Best JM. Persistence of specific IgM and low avidity specific IgG1 following primary rubella. *J Virol Methods* 1992 Sep;39(1-2):149-55.
62. Stone KM, Reiff-Eldridge R, White AD, Cordero JF, Brown Z, Alexander ER, et al. Pregnancy outcomes following systemic prenatal acyclovir exposure: Conclusions from the international acyclovir pregnancy registry, 1984-1999. *Birth Defects Res A Clin Mol Teratol* 2004 Apr;70(4):201-7.

Guidance on the investigation, diagnosis and management of viral rash illness, or exposure to viral rash illness, in pregnancy

63. Pasternak B, Hviid A. Use of Acyclovir, Valacyclovir, and Famciclovir in the First Trimester of Pregnancy and the Risk of Birth Defects. *JAMA*. 2010 Aug; 304(8): 859-66.
64. Wallace MR, Bowler WA, Murray NB, Brodine SK, Oldfield EC, III. Treatment of adult varicella with oral acyclovir. A randomized, placebo-controlled trial. *Ann Intern Med* 1992 Sep 1;117(5):358-63.
65. Cohen J, Breuer J. Chickenpox: treatment. *Clinical Evidence* 2015 Jun;06:912.
66. Kempf W, Meylan P, Gerber S, Aebi C, Agosti R, Buchner S, et al. Swiss recommendations for the management of varicella zoster virus infections. *Swiss Med Wkly* 2007 May 5;137(17-18):239-51.
67. Ogilvie MM. Antiviral prophylaxis and treatment in chickenpox. A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect* 1998 Jan;36 Suppl 1:31-8.
68. Paediatric Formulary Committee. *British National Formulary for Children*. London: BMJ Group; 2018.
69. Maple PAC, Gunn A, Sellwood J, Brown DWG, Gray JJ. Comparison of fifteen commercial assays for detecting varicella zoster virus IgG with reference to a time resolved fluorescence immunoassay (TRFIA) and the performance of two commercial assays for screening sera from immunocompromised individuals. *J Virol Methods* 2009;155:143-9.
70. Miller E, Marshall R, Vurdien J. Epidemiology, outcome and control of varicella-zoster infection. *Rev Med Microbiol* 1993;4:222-30.
71. Paediatric Formulary Committee. *British National Formulary for Children*. London: BMJ Group; 2018.
72. Public Health England. *Green Book (2015)*. Chapter 34: varicella. Immunisation against Infectious Diseases.
73. UK National Screening Committee. Parvovirus B19 Infection in Pregnancy. A Brief Review of Literature: External review against programme appraisal criteria for the UK National Screening Committee (UK NSC). Jun 2014. Retrieved from: legacyscreening.phe.org.uk/policydb_download.php?doc=444
74. UK National Screening Committee. UK NSC recommendation on screening for varicella susceptibility. Mar 2016. Retrieved from: legacyscreening.phe.org.uk/policydb_download.php?doc=621
75. Public Health England. Rubella susceptibility screening in pregnancy to end in England. 2016. Retrieved from: www.gov.uk/government/news/rubella-susceptibility-screening-in-pregnancy-to-end-in-england
76. Public Health England. *Green Book (2016)*. Chapter 28a: Shingles (Herpes Zoster). Immunisation against Infectious Diseases.