A summary of guidance related to viral rash in pregnancy

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Introduction

- Viral exanthema can cause rash in pregnant women and should be considered even in countries with comprehensive vaccination programmes.

- It is important to be aware of their presentation due to the possibility of serious consequences for both mother and foetus.
Viral infections that commonly present with generalised rash illness in the UK include:

1. Varicella (chickenpox)
2. Parvovirus B19 (e.g. slapped cheek syndrome)
3. Rubella
4. Measles
5. Epstein-Barr Virus
6. Cytomegalovirus
7. Human Herpes Virus 6 and 7
8. Enterovirus (e.g. hand, foot and mouth)
More recently, Zika virus has been a concern worldwide, due to its link to microcephaly and birth defects. It should also be given due consideration as a potential diagnosis.

Public Health England Zika Virus guidance for Primary Care updated November 2016
Points to note in the history

- **Duration of pregnancy** – exposure/infections in the first trimester may have different consequences to that in the last trimester

- Location, speed and date of onset of rash

- **Associated symptoms.** Fever, sore throat and malaise suggest an infectious cause compared to itching, for example

- Vaccination history
- History of chickenpox or having received the vaccine

- **Country of origin** – vaccination coverage varies globally

- **Recent travel** to countries where rubella and measles are endemic. Travel to South America or the Caribbean in the previous 2 weeks should prompt consideration of Zika virus infection

- **Contact with unwell people** with a rash or with someone who has travelled to an endemic country
- **Sexual history** – relevant with regards to Zika virus and HIV

- **Past medical history/problems in previous pregnancies**

- **Drug history** – If a patient is on immunosuppressants or steroids, herpes zoster may be more likely
Varicella

- Endemic in the UK, more than 85% adults having been infected. Presents with a vesicular rash.

- **Incubation** period is **10-21 days** and can be prolonged if the patient is immunosuppressed.

- For investigation and consideration of VZIG (Varicella Zoster Immunoglobulin) or contact management, the patient is considered **infectious 48 hours before the rash appears and until vesicles crust over.**
Maternal risks of chickenpox infection

- Risk of pneumonia in pregnant women with chickenpox is increased towards term and fatality increases to 20-40% if untreated.

- Highest risk of maternal pneumonia is associated with infection after 18-20 weeks of pregnancy.

- Encephalitis is a rare complication with mortality of 5-10%.
Foetal risks of maternal chickenpox infection

- There is little evidence to suggest infection in the first trimester is more likely to lead to foetal loss.

- Chickenpox during the first two trimesters can lead to intrauterine infection in up to 25% of cases but only a small proportion of these will develop congenital varicella syndrome.

- 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.
The risk of congenital varicella syndrome is 0.4% in maternal infection between conception and 12 weeks gestation and 2% between 12 and 20 weeks gestation.

Risk of shingles of infancy or early childhood (0.8-1.7% risk in first 2 years of life) in babies born to mothers infected between 20-37 weeks gestation.

Foetuses exposed to chickenpox between 20 and 7 days before delivery may develop neonatal chickenpox. This is usually less severe due to transplacentally transmitted antibodies partially protecting the foetus.
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 fuminans. Neonatal death may occur.
Localised maternal shingles (herpes zoster) reflects reactivation of the latent virus. There is a theoretical risk of postnatal transmission of chickenpox to the baby from maternal shingles on the chest, abdomen or exposed areas. **There is no other observed risk to the foetus or neonate of localised maternal shingles.**
Management of confirmed chickenpox in the pregnant woman

- Diagnosis can usually be made clinically.

- If the woman presents within 24 hours of onset of the rash and she has reached 20 weeks gestation she should be offered antiviral treatment for 7 days. Aciclovir 800mg 5 times per day. This is to reduce the risk of pneumonia.

- Aciclovir should be used cautiously before 20 weeks gestation.

- If it is more than 24 hours after the onset of the rash, antivirals are not advised as there is no evidence of benefit.
- VZIG has no place in treatment once the rash appears.

- Referral to hospital is indicated if there is deterioration, fever persists, the cropping of the rash continues after 6 days or if respiratory or other symptoms develop.

- IV treatment with Aciclovir is indicated if the chickenpox is severe or complications are present.
Management of confirmed chickenpox exposure in utero

- There is **no** evidence of **benefit** of immunoglobulin or aciclovir treatment in preventing vertical transmission or congenital varicella syndrome.

- Chickenpox during pregnancy does not justify termination without prior prenatal diagnosis as only a minority of foetuses will be infected and not all of those will develop congenital varicella syndrome. Parental counselling should be offered in a specialist unit.
Management of the neonate exposed to chickenpox

- The HPA (Health Protection Agency) recommends infants whose mothers develop chickenpox (but not shingles) between 7 days before to 7 days after delivery should be given VZIG without antibody testing of the infant.

- If severe chickenpox develops despite VZIG, high dose IV aciclovir should be given.

- If other children in the family have chickenpox and the mother has had chickenpox or is known to have varicella-zoster virus antibody, there is no reason to prevent a new baby going home.
If the mother is susceptible, then contact with siblings should be delayed till baby is 7 days of age, in order to prevent disease in first month of life which carries greater risks of severe illness.

Mothers with chickenpox should be allowed to breastfeed. If the nipple is affected the mother should express the milk until the lesions are crusted over. This milk can be fed to baby if it is covered by VZIG and/or aciclovir.
Contact with confirmed chickenpox during pregnancy

- If the woman:
  - has a past history of chickenpox or shingles
  - **OR** has had 2 doses of varicella vaccine
  - **AND** is not immunosuppressed – Reassure her that protection can be assumed and no further action is needed.

- If the above criteria are not met then the woman needs urgent assessment of susceptibility by testing for VZV IgG serum antibody. Absence of the antibody indicates susceptibility.

- VZIG should be offered to susceptible women **within 10 days of the exposure**, irrespective of gestation.
VZIG does not always prevent chickenpox. The woman should be managed as possibly infectious from 8-28 days after VZIG and asked to see her doctor if she develops a rash.
Parvovirus B19

- Parvovirus B19 infection is common with approximately 50-60% of adults having been infected.

- An increased incidence occurs every 3-4 years, mostly in schoolchildren.

- Infection has a wide range of presentations from minor febrile illness to slapped cheek syndrome, a generalised rash illness similar to rubella, aplastic crises in susceptible patients, arthropathy and persistent infection in the immunocompromised.
- Incubation period is 14 to 21 days.

- Infectious period is from 10 days before rash to day of rash onset.
Foetal risks of parvovirus B19 infection

- Intrauterine death if maternal infection occurs in first 20 weeks of pregnancy – 15% risk compared with a control group risk of 5%

- Hydrops foetalis – risk is 3% if infection between 9-20 weeks, of which half die.

- These consequences usually occur 3-5 weeks after maternal infection, but can be later.
Management of parvovirus B19 infection

- Confirm or exclude recent infection by testing for parvovirus specific IgM antibody.

- Failure to detect parvovirus specific IgM antibody excludes infection in the 4 weeks prior to collection of the serum. Hence, infection cannot be excluded if investigation done 4 weeks after onset of rash illness.

- If parvovirus specific IgM is detected in the first 20 weeks of pregnancy, further testing is required to confirm the diagnosis with an alternative assay.
- Specialist input and serial ultrasound scanning would be required to assess for development of hydrops foetalis.

- Intrauterine transfusion of the foetus may be considered due to some evidence of improved outcomes.
Contact with suspected parvovirus B19 infection during pregnancy

- The pregnant woman should be investigated for asymptomatic infection as it is at least as likely to cause foetal damage as symptomatic infection AND active management of the foetus may reduce the risk of adverse outcomes.

- Serum should be collected as soon as possible and tested for B19V-specific IgG and IgM.
If IgG positive and IgM not detected – reassure the woman that the test shows parvovirus B19 infection at some time but not recently.

If neither antibody is detected – repeat sample at one month. If still not detected – reassure that there no evidence of recent infection but she is susceptible to it.

If IgM detected and no IgG – repeat sample immediately and if again IgM detected, manage as suspected infection with specialist input.
Rubella

- Clinical diagnosis can be unreliable.

- Symptoms include low grade fever, mild URTI symptoms, maculopapular rash (begins at hairline and spreads down), Pale pink discrete lesions fading to brown over 4 days

- **Incubation** period is **14 to 21 days**

- **Infectious** from **7 days before rash to 10 days after**
Maternal risks of rubella infection

- Arthritis
Foetal risks of maternal rubella infection

- Congenital Rubella Syndrome (triad of sensorineural deafness, eye abnormalities and congenital heart disease) in 90% of foetuses if infection occurs at less than 11 weeks gestation.

- At 11-16 weeks gestation – 20% risk of congenital rubella syndrome.

- At 16 - 20 weeks gestation – minimal risk of deafness only.

- Over 20 weeks gestation – no increased risk.
Management of suspected rubella infection

- Laboratory testing for serum IgM and IgG. A positive IgM antibody may indicate recent infection but the woman would require further tests before confirmation of the diagnosis.

- Management would be dependent on the gestation of pregnancy and individual circumstances of the woman and may include termination of pregnancy.
Contact with suspected rubella during pregnancy

- Reassure the woman that the possibility of infection is remote and specific rubella testing is not required if she has had one of the following:
  - At least 2 documented doses of the 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 2 previous rubella antibody screening tests which have detected antibody, in at least one of which rubella antibody is ≥ 10 IU/ml
If these criteria are not met then testing for IgM and IgG antibody should be done as soon as possible.

- If Rubella IgG detected and IgM not detected – reassure that there is no evidence of recent infection but she should see her GP if a rash develops.

- If Rubella IgG not detected and IgM not detected – the woman is susceptible and repeat testing should be done after 1 month to ensure IgM is still absent.
- If IgG is negative, the woman should be immunised with MMR after delivery in line with national guidelines as she is susceptible to infection.

- If Rubella IgM detected – needs further testing and specialist input regarding management.
Measles\textsuperscript{1}

- Clinical features and complications of measles include disseminated rash, coryza, conjunctivitis, pneumonia, otitis media and encephalitis.

- **Incubation** period is **8-14 days**

- **Infectious** from **4 days before onset of rash to 4 days after**
Maternal risks of measles infection

- Severe measles, including pneumonia
Foetal risks of maternal infection

- Increased foetal loss and premature delivery at any gestation.

- Low birth weight.

- Perinatal risk of severe measles.
Management of suspected measles infection

- Obtain serum sample for measles specific IgM and IgG testing.

- In confirmed infection, the management of the pregnancy should be continued as normal.

- Although no congenital infection or damage would be anticipated, follow up of the infant should be considered.
Management of the neonate born to a measles infected mother

- Administration of HNIG (Human Normal Immunoglobulin) immediately after birth or postnatal exposure is recommended for neonates born to mothers in whom the rash appears 6 days before to 6 days after birth.
Contact with suspected measles during pregnancy

- If the woman has a documented history of 2 doses of measles containing vaccine or is known to be immune reassure her that the risk of measles is remote but she should see her GP if she develops a rash.

- If the index case is a confirmed epidemiologically linked or likely case of measles and contact has been within 6 days of onset of rash then test for Measles IgG.

- If Measles IgG detected – reassure her that she has evidence of immunity to measles and advise her to see her GP if she develops a rash.
If Measles IgG not detected – arrange HNIG via Health Protection Unit and advise a 2 dose course of MMR vaccine after completion of pregnancy.
Epstein-Barr virus

- Infectious mononucleosis is a common presentation of Epstein-Barr Virus (EBV) characterised by generalised lymphadenopathy, fever and sore throat. A generalised maculopapular rash may be an associated feature.

- Primary EBV infection during pregnancy carries no specific risk to the foetus.
Cytomegalovirus

- Cytomegalovirus (CMV) can be another cause of infectious mononucleosis but rarely presents with a rash.

- The foetus can be infected either during primary infection or reactivation of the virus and is a common cause of congenital viral infection. The overall birth prevalence is estimated at 3/1000 in the UK. There is no treatment recommended currently to prevent or reduce mother to child transmission.

- If infection is suspected, specialist advice should be sought.
Human herpes virus 6 and 7 (HHV 6/7)

- These are closely related to CMV
- Primary infection during infancy and early childhood is universal and a proportion of children develop roseola infantum as a result.
- No clinical implications or consequences of congenital infection have been identified up to present.
Enterovirus\textsuperscript{1}

- Hand, foot and mouth disease is an Enteroviral infection characterised by vesicular lesions of hands, feet and mouth.

- Pregnant women presenting with features of infection or who have been in contact with the infection may be reassured that there are no adverse consequences for the foetus.
Algorithm for follow-up of women exposed to rash in pregnancy\(^1\)
Take home messages

- There are many common viral infections that can present with a rash illness. It is important to be aware of their presentations in order to assess and advise pregnant women appropriately.

- Infections such as infectious mononucleosis and hand, foot and mouth have no implications for the foetus and pregnant women can be reassured regarding these.

- Guidelines provide a framework for assessment and management of pregnant women with suspected viral rash illness or exposure to such infections but do not replace seeking specialist advice when indicated.
References

1. HPA guidance on viral rash in pregnancy updated 2016

2. A suspected viral rash in Pregnancy. BMJ March 2017

3. Public Health England Zika Virus guidance for Primary Care updated November 2016

4. Fit for Travel website