

Infections in Pregnancy: A Guide for Maternity Services When Requesting Serological Testing

A Consultation Document

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In conjunction with Antenatal Screening Wales (ASW)

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Preface

This consultation document is intended to provide an explanation to the relevance of serological testing in pregnancy, particularly for junior doctors and midwives who may be asked questions about whether tests are advisable as part of antenatal care.

It is important that women are offered tests appropriately and in a more standardised way to ensure an equality of care.

The aim of this document is to provide guidance to obstetricians and midwives on when serological tests should and should not be offered in pregnancy and which tests may be relevant following specific ultrasound findings.

It is anticipated that agreement on these issues will inform the development of the Welsh Pathology Handbook, test requesting and results reporting (TRRR) and laboratory information management system (LIMS).

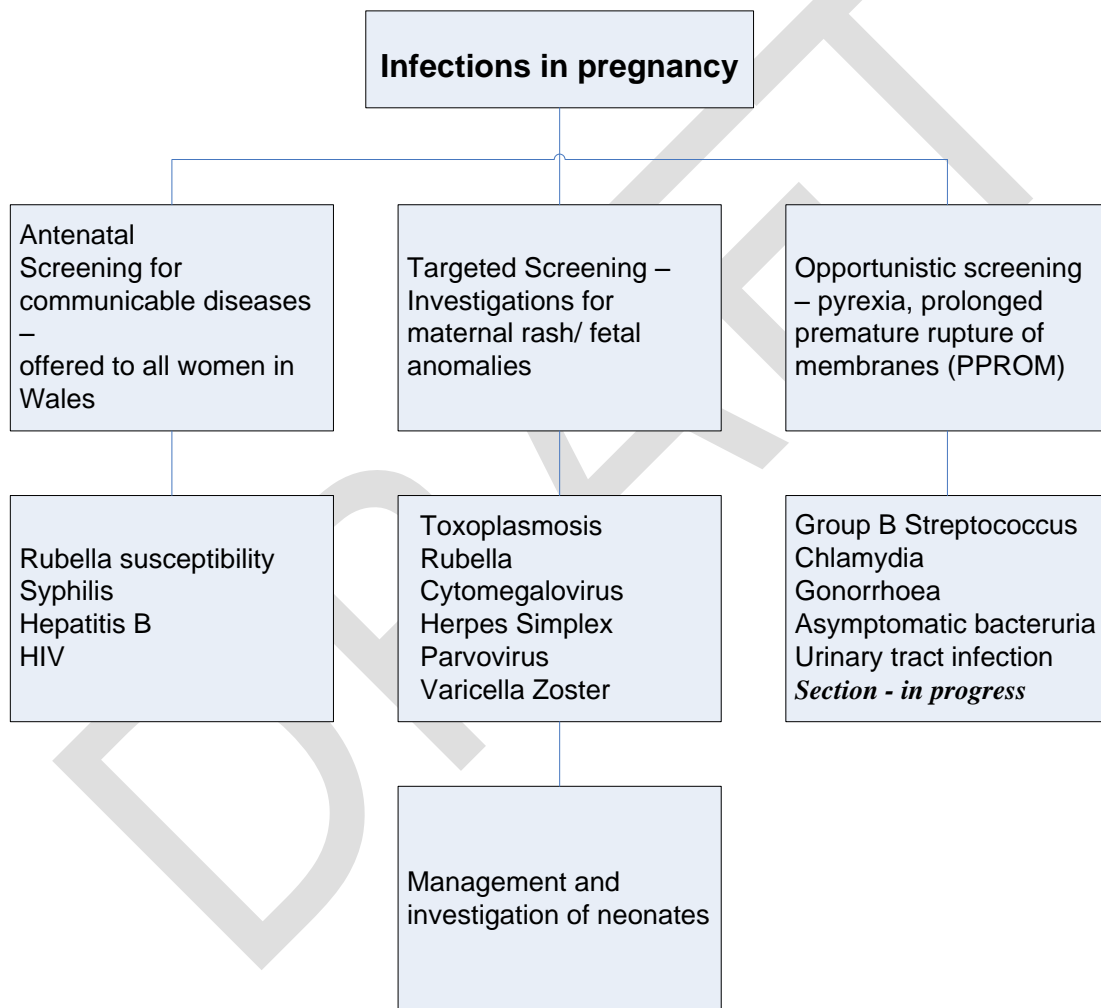
This document is intended to complement, and should be used in conjunction with, nationally agreed guidelines.

DRAFT

1.0 Introduction

1.1 Infections in pregnancy

Infections in pregnancy are discussed in this guideline. The infections have been categorised into three groups: those diagnosed as part of routine antenatal screening for communicable diseases (HIV, hepatitis B, syphilis and rubella susceptibility), those identified as result of targeted screening due to presence of fetal anomalies and those identified following opportunistic screening.



These guidelines are not exhaustive.

Advice from senior obstetricians, microbiologists, virologists, GUM/sexual health specialists and the public health teams may be required.

The neonatologists need to be consulted and a care plan developed for a pregnant woman who has an infection that could affect the fetus.

2.0 Antenatal screening in Wales

All women in Wales should be offered antenatal screening for HIV, hepatitis B, syphilis and rubella susceptibility, usually before 13 weeks gestation (see table 1). Urine should also be routinely sent for microscopy, culture and sensitivity (M/C&S) when the woman first attends for maternity care (see table 2).

The blood samples should be sent to the microbiology laboratory (during the working hours of Monday to Friday). For women who access maternity care after 35 weeks gestation, the laboratory should be informed. The consultant microbiologist/virologist should be contacted if the woman presents in labour as urgent tests may be required.

Table 1. Antenatal Screening Tests

Infectious Agent	Laboratory Investigation	Purpose
Rubella	Rubella IgG	Women who are susceptible to rubella are offered vaccination postpartum.
Syphilis	Syphilis ELISA (combined IgG and IgM)	Women who have a confirmed syphilis infection are offered treatment to prevent fetal/neonatal infection. Neonates require follow up.
Hepatitis B	Hepatitis B surface antigen	Babies born to women who have a hepatitis B infection are offered hepatitis B vaccination at birth to prevent vertical transmission. Babies require follow up.
HIV	HIV Ag/Ab combination assay	Women who have an HIV infection are offered treatment to prevent fetal/neonatal infection. Neonates require follow up.

Table 2. Tests Offered as Part of Pregnancy Management

Test offered to all women as part of pregnancy management		
Urine	Urine culture to detect asymptomatic bacteruria	Urine should be routinely sent for microscopy culture and sensitivity (M/C&S) when the woman first attends for maternity care. Woman with asymptomatic bacteruria are at increased risk of pyelonephritis.

Table 3. Tests Offered to Individuals if Clinically Indicated

Antenatal tests which may be offered to individuals but are not part of the antenatal screening programme		
Infectious Agent	Laboratory Investigation	Purpose
VZV chickenpox (varicella)	VZV IgG	Only useful if women are in contact with chickenpox during pregnancy.

2.1 Rubella (German Measles)

Introduction

German measles is an infection caused by the rubella virus. It occurs most commonly in young children, but can affect anyone. The illness is usually mild, though during pregnancy it can cause serious damage to the fetus specially if caught during the first 16 weeks of pregnancy. This is called 'congenital rubella syndrome (CRS)'.

At least 2% of women in their first pregnancy in England and Wales are susceptible to rubella infection.

All pregnant women should be offered serum screening for rubella susceptibility.

Symptoms of rubella

Adult infection is often asymptomatic

The symptoms are usually mild and include fever, headache, joint pains and a sore throat. A distinctive red-pink, non-vesicular rash usually appears shortly after the glands swell.

Risk of developing congenital rubella syndrome related to timing of primary maternal infection

The risk to the fetus from maternal primary rubella infection in the first 16 weeks of pregnancy is substantial:

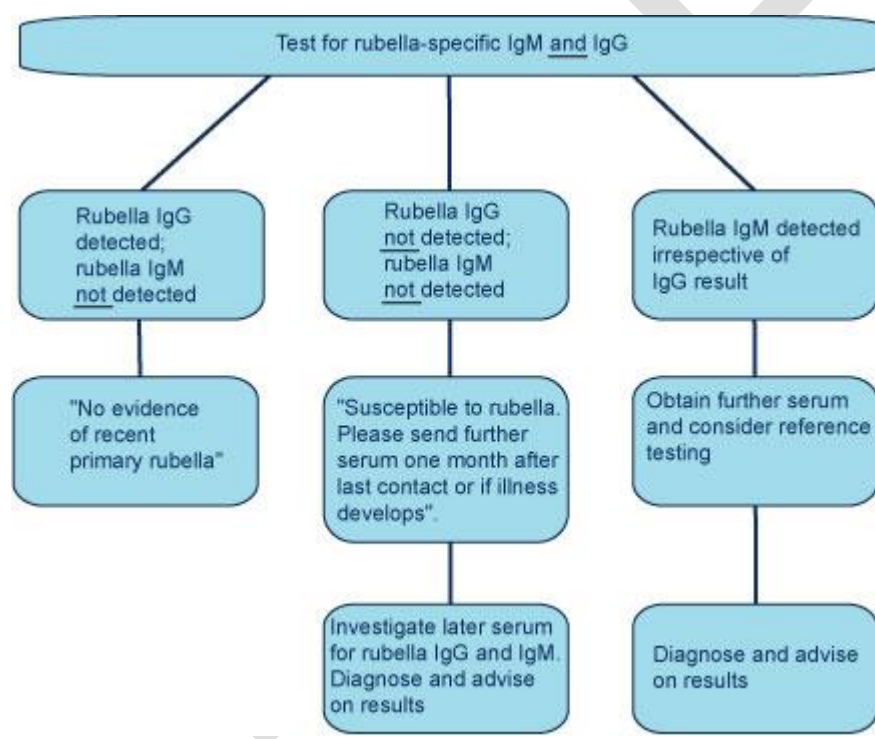
- <10 weeks: 80–90%
- 11–16 weeks: 10–20%
- 16–20 weeks: 20% (deafness)
- >20 weeks: <1 %

The option of termination of pregnancy should be discussed with the woman, specifically if the gestation is before 16 weeks.

If susceptible to rubella and pregnant

All pregnant women with an infectious rash/illness, or who have had significant contact with a person with an infectious rash/illness, should be tested for rubella and other relevant viral infections (see section 4.0 Management and investigation of rashes and contact with rashes in pregnancy).

Possible results from rubella susceptibility screening:



A positive IgM indicates possible recent infection, or reinfection, depending on history.

If susceptible to rubella and not pregnant

- Offer two measles, mumps and rubella (MMR) vaccinations, with four weeks between the first and second vaccination.
- Women should be advised to avoid getting pregnant for at least one month after completion of the vaccines because it is a live vaccine.

MMR postpartum

- Women susceptible to rubella should be offered two MMR vaccinations post delivery. There is no contra-indication to breastfeeding following MMR vaccination.

Rubella infection

Any pregnant woman who is suspected to have contracted rubella before 20 weeks gestation needs to be referred to a fetal medicine unit for counselling regarding CRS. It is advisable to repeat the blood samples for rubella serology and discuss with the consultant virologist/microbiologist.

Evidence base

- Morgan-Capner, P. and Crowcroft, N. S. on behalf of the PHLS Joint Working Party of the Advisory Committees of Virology and Vaccines and Immunisation (2002), Guidelines on the management of, and exposure to, rash illness in pregnancy. *Communicable Disease and Public Health*. 5(1) pp. 59–71.
- Morgan-Capner, P. (1988), Laboratory diagnosis of rubella. Summary of recommendations of PHLS Working Party. *PHLS Microbiology Digest*. 5. pp. 49–52.
- Department of Health (2006), Immunisation Against Infectious Diseases – 'The Green Book' Available from: www.dh.gov.uk/en/Publichealth/Healthprotection/Immunisation/Greenbook/DH_4097254. (Accessed on 10/03/11).

2.2 Treponema pallidum – Syphilis

Introduction

Syphilis is caused by a spirochete bacterium, *Treponema pallidum*, which, if not treated promptly, can result in serious short and long-term morbidity.

The incidence of syphilis has been increasing over the past five years in the United Kingdom. Most cases of infectious syphilis are either acquired abroad, notably in Eastern Europe, or from men who have sex with men.

Antenatal screening for syphilis should be offered to all pregnant women in Wales. Syphilis may be transmitted via the placenta, at any stage of pregnancy, and may result in miscarriage, pre-term labour, stillbirth, hydrops and congenital syphilis.

Antenatal management

All pregnant women should have been offered screening for syphilis at the initial antenatal visit. If, during pregnancy, the woman changes her partner or is worried that she may have contracted HIV, hepatitis B, or syphilis, the midwife can repeat the test at any time during the pregnancy.

- If a screening sample is positive then appropriate further serological investigations will be performed on the booking sample to confirm infection and assist with staging of the infection.
- Women should be given a positive result by a health professional with suitable skills and knowledge; this is usually the screening coordinator, or her deputy. (Antenatal Screening Wales (ASW) 'Revised Policy, Standards and Protocols to Support the Provision of Antenatal Screening in Wales' 2010).
- Women with syphilis positive results should be referred to a GUM or Sexual Health Service specialist for treatment and follow up.
- Where fetal damage is suspected referral to a fetal medicine unit is recommended.
- Written information should be given to pregnant women who have a positive syphilis result.
- A referral letter should be sent to a paediatrician with an interest in infectious diseases by the obstetrician/antenatal screening coordinator to ensure follow up of neonate.

Transplacental transmission can occur at any stage of pregnancy. Maternal early stage syphilis and high titre RPR/VDRL are risk factors for congenital infection, though transmission rates of 10% have been reported in late disease. Maternal co-infection with HIV may increase the risk of transmission of syphilis. Any organ damage already caused by the disease cannot be reversed. Careful assessment of clinical and microbiological tests must be undertaken prior to clinical advice and treatment, hence the need for referral to GUM or Sexual Health Service.

Recommended treatment regimen

Primary syphilis

- Benzathine penicillin G 2.4 MU i.m. single dose in the first and second trimesters. When maternal treatment is initiated in the third trimester, a second dose of benzathine penicillin G 2.4 MU i.m. should be given after one week (day 8).

Alternative regimens

- Amoxicillin 500 mg PO q.d.s. plus probenecid 500 mg PO q.d.s. for 14 days.
- Ceftriaxone 500 mg i.m. daily for 10 days.
- Erythromycin 500 mg PO q.d.s. for 14 days or Azithromycin 500 mg PO daily for 10 days plus evaluation and treatment of neonates at birth with penicillin.

Secondary syphilis

- Benzathine penicillin 2.4 MU i.m. weekly for two weeks (three doses).

Alternative regimens

- Amoxicillin 2 g PO t.d.s. plus probenecid 500 mg q.d.s. for 28 days.

Intrapartum care

- Caesarean delivery is not indicated.
- Breastfeeding is not contraindicated.

Postnatal care

- The paediatrician should be informed following the delivery and postnatal/neonatal clotted and EDTA samples taken.
- A 5 ml plain tube from the mother and a neonatal sample of at least 0.5 ml venous blood (not cord blood) should be taken and sent to the laboratory. These samples need to be taken on the same day and 'linked' to ensure that the laboratory is aware of the connection, as they require testing in parallel.
- NPA (nasopharyngeal aspirate) for syphilis PCR may also be indicated and requires discussion with the virology consultant/microbiology consultant prior to being sent.
- There is no facility to test these samples out of hours.

Management of the neonates

Most babies born to mothers diagnosed with syphilis in pregnancy will not require treatment.

Exceptions are:

- IgM detected in neonate
- A four-fold higher titre in the neonate VDRL/RPL compared to the mother
- Inadequately treated maternal infection
- Organisms detected in neonate's NPA sample
- Undiagnosed maternal infection until late in pregnancy.

Treatment of the neonate

- Benzyl penicillin sodium 100,000–150,000 u/kg daily IV (in divided doses given as 50,000u/kg 12 hourly for first 7 days and 8 hourly thereafter for 10 days.
- Treatment of the neonate should only be commenced after discussion with consultant paediatrician or consultant in medical microbiology or virology.

Evidence base

- Clinical Effectiveness Group (2008), UK National Guidelines on the Management of Syphilis 2008. *International Journal of STD & AIDS*. 19. pp. 729–740.
- Lewis, D. A., Young, H. Syphilis. In: Ross, J., Ison, C., Carder, C., Lewis, D., Mercey, D., Young, H. (2006), *Sexually transmitted infections: UK national*

screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); pp. 33–39.

- Antenatal Screening Wales (ASW) (2010), *Revised Policy, Standards and Protocols to Support the Provision of Antenatal Screening in Wales*. Cardiff: Public Health Wales.
- Chakraborty, R. and Luck, S. (2008), Syphilis is on the increase: the implications for child health. *Archives of Disease in Childhood*. 93 (2). pp. 105–109.

2.3 Hepatitis B

Hepatitis B is an infectious disease of the liver caused by the hepatitis B virus, resulting in both acute and chronic infection. In Britain, the prevalence of hepatitis B carriers among pregnant women is estimated at 0.15% (1–2 per 1000 women). This proportion varies across different ethnic groups and is higher among groups from countries where the disease is endemic, e.g. 67% of hepatitis B carriers are African, Chinese or South Asian.

Hepatitis B can be detected in blood, semen and saliva and can be transmitted:

- vertically from mother to baby
- through contact with contaminated blood products
- through sexual contact
- through close prolonged household contact with an infected person.

Antenatal diagnosis of hepatitis B infection is usually made by screening antenatal booking bloods for the presence of hepatitis B surface antigen (HBsAg). In pregnancy, women are more likely to have chronic hepatitis B infection, i.e. those who remain HBsAg positive for longer than six months following acute hepatitis B infection. Samples that screen positive for HBsAg will automatically be tested for all markers for hepatitis B to determine the stage of infection. Mothers with HBsAg can transmit infection to their baby during the birth process. Neonates who acquire infection from their mother have a high chance of becoming long-term carriers of hepatitis B and are therefore at risk of developing liver disease as adults. Twenty per cent of babies infected in infancy may develop cirrhosis or hepatocellular carcinoma in later life.

Antenatal screening for hepatitis B is offered to all pregnant women to identify infants at risk of perinatal hepatitis B infection and therefore enable a programme of active and passive vaccination for the baby after birth. This is extremely effective at reducing vertical transmission of hepatitis B.

Antenatal management of women found to be positive for HBsAg

- Refer for consultant-led care.
- Women should be given a confirmed positive result by a health professional with suitable skills and knowledge; this is usually the consultant obstetrician, antenatal screening coordinator, or her deputy (ASW, 2010).

- Pregnant women who are hepatitis B positive should be offered written information (ASW, 2010).
- Verbal information should be given about the importance of the baby completing a hepatitis B vaccination programme (vaccinations are given at birth, 1 month, 2 months and 12 months). The woman should be advised about screening of family members, such as partners and existing children for the infection, in order that they may be referred, or vaccinated, as appropriate.
- The woman should be referred to an infectious diseases specialist, gastroenterologist, or a hepatologist.
- The Health Protection Team should be informed of the results. Each Health Board should have a local pathway for informing the Health Protection Team.
- A second sample is required to confirm results and patient identity.

Most babies require only hepatitis B vaccination, however, there are some women who have a higher risk of transmitting infection to their babies and whose babies will require both hepatitis B immunoglobulin and vaccination (see Table 4). This information should be documented in the intrapartum care plan and on the neonatal hepatitis B checklist, which is filed in the same section.

Table 4. Hepatitis B vaccine and HBIG guidance

Hepatitis B status of mother	Baby should receive	
	Hepatitis B vaccine	HBIG
Mother is HBsAg positive and HBeAg positive	Yes	Yes
Mother is HBsAg positive, HBeAg negative and anti-HBe negative	Yes	Yes
Mother is HBsAg positive where e-markers have not been determined	Yes	Yes
Mother had acute hepatitis B during pregnancy	Yes	Yes
Mother is HBsAg positive and anti-HBe positive	Yes	No
A woman who is HBsAg sero-positive and known to have an HBV DNA level equal or above 1×10^6 IU/ml in an antenatal sample*	Yes	Yes
If baby is pre-term and weighs less than 1500g irrespective of maternal 'e' antigen status	Yes	Yes

* Where viral load testing has been performed to inform the management of the mother (adapted from DoH 2010).

The antenatal screening coordinator should be responsible for organising a referral to the infectious disease specialist/hepatologist.

All Health Board employees should adhere to the local universal precautions policy.

Intrapartum management

- Hepatitis B vaccine (and hepatitis B immunoglobulin HBIG if required) should be given to the baby within the first 24 hours of life. See local policy for details on co-ordination and responsibility.
- Universal precautions should be taken for control of infection.
- There is no need for elective caesarean section.
- Breastfeeding is not contraindicated.

Neonatal management

- The paediatrician should be informed following delivery to prescribe and administer hepatitis B vaccine and HBIG if indicated.
- The dose of hepatitis B vaccine varies according to the brand used, so it should be prescribed by brand name not as hepatitis B vaccine. The dose is 5 micrograms for children up to 16 years.

Note: if the woman's baby is identified as requiring both hepatitis B immunoglobulin and vaccination at birth:

- Hepatitis B immunoglobulin and hepatitis B vaccination should be given as soon as possible and within 24 hours of delivery. If both need to be given, they should be given at the same time in separate sites.
- The baby will require three more vaccinations and the timing for these are:
 - one month old
 - two months old
 - twelve months old.
- The baby requires a blood test to establish immunity when the course is finished.

These vaccinations are co-ordinated by the public health nurse.

Evidence base

- Department of Health (2006), Immunisation Against Infectious Diseases – 'The Green Book' Available from www.dh.gov.uk/en/Publichealth/Healthprotection/Immunisation/Greenbook/DH_4097254. (Accessed on 10/03/11).

- Ramsey, R. (2008), *Policy on the use of passive immunisation with hepatitis B immunoglobulin (HBIG) for infants born to Hepatitis infected mothers*. London: Health Protection Agency.

2.4 Human Immunodeficiency Virus (HIV)

The Human Immunodeficiency Virus (HIV) is a retrovirus that attacks and destroys T-lymphocytes, resulting in immune-suppression that eventually leads to acquired immune deficiency syndrome (AIDS). Two forms of the virus have been identified, HIV-1 and HIV-2. The commonest and most virulent form is HIV-1. HIV-2 is relatively uncommon in Western countries.

Ninety-five per cent of the total HIV positive population lives in the developing world. Over 90% of infected babies live in sub-Saharan Africa. In the UK one pregnant woman in every 486 is infected with HIV. Mother to child transmission of HIV was diagnosed in 110 babies born in the UK in 2008.

HIV infection is transmitted through infected body fluids such as blood, semen and vaginal secretions, or vertically from an infected mother to her baby during pregnancy, birth and breastfeeding. Without intervention mother to child transmission rates of HIV are between 15 to 25%. Drug therapy, careful management of delivery and avoidance of breastfeeding can reduce the risk of vertical transmission to around 1%.

Antenatal care

- Women should be given a confirmed positive result by a health professional with suitable skills and knowledge. This is usually the consultant obstetrician, screening coordinator, or her deputy with support from the HIV specialist team. A second sample to confirm the result and patient identity is required.
- Women should be given written information about being HIV positive in pregnancy (ASW, 2010).
- The woman's care should be transferred to consultant-led care (see local protocols).
- Women should be referred to GUM, or infectious diseases specialists, for HIV treatment and blood tests, such as viral load testing.
- A multidisciplinary HIV team meeting should be arranged in the antenatal period to discuss the case and complete the intrapartum care plan.
- A detailed care plan should be discussed, developed and agreed with the woman (see local protocols).
- The antenatal screening coordinator should be responsible for coordinating the care plan.

- The woman should be offered the opportunity to meet the paediatric team during pregnancy to explain the care of baby.

Intrapartum care:

- The woman's labour plan, intrapartum guidelines and treatment regime should be available in the maternity notes and obvious to the person providing intrapartum care.
- Women whose viral load is undetectable can be offered a vaginal delivery, although historically women with HIV have had planned caesarean sections.
- The decision regarding mode of delivery should be documented in the labour plan.

Elective Caesarean Section (EL LSCS)

- Admit to the maternity unit the day before EL LSCS.
- Oral antiretroviral drugs should be prescribed and administered as requested and documented. It is vital that the woman has this medication at the same time each day; otherwise the viral load may become detectable.
- IV Zidovudine should be commenced at 12 midnight and continued until the baby is born.
- On the day of EL LSCS ensure that the woman has oral antiretroviral drugs.

Planned vaginal delivery

- IV Zidovudine should be prescribed and administered as soon as labour is established.
- If spontaneous rupture of membranes (SROM) occurs the woman should deliver within four hours unless an alternative care plan has been documented. (Mother to baby transmission is increased if the membranes are ruptured for more than four hours (BHIVA guidelines)).
- If the agreed plan is to deliver vaginally, IV Zidovudine (AZT) should be prescribed and administered, ideally 6 to 8 hours before delivery.

Postnatal/neonatal management

- Universal precautions are recommended when taking blood samples.
- There is no need for a side room, or a separate toilet, unless requested by the woman.
- Ensure that the paediatrician is contacted whilst the woman is still on the delivery suite to ensure that the neonate's medication is prescribed.
- Ensure that the blood sample from neonate and mother are taken the next working day after delivery. (EDTA samples required).

Neonatal medication

- Oral Zidovudine is usually prescribed twice a day for one month.
- Infants who are at higher risk of becoming infected may require triple therapy. This will normally be determined prior to delivery.
- On rare occasions medicines will be altered after the results of the blood tests are known, usually between three to five days post delivery.

Blood samples

- These should be taken from both the mother and baby and sent together. The laboratory should be phoned to inform them that the blood samples are being sent. (Local protocols should be followed).
- Blood samples should not be sent after 4pm, or weekends, as they will not be processed. In this event, blood samples should be taken the next working day.
- Ensure one of the HIV team is aware of delivery to coordinate postnatal care appointments.
- More details should be available in the local HIV protocol and in the woman's maternity notes.

Evidence base

- de Ruiter, A., Mercey, D., Anderson, J., Chakraborty, R., Clayden, P., Foster, G., Gilling-Smith, C., Hawkins, D., Low-Beer, N., Lyall, H., O'Shea, S., Penn, Z., Short, J., Smith, R., Sonecha, S., Tookey, P., Wood, C., and Taylor, G. (2008), British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. *HIV Medicine*. 9. pp. 452-502.
- Antenatal Screening Wales (ASW) (2010), *Revised Policy, Standards and Protocols to Support the Provision of Antenatal Screening in Wales*. Cardiff: Public Health Wales.
- HPA (2009), HIV in the United Kingdom. Found at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/HIV/> (Accessed on 06/08/11).

3.0 Targeted investigations

3.1 Brief overview of diagnostic tools and strategies

The acronym TORCH is obsolete. It was developed in the 1970s to facilitate the diagnosis of infections in pregnancy, but has long since passed its usefulness. The advent of more complex and sensitive assays requires the clinicians to be more proactive and direct investigations in a more focused way, i.e. targeted investigations looking for specific infectious agents depending on clinical presentation.

This chapter provides guidance on what infections and subsequent investigations are relevant in specific conditions.

Principles of targeted investigations

- Maternal serological investigations provide information that relates ONLY to maternal infection. The value of maternal investigations is to identify recent maternal infections thereby allowing more targeted investigations of the neonate, or fetus.
- Investigations for fetal infection will require invasive samples such as amniotic fluid, CVS, or fetal blood and often require expensive investigations, some of which are only available from reference laboratory services.
- Neonatal investigations require careful interpretation with targeted molecular assays; the presence of passive maternal IgG and the inability of the neonate to make IgM antibodies means that serological investigations of the neonate are difficult to interpret and are often unsatisfactory as an investigative tool.

Brief overview of investigative tools

Investigation of the mother

- **IgG** – This antibody is present when an individual has had an infection in the past. It is not useful in determining when that infection occurred. IgG is not always present in early infection (i.e. at the time of the rash or symptoms). The exception to this general rule is parvovirus B19. Demonstration of the absence of parvovirus specific IgG to the presence of parvovirus specific IgG over a time period may allow the timing of the infection to be determined. Hence the request for booking blood samples to be compared with later samples (clotted or EDTA as per local protocols).
- **IgM** – This antibody is produced when a recent infection has occurred. It persists for at least a month, but usually longer. It usually develops several days after the symptoms, as with IgG. It can, however, be detected when latent infections re-activate, such as CMV or VZV (chickenpox/shingles). (Clotted or EDTA as per local protocols.)

Investigation of the fetus

Serological investigations

Fetal blood sample

- Fetal blood sample is often of less clinical value than amniotic fluid and requires prior discussion with laboratories to ensure that this sample is appropriately used. (Clotted or EDTA sample is required.)
 - **IgG** is not often useful as all that is detected is passive maternal antibody.
 - **IgM** is not a useful marker in the fetus, or the neonate, as the fetus cannot produce IgM before 28 weeks gestation and both the fetus and the neonate will not produce IgM in acute infections in up to 30% of cases.
- EDTA sample of fetal blood can be sent for specific molecular investigations, however, they require 'targeting' as these are often only available at reference facilities.

Amniotic Fluid (AF) samples

Amniotic fluid sample is the most useful for investigating fetal infections. The presence of the virus itself can be determined using specific molecular probes. The presence of the virus in amniotic fluid is the best indicator of fetal infection. In parallel with maternal infection history and presentation, maternal serological investigations can be useful in determining which virus to look for in amniotic fluid.

Molecular investigations are expensive and may require the use of reference laboratory facilities; hence the requirement for using targeted investigations appropriately.

The limitation of amniotic fluid samples is that they are obtained by performing an invasive procedure, which can cause a miscarriage in 1% of cases and false negative results can occur if sampling occurs before 21 weeks gestation.

Investigation of the neonate

Neonatal blood samples

Serological investigations in neonates are difficult because of passive maternal IgG and the limited production of IgM. Transfusions and receipt of blood products also complicate interpretation.

EDTA neonatal blood samples are useful for molecular investigations, but require 'targeting'. It is often useful to exclude recent infections during the pregnancy by investigating the mother.

Urine samples

The diagnostic tool of choice for congenital cytomegalovirus (CMV) infection is urine taken in the first 3 weeks of life. The presence of CMV DNA confirms congenital CMV infection. Urine may also be useful for other infections.

Swabs

Swabs from nose, throat, ear, umbilicus and skin lesions may be useful for investigation of neonatal herpes. Faecal samples, or rectal swab, are useful in 'neonatal sepsis' where enteroviral infections require excluding.

Local laboratory protocols should be reviewed regarding appropriate swabs type, i.e. dry swabs, or in fluid.

3.2 Details of specific infections

3.2.1 *Toxoplasma gondii*

Introduction

Toxoplasmosis is an infection caused by a parasite called *Toxoplasma gondii*. The organism lives in the muscle tissue of some animals. Pregnant women can become infected by ingesting anything infected with the parasite, such as raw or undercooked meat, or unpasteurised goat's milk. Infected cats also excrete this organism in their faeces; soil is often contaminated with cat faeces.

Pregnant women should therefore:

- Avoid eating unwashed fruits and vegetables, undercooked meat and unpasteurized milk.
- Ensure good hand washing when preparing raw meat and vegetables.
- Wear gloves for gardening.
- Avoid changing cat litter, or change it daily, and wear gloves.

It is estimated that 15% of women booking for antenatal care are immune to toxoplasma infection. Pregnant women may not know that they are immune to toxoplasma infection. Therefore, all pregnant women should be advised on how to avoid becoming infected.

Routine antenatal screening, or routine testing of groups perceived to be at higher risk of contracting toxoplasmosis, is not advised as primary infection in pregnancy is rare in the UK and the incidence of congenital toxoplasmosis is very small: only 3 babies in every 100,000. The NSC concluded in 2001 that there are known harms associated with fetal diagnosis (1% miscarriage from an amniocentesis procedure) and no evidence that diagnosis leads to a beneficial change in antibiotic treatment.

Symptoms

Toxoplasmosis is often asymptomatic, therefore making diagnosis difficult. Women can have mild flu like symptoms and occasionally may experience a more long-term illness similar to glandular fever.

Not all women who become infected during pregnancy will pass this infection onto the fetus. Not all fetal infections will cause fetal damage. This depends on a number of factors, most important of which is the gestation at the time of maternal infection.

Risk of vertical transmission related to timing of maternal infection

- **First trimester:** low risk (5–15%) of transplacental transmission, but if infected high risk (60–80%) of fetal damage.
- **Second trimester:** intermediate risk (25–40%) of transplacental transmission, but if infected intermediate risk (15–25%) of fetal damage.
- **Third trimester:** high risk (30–75%) of transplacental transmission, but if infected low risk (2–10%) of fetal damage.

Serology investigations in the pregnant woman

The purpose of a serology investigation is to investigate whether the pregnant woman has ever been infected with toxoplasmosis and, if so, to try and determine when.

Possible results and guidance on interpretation

- **IgG –ve with or without IgM –ve:** the pregnant woman is susceptible to toxoplasmosis. There is no serological evidence of toxoplasmosis therefore the fetus has never been exposed to the parasite. The pregnant woman should be given information on how to avoid exposure during current and subsequent pregnancies. No need to investigate further for toxoplasmosis.
- **IgG +ve and IgM –ve:** shows past infection. The pregnant woman has been exposed to toxoplasmosis at some time. If this is early in pregnancy (<12 weeks) it is unlikely to be a recent exposure due to absence of IgM. However, if this is later in pregnancy, or if a fetal anomaly identified by an ultrasound scan is such that toxoplasmosis is suspected, comparison with booking blood is warranted. A change from IgG negative to IgG positive (booking blood compared to later sample) indicates a recent infection. Advice should be sought on subsequent investigations on mother and fetus from a consultant microbiologist.
- **IgG +ve and IgM +ve:** suggests possible recent infection therefore further testing will be required for confirmation. Seek advice from consultant virologist/microbiologist and refer patient to a fetal medicine unit.

Vertical transmission may be reduced by treating the pregnant woman with an antibiotic called spiramycin. Expert advice should be sought from a consultant microbiologist.

Evidence base

- Peyron, F., Wallon, M., Liou, C., Garner, P. Treatments for toxoplasmosis in pregnancy. Cochrane Database of Systematic Reviews 1999, Issue 3. Art. No.: CD001684. DOI: 10.1002/14651858.CD001684.

- Antenatal and Newborn Screening for Toxoplasmosis. Report of the Working Group—October 2001. Available at: www.nhs.uk/conditions/toxoplasmosis/pages/introduction.aspx (Accessed on 06/08/11).

3.2.2 Cytomegalovirus

Introduction

Cytomegalovirus (CMV) is a member of the herpes virus family. It is a common viral infection and about fifty per cent of the population of Britain have been infected with it at some time. CMV infection usually causes no symptoms in infected children and adults. It is most common in young children and is the leading cause of congenital infections in the UK.

Pregnant women can be infected with CMV through sexual contact, blood transfusions, and non-sexual, close contact with infected persons, especially young children.

CMV is a herpes virus and all herpes viruses can be latent. A primary infection is the first time an individual is infected with the virus and it is a primary CMV infection that is more likely to result in a severe fetal infection. Because the virus can remain latent, during pregnancy a previous CMV infection can be reactivated, or the woman may become infected with a different strain of virus. Reactivation, or reinfection, has a less than 1% risk of transmission from mother to fetus. It is uncommon for the fetus to develop any serious CMV related problems following reinfection or reactivation.

The incidence of primary CMV infection in pregnancy is estimated to be 6/1000 pregnancies. The risk of transmission to the fetus in pregnant women with primary CMV infection is approximately 40%. This appears to be independent of the gestational age at which maternal infection takes place. Most infected fetuses do not develop the disease. It is only a small percentage that can be severely affected with fetal abnormalities; babies apparently normal at birth may develop sensorineural deafness later in life.

Risk of transmission

The risk of transmission is distributed equally between the three trimesters.

However:

- Risk of severe adverse neurological outcome is more likely in primary infection in first half of pregnancy
- A fetus affected late in pregnancy is more likely to have acute visceral disease (hepatitis, pneumonia, purpura and severe thrombocytopenia).

Routine antenatal screening is not advised in the UK

Antenatal screening for CMV is not recommended by the NSC as it is not currently possible to determine accurately which pregnancies are likely to result in the birth of an infected infant and there is no method to determine which infected infants will develop abnormalities as a result of CMV infection. There are currently no available vaccines or prophylactic therapies for the prevention of transmission and no procedures to determine whether maternal to fetal transmission has occurred.

Indications for antenatal testing

- Exposure to known CMV infected individual
- Abnormalities in routine antenatal ultrasound (microcephaly, ventriculomegaly, intracranial calcification, intrauterine growth restriction (IUGR), ascites, pleural and pericardial effusions, hepatomegaly, echogenic gut). See Table 5.

Results of maternal serological – interpretation for guidance

- **IgG –ve with or without IgM –ve:** shows susceptibility. This means that the pregnant woman has never had CMV and therefore the fetus has not been exposed to the virus. No further investigations for CMV are indicated.
- **IgG +ve/IgM –ve:** this means that maternal infection has occurred at some time. If there are concerns regarding the pregnancy then the booking blood should be compared with current blood to look for differences in serostatus (i.e. IgG negative at booking). CMV as a cause for fetal abnormality cannot be excluded, but is unlikely in the absence of a recent sero-conversion. To completely exclude CMV as a cause, amniotic fluid samples should be sent for CMV PCR after 21 weeks gestation.
- **IgG +ve and IgM +ve:** this may indicate recent infection, reactivation, or reinfection. Further investigations to determine whether the fetus has been infected should be considered on the basis of clinical history. Comparison with booking blood may help in determining whether this is primary infection, or reinfection/reactivation. CMV avidity tests may also be useful. Amniotic fluid samples should be submitted for CMV PCR. Due to the nature of the fetal kidney, amniotic fluid samples taken before 21 weeks gestation can give rise to false negative result. Women with these results should be referred to a fetal medicine unit for detailed ultrasound scan and further management.

Management of the neonate

- If neonatal infection is suspected, a review of all the maternal investigations during pregnancy should be undertaken.
 - Maternal investigations should include a current, post-delivery maternal blood sample, which should be tested in parallel with the maternal booking blood sample.

- Urine from the baby is the diagnostic test of choice and this should be submitted for CMV PCR. The presence of CMV DNA in this sample, if taken in the first 3 weeks of life, is diagnostic of congenital CMV infection.
- There are currently clinical trials reviewing the usefulness of treating CMV infected neonates with ganciclovir.
- Children with proven CMV infection should be referred to the paediatric infectious diseases consultant, or clinical virologists, to discuss enrolment into trials.

Evidence base

- Revello, M. G. and Gerna, G. (2002), Diagnosis and Management of Human Cytomegalovirus Infection in the Mother, Fetus, and Newborn Infant. *Clinical Microbiology Reviews*. 15 (4). pp. 680–715.
- Kimberlin, D. W., Lin, C. Y., Sanchez, P., Demmler, G., Dankner, W., Shelton, M., Edwards, K., Jacobs, R. F., Robinson, J., Wright, J., Lakeman, F. D., Kiel, L. J.M., Soong, S. J. and Whitley, R. J. (2000). Ganciclovir (GCV) Treatment of Symptomatic Congenital Cytomegalovirus (CMV) Infections: Results of a Phase III Randomized Trial. *Abstract Interscience Conference on Antimicrobial Agents and Chemotherapy*. 40. p. 274.
 - [Phase III Randomized, Controlled Study of Ganciclovir for Symptomatic Congenital Cytomegalovirus Infection](#) - This study has been completed (Current: 23 Nov 2006) - ganciclovir.
 - [Phase I/II Study of Human Anti-Cytomegalovirus \(CMV\) Monoclonal Antibody MSL-109 in Newborns With Symptomatic Congenital CMV Infection Without Central Nervous System Disease](#) - This study has been completed (Current: 23 Nov 2006) - SDZ MSL-109.
 - [Valganciclovir in Congenital CMV Infants](#) - This study is no longer recruiting patients (Current: 23 Nov 2006) - Ganciclovir, Valganciclovir.
 - [Genotyping of Cytomegalovirus From Patients in Israel](#) - This study is currently recruiting patients (Current: 23 Nov 2006).

3.3 Abnormal antenatal ultrasound findings and serological testing

Women are offered two ultrasound scans in pregnancy; the first is before 13 weeks and the second is at 18–20 weeks. While most abnormalities are because of a structural, or genetic cause, some abnormalities can have an infectious cause.

Requesting a large number of tests when there are abnormal ultrasound findings is both expensive and causes the woman additional, unnecessary worry. A rationalisation of the serological testing offered to women who have abnormal

ultrasound scan findings is proposed in Table 5. These tests should only be offered after discussion with a consultant obstetrician with a special interest in fetal medicine and a full discussion with the woman is required.

Table 5. Serological investigation on maternal serum following the detection of fetal abnormality diagnosed by ultrasound

	Infection					
	Rubella	CMV	Toxoplasmosis	Parvovirus	Syphilis	VZV
Before considering serological tests a relevant maternal history should be taken to indicate whether the test is required	Testing not required if evidence of previous immunity on two occasions, or 2 documented doses of MMR given				Review previous antenatal serology results and consider if the woman is in a high risk group, e.g. asylum seeker. (If in high risk group, or previous serology equivocal test.)	Only consider testing if there is recent history of confirmed chickenpox infection.
Fetal ultrasound finding						
Fetal growth restriction <10th centile	Yes	Yes	Yes	No	Yes	Yes
Microcephaly head circumference less than 5th centile as measured by trained sonographers	Yes	Yes	Yes	No	No	Yes
Ventriculomegaly	Yes	Yes	Yes	No	No	No
Hydrocephalus	Yes	Yes	Yes	No	No	No
Echogenic gut	No	Yes	No	No	No	No
Intra-cranial calcification	No	Yes	Yes	No	No	No
Liver calcifications	No	Yes	Yes	No	No	No

	Infection					
	Rubella	CMV	Toxoplasmosis	Parvovirus	Syphilis	VZV
Cardiac abnormality	Yes	No	No	No	No	No
Non immune hydrops	No	Yes	No	Yes	Yes	No
Raised nuchal measurement >3.5 at 11–13 weeks only if persists to 16 weeks	No	No	No	Yes	No	No
Nuchal thickening > 6.1mm at 18-22 weeks	No	No	No	Yes	No	No
Cystic Hygroma - no investigations indicated	No	No	No	No	No	No
Limb contraction/ Skin contraction due to scarring (exceptionally rare – discuss)	No	No	No	No	No	Yes
Oligohydramnios – no investigations for infection indicated	No	No	No	No	No	No
Polyhydramnios – no investigations for infection indicated	No	No	No	No	No	No
Recurrent miscarriage	No	No	No	No	No	No
Small for dates on palpation or measurements IS NOT an indication for investigation, ONLY if ultrasound indications as above	No	No	No	No	No	No

Yes = consider investigating for.

No = investigations not indicated.

4.0 Management and investigations of rashes and contact with rashes in pregnancy

4.1 Overview of rashes in pregnancy

This section deals only with infections that present with rashes and are of concern in pregnancy.

These are:

- Parvovirus B19
- Rubella
- Measles Chickenpox (VZV)
- Herpes simplex (primary infection)
- Hand, foot and mouth

4.2 Description of rashes

Rashes are broadly broken up into two categories. These are maculopapular rashes and vesicular rashes.

4.2.1 Maculopapular rashes

Macule means 'spot' and papule means 'little bump'. Generally this term is used to describe uniform small red spots which, when felt, the skin may feel slightly 'bumpy'. It is often impossible to distinguish the viral infections on the bases of rashes alone.

Maculopapular rashes are seen in:

- Rubella (German measles)
- Parvovirus B19
- Measles

Clinical presentation

Rubella (German measles)

- Incubation period is 14 to 21 days
- Period of communicability is seven days before the rash appears until four days after the rash
- A prodrome (a symptom indicating the start of a disease) of feeling unwell with low grade pyrexia may, or may not, precede the rash
- Post auricular (behind the ears), occipital (back of the head) and posterior cervical (under the jaw) lymphadenopathy is the most characteristic clinical feature, which precedes the rash by five to ten days
- Evidence of immunity from previous pregnancy, or a history of two MMR vaccinations, makes the diagnosis of rubella so unlikely as not to be appropriate to test.

Parvovirus B19 (Fifth disease or slapped cheek)

- Incubation period is four to twenty days
- Period of communicability is four days before the rash until the rash appears
- This rash typically presents as very red cheeks in children hence its name 'slapped cheek disease'. The rash is described as lace like on the trunk and extremities that fades during the day, but becomes more apparent after baths, or after exposure, to sunlight
- Symptoms are usually mild
- Parvovirus infection in dogs is a different disease and this type of parvovirus does not infect humans.

Measles

- Incubation period is 10 to 12 days
- Period of communicability is one day before prodrome until four days after rash has appeared
- Measles is by far the most severe of these viral infections. Patients presenting with measles are often unwell. Children in particular are miserable and usually also have conjunctivitis, cough and a runny nose. The rash appears four to seven days into the illness and begins on the face, before becoming more widespread. On the buccal mucosa white or bluish white spots can be seen, these are known as Koplik's spots. As the rash fades the skin desquamates and has a brownish tint.

4.2.2 Vesicular rashes

Vesicular rashes are described as small blisters. They are raised and have fluid filled vesicles (little blisters).

Vesicular rashes are seen in

- Chickenpox – all over the body
- Shingles (herpes zoster) – localised
- Herpes simplex – localised to mouth, or genital regions
- Hand, foot and mouth – localised to hands, feet and mouth and occasionally knees!

Clinical presentation

Chickenpox

- Incubation period is 10 to 21 days
- Period of communicability is 48 hours before onset of rash until lesions have crusted – about five days
- Chickenpox rash starts with a sudden onset of fever and mild constitutional malaise. The rash begins as a maculopapular rash on the face, but within a few hours becomes vesicular, i.e small blisters appear. Vesicles continue to appear for several days in small crops. Generally after five days all the lesions have crusted over and the patient is then

considered to be non-infectious. Chickenpox is generally easy to diagnose clinically, but can be more difficult in adults and dark-skinned people.

Shingles (Herpes Zoster)

- Shingles is a reactivation of the chickenpox virus and presents as a rash over a single dermatome. Shingles only occurs in individuals who have previously had chickenpox. Shingles does not cause any problems to the developing fetus therefore women presenting with shingles should be reassured.
- Pregnant women who have never had chickenpox can 'catch' chickenpox from individuals with shingles, but only if they are in very close contact with exposed lesions (vesicles) for a prolonged period. Therefore, most women exposed to shingles during pregnancy will not require any intervention.

Herpes Simplex

- Herpes simplex virus 1 and 2 cause cold sores and genital herpes. Genital infection can result in neonatal herpes if the mother acquires a genital herpes infection for the first time during the last trimester of pregnancy. Neonatal herpes in the UK is very rare.

Hand, foot and mouth disease

- Hand, foot and mouth disease can rarely be confused with chickenpox. Hand, foot and mouth is a common infection in children and is of no real consequence in pregnancy.
- It usually presents as vesicles in the mouth, hands and feet. During later pregnancy, vesicles may also be apparent on the stretched abdominal skin.
- It may occasionally be seen with a maculopapular rash on the buttocks. It is self-limiting and caused by an enterovirus.
- Enteroviruses can cause significant disease and mortality in neonates.
- Enteroviral infections should be excluded in neonates who present with sepsis. If women present in labour with a rash, enteroviruses should be considered.

4.3 Management of contact with rashes in pregnancy

Once a woman reports contact with a rash, it is important to determine whether this contact was with a maculopapular rash, or a vesicular rash. This will be determined by the history and description of the rash. It is unusual not to be able to make this distinction.

Information that is required to inform management is:

- Nature of the rash, i.e. vesicular or maculopapular
- Date of last contact with the rash
- Nature of contact with the rash (same room for >15 minutes, household contact, conversation with a person with a rash)
- Duration of contact with rash
- Gestation of pregnancy
- Previous history of infection with rubella, measles, parvovirus, chickenpox, etc.
- Vaccination history (rubella, measles, chickenpox).

Once an accurate history is obtained a clotted blood sample should be sent for testing.

Women who have been in contact with a person with maculopapular rash should have diagnostic tests to look for both immunity and current infection with measles, parvovirus and rubella.

Women who have been in contact with a person with a vesicular rash should have a diagnostic test for immunity to chickenpox.

Refer to the antenatal screening section for information on rubella.

4.3.1 Rubella (German Measles)

Please refer to the first chapter on Antenatal Screening 2.1

4.3.2 Parvovirus B19

Introduction

Parvovirus B19 is a virus that only affects humans. It is also known as erythrovirus, fifth disease, slapped cheek, or erythema infectiosum.

It is thought that 60% of all adults in the UK have been infected with parvovirus B19 at some point. An increase in the number of infections occurs every 3 to 4 years, usually in schoolchildren. Once infected, immunity is lifelong.

The risk of acquiring parvovirus during pregnancy, over epidemic and non-epidemic years, is about 1 in 400.

Routine antenatal screening is not recommended as there is no vaccine, or prophylaxis available.

Consequence of infection with parvovirus during pregnancy

- There is a 50% risk of transmission from an infected mother to the fetus
- Parvovirus contracted before 20 weeks gestation has a risk of adverse fetal outcome as it destroys fetal red blood cells, resulting in fetal anaemia and hydrops. Infection acquired before 20 weeks has around 9% increase in the risk of fetal loss
- Parvovirus does not result in fetal abnormality other than hydrops.

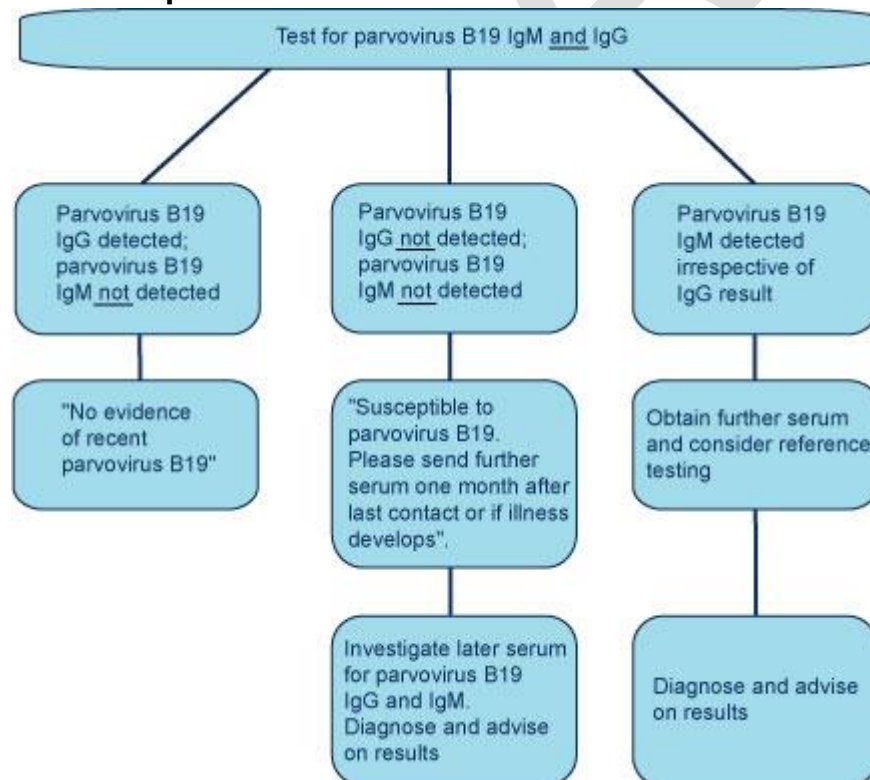
Symptoms

- Adults are often asymptomatic, or they can present with a non-specific illness, rash and/or arthralgia
- Women who are susceptible to catching parvovirus are as follows:
 - living in a household setting with an infected person
 - sharing a meal with an infected person
 - being in the same room for over half an hour with an infected person.

Diagnosis of infection following contact or illness with non-vesicular rash during pregnancy

- A maternal blood sample is required for parvovirus serology to look for the presence of antibodies. Rubella serology should also be requested as symptoms are similar.

Interpretation of serological investigation for parvovirus B19 of pregnant woman exposed to rash illness



Management of parvovirus B19 infection

- Woman found to have been recently infected with parvovirus should have bi-monthly ultrasound scans until 30 weeks gestation to look for early signs of hydrops. Referral to a fetal medicine unit should be discussed.

Evidence base

Morgan-Capner, P. and Crowcroft, N. S. (2001), Guidelines on the management of, and exposure to, rash illness in pregnancy (including consideration of relevant antibody screening programmes in pregnancy). *Communicable Disease and Public Health*. 5 (1). pp 59–71.

4.3.3 Varicella Zoster virus (chickenpox)

Introduction

Varicella zoster virus (VZV) causes chickenpox as a primary infection. VZV is a DNA virus, which is highly contagious and spread by respiratory droplets. The incubation period is 10 to 21 days.

Shingles is a reactivation of latent VZV virus. Shingles cannot be caught following contact with chickenpox (or shingles). However, susceptible individuals can catch chickenpox from exposed shingles lesions on rare occasions. Exposed shingles is much less contagious than chickenpox and covered 'shingle' lesions pose no threat to pregnant women.

Maternal shingles carries no risk to the fetus, or neonate.

Definition of contact with chickenpox

- Household member has chickenpox
- Face-to-face conversation with a person with chickenpox
- Same room as a person with chickenpox for at least 15 minutes.

The person with chickenpox is infectious for 48 hours before the onset of the rash and until the lesions have crusted over (usually 5 days).

Risks of chickenpox in pregnancy

Chickenpox (primary VZV infection) is unusual as it can cause complications in pregnant women, the fetus and the neonate.

Complications for pregnant woman

Pregnant women are at risk of more severe infection and complications, such as:

- Pneumonia (up to 10% if smokers)
- Hepatitis
- Encephalitis
- Death (mortality rate <1%).

Risks to fetus

The fetus is at greatest risk if maternal infection occurs before 20 weeks gestation. There is some controversy as to whether there remains a small risk to

the fetus up to 28 weeks gestation. Pregnant women with chickenpox infection are not at an increased risk of miscarriage. Fetal Varicella Syndrome (FVS) occurs in less than 2% of pregnancies with maternal chickenpox before 20 weeks gestation.

The fetus can present with abnormalities such as:

- Skin scarring in dermatome distribution
- Eye defects
- Limb hypoplasia
- Neurological abnormalities.

Neonatal infection

Babies born to mothers who have contracted chickenpox within 7 days of delivery, or 7 days following delivery, are at high risk of developing neonatal varicella which carries a mortality of 30%. Urgent advice from microbiologist, or virologists, should be sought regarding prophylaxis, or treatment for the neonate.

Management of pregnant women exposed to chickenpox during pregnancy

- Previous maternal chicken pox: reassure and no action required.
- No history, or uncertain past history, of chicken pox:
 - check for presence of maternal IgG. Same day testing is available Monday–Friday.
 - booking blood samples can be used if the woman has already booked.
 - the laboratory should be contacted to request urgent testing.
- If VZV IgG is absent, Varicella Zoster Immune Globulin (VZIG) should be considered.
- VZIG is available from the consultant virologist/microbiologist and can only be made available following discussion with an obstetrician.
- Out of hours contact consultant virologist/microbiologist via switchboard to determine if out of hours testing indicated VZIG.

Management of pregnant women if exposed to shingles during pregnancy

- In the absence of a history of chickenpox it is unusual to offer any prophylaxis for contact with shingles. This may occasionally be warranted if the pregnant woman has had significant exposure, such as dressing a lesion, or if she is the primary carer of an individual suffering with shingles.

Management of pregnant woman with chicken pox

- VZIG is not recommended in the management of women who present with chickenpox.
- Acyclovir should be offered if the woman presents within 24 hours of the onset of the rash.
- The woman should be advised to avoid contact with other susceptible individuals.
- The woman should be advised to seek urgent medical attention if she develops breathlessness, becomes confused, or develops a haemorrhagic rash as this indicates severe infection and the need for antiviral therapy.

Evidence base

- Royal College of Obstetricians and Gynaecologists (2007), Chicken pox in Pregnancy. *Green Top Guideline No. 13*. RCOG: London.
- Department of Health (2006), Immunisation Against Infectious Diseases – 'The Green Book' Available at: www.dh.gov.uk/en/Publichealth/Healthprotection/Immunisation/Greenbook/DH_4097254. (Accessed on 10/03/11).

4.3.4 Genital Herpes

Introduction

Genital herpes simplex virus (HSV) infection is one of the most common viral sexually transmitted infections. HSV can cause cold sores on the face and lips (HSV 1 usually), or sores on the genitals (HSV 2 usually). Once infected with either type, the virus remains within the body for life and the symptoms can re-emerge; these are called recurrences. The majority of women with genital herpes will have a recurrence during pregnancy. Transmission of the virus from mother to fetus typically occurs by direct contact with virus in the genital tract during birth.

Neonatal HSV is a very severe viral infection with a high mortality. It is fortunately very rare in the UK; surveillance data in the late 1980s indicated an incidence of 1.65:100 000 live births are affected. This means the majority of women with genital herpes give birth to healthy babies.

HSV infection in pregnancy

The management of genital herpes in pregnancy depends on whether the infection is primary or recurrent:

- **A primary infection** of genital herpes is when the mother becomes infected for the first time with any HSV virus. The risk of transmission of HSV infection to the newborn can be as high as 33 to 50% if the woman becomes infected in the third trimester of pregnancy (see section A below for management)

- **First episode of HSV genital infection.** If the woman has been previously infected with an HSV 1 virus and she subsequently acquires a genital infection with the HSV 2 virus, these women are described as having a 'first episode genital infection'. These mothers are at a lower risk of transmitting infection to their babies (see section A below for management)
- **Recurrent infection.** Women with a history of recurrent genital HSV infection have a much lower risk of transmitting infection. This risk is around 2% if there are genital lesions present at the time of delivery and is as low as 0.04% in the absence of lesions (see section B for management)

The difficulties arise in identifying these patients groups. Detailed history taking is essential. There are serological tests that can differentiate between HSV 1 and HSV 2 antibodies, however, these are not readily available and accessing these investigations requires a discussion with a microbiologist, or virologist.

Management of HSV infection in pregnant women

A. Genital herpes: primary infection, or first episode genital herpes

- ***Lesions present at onset of labour:***
 - caesarean section (CS) is recommended unless the membranes have been ruptured for greater than four hours. Treat with IV acyclovir (ACV) 5mg/kg tds for five days.
- ***Lesions within 6 weeks of expected date of delivery:***
 - consider CS. If the woman chooses a vaginal delivery, invasive procedures such as fetal scalp electrodes, or fetal blood sampling should be avoided.
- ***Lesions more than 6 weeks before expected onset of labour:***
 - CS not indicated.

B. Recurrent genital herpes with active lesions

- **Lesions at onset of labour**
 - CS should be considered unless the membranes have been ruptured for greater than four hours, BUT risk is small (0-3%) so this should be considered against the risk of a CS to the mother. Treat with ACV 200mg 5 x day for 5 days.
- **Lesions before onset of labour**
 - no indication for CS. Consider suppressive ACV 400mg bd for last four weeks of pregnancy.

Neonatal HSV infection

Neonates with HSV infection manifest the disease in three different ways:

1. SEM – Skin, eye and mucous membrane diseases. This accounts for approximately 20% of all neonatal HSV infections. It usually presents at 10 to 12 days post birth and the lesions often appear at the site of trauma. At this stage neonates are not systemically unwell, but can progress to disseminated disease without treatment. With active treatment prognosis is good.
2. Disseminated infection accounts for 25% of HSV infections in newborns. This usually manifests earlier around the first few days of life. The neonate presents with jaundice, hepatomegaly, respiratory dysfunction and the disease progress can be rapid. Skin lesions are not always present, or obvious.
3. Encephalitis is the sole manifestation in approximately 30% of babies. Presentation usually occurs within the first 2 to 3 weeks of life with lethargy, irritability and focal seizures. Without treatment prognosis is poor; those children who survive have severe neurological impairment.

Babies suspected of having neonatal HSV infection

- Treatment with high dose acyclovir (ACV) is recommended (60mg/kg/day in 3 divided doses) for 21 days.
- Send Nasopharyngeal aspirate (NPA), plus swabs from nose, throat, ear, axilla, umbilicus and a swab from a lesion. The local laboratory should be contacted as to which type of swabs are required (i.e whether dry swabs, or swabs in media).
- Send cerebral spinal fluid (CSF) for PCR.
- Inform the laboratory of the suspected diagnosis.
- Isolate baby.
- Ensure good hand washing by both mother and staff.
- Refer to local infection control policies.

Management of neonates born to mothers with genital herpes

A. Well baby, but mother with primary or first episode of genital HSV at delivery

- Isolate baby and observe.
- Send samples from baby (detailed above) 48 hours after delivery.

- Advise five days of IV ACV if vaginal delivery, or if membranes ruptured for more than four hours prior to caesarean section.

B. Well baby, mother with recurrent genital herpes with active lesions at delivery

- Isolate baby and observe.
- Send samples from baby 48 hours after delivery for HSV PCR. Samples sites are axilla, umbilicus, ear, nose, throat and mouth.
- Consider five days of IV ACV if vaginal delivery, or if membranes ruptured for more than four hours prior to caesarean section, or if invasive monitoring used [evidence lacking as to benefit].

C. Well baby, but mother with past history of genital HSV but no Evidence of current active infection

- No special management required.
- Breastfeeding is not contraindicated except if the mother has lesions on the breast. This indicates severe infection and the need for antibiotics.

Evidence base

- Royal College of Obstetricians and Gynaecologists (2007), Management of Genital Herpes in Pregnancy. *Green Top Guideline No. 30*. RCOG: London.
- Scottish Clinical Virologists Consultant Group (2004), Protocol: Herpes Simplex Infection In Pregnancy And Neonate. Available at: <http://www.bing.com/search?q=%E2%80%A2%09Scottish+Clinical+virologists+Consultant+group+%E2%80%93+Protocol%3A+&src=IE-SearchBox>. [Accessed 11/1/11].
- Money, D., Steben, M. (2008), Guidelines for the Management of Herpes Simplex Virus in Pregnancy. *Journal of Obstetrics and Gynaecology Canada*. 30(6). pp. 514–519.
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- Canadian Paediatric Society (2003), Paediatric infectious disease notes – Current management of Herpes simplex infection in pregnant women and their newborn infants. *Paediatric Child Health*. 8(6). pp. 363–365.
- Malkin, J. E., Beumont, M. G. (1999), Herpes Simplex Virus Infection in Pregnancy. *Herpes*. 6(2). pp. 50–54.

4.3.5 Measles

Introduction

Measles is by far the most severe of the common childhood viral infections. Patients presenting with measles are often unwell. It is highly infectious and cases are infectious one day before the prodrome, which may be as long as four days before the rash appears and they continue to be infectious for four days after the rash appears.

Measles used to be very rare in the UK, but as a result of unfounded anxiety surrounding MMR vaccine the uptake of MMR was reduced and therefore measles has become more prominent.

A previous history of measles, or a history of vaccination with MMR, makes measles an unlikely diagnosis.

Seroprevalence studies indicate that <1% of individuals born before 1970 and <10% of individuals born after 1970 are susceptible to measles.

Management of pregnant women

Pregnant women who are susceptible to measles and have been exposed to a confirmed case of measles

- Pregnant women who are susceptible to measles and have been exposed to a confirmed case of measles can be offered Human Normal Immunoglobulin (HNIG). The purpose of this blood product is to try and attenuate maternal infection. Ideally it should be given by I.M. injection within 72 hours of contact, but may be of benefit up to six days after exposure.
- Supplies of HNIG are limited and can only be obtained from the Health Protection Agency (HPA) in London. HNIG is a blood product and therefore should only be offered appropriately. Discussion with local microbiologist, virologist, or health protection teams may be useful to determine the urgency for testing for maternal immunity (IgG) and to undertake a full risk assessment of the contact.
- Measles is highly infectious, but the clinical diagnosis of measles is difficult due to the relatively rarity of the infection.

Pregnant women who are infected with measles

- Women who have become infected with measles are thought to be at risk of more severe infection and the complications of measles such as pneumonitis.
- HNIG is offered to women to try and attenuate the risk to the mother; there is no evidence that it provides any protection to the fetus.

- Women who are infected with measles may have a spontaneous miscarriage as a result of maternal illness.
- There are no fetal abnormalities associated with measles and if the pregnancy continues the fetus is not at any greater risk of abnormality.

Management of the neonate following maternal measles during pregnancy

- As there is no evidence of increased risk of fetal abnormalities following maternal infection no interventions are required for the neonate.
- Measles is notifiable on clinical suspicion. The public health teams should be informed of suspected cases of measles.

Evidence base

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