PERINATAL INFECTIONS

4th stage
Infectious diseases contracted during pregnancy can have a serious impact on both the mother and the fetus. Some infections cause congenital abnormalities in the fetus (rubella, syphilis, toxoplasmosis, cytomegalovirus, chickenpox). Other infections can be transmitted from mother to baby during pregnancy (parvovirus) or around the time of delivery (human immunodeficiency virus (HIV), hepatitis B, hepatitis C, herpes, group B streptococcus).
For several infectious diseases, screening programmes and effective interventions can improve the outcome for the fetus. For other diseases, early diagnosis and appropriate treatment can be of benefit to both mother and baby.
Rubella

Infecntive organism

Rubella virus is a togavirus spread by droplet transmission.

Prevalence

Since the introduction of the measles, mumps and rubella vaccine (MMR), an average of three births affected by congenital rubella a year and four rubella associated terminations were registered from 1996 to 2000 in the UK. In the 1990s there was reduced uptake of the MMR vaccine for infants due to concern about a possible link with autism. It is too soon to say whether this will eventually lead to an increase in the prevalence of rubella in the community and an increase in incidence of congenital rubella when this cohort of non-immunized infants reach childbearing age.
Screening

In the UK, NICE recommendations are that all women should be offered rubella susceptibility screening early in their pregnancy to identify women at risk of contracting rubella infection and to enable vaccination in the post-natal period for the protection of future pregnancies.

For pregnant women who are screened and rubella antibody is not detected, rubella vaccination after pregnancy should be advised. Vaccination during pregnancy is contraindicated because of a theoretical risk that the vaccine itself could be teratogenic, as it is a live vaccine. No cases of congenital rubella syndrome resulting from vaccination during pregnancy have been reported. However, women who are vaccinated postpartum should be advised to use contraception for three months.
Rubella infection is characterized by a febrile rash but may be asymptomatic in the mother in 20–50 per cent of cases.

Features of congenital rubella syndrome can include sensorineural deafness, congenital cataracts, blindness, encephalitis and endocrine problems.
Rubella syndrome

- Microcephaly
- PDA
- Cataracts
The risk of congenital rubella infection reduces with gestation. If infection of the fetus does occur the defects caused are also less severe with more advanced gestations. One hundred per cent of infants infected during the first 11 weeks of pregnancy have rubella defects, whereas primary rubella contracted between 16 and 20 weeks of gestation carries only a minimal risk of deafness. Rubella infection prior to the estimated date of conception or after 20 weeks gestation carries no documented risk to the fetus.
Blueberry muffin rash in congenital rubella
Management

If infection during pregnancy is confirmed, the risk of congenital rubella syndrome should be assessed depending on the gestation when infection occurred. If infection occurred prior to 16 weeks gestation, termination of pregnancy should be offered. If the infection occurs later in pregnancy the woman should be given appropriate information and reassured.
Syphilis

Infective organism
Syphilis is a sexually acquired infection caused by Treponema pallidum.

Prevalence
The increase has mainly been seen in rates of infection in homosexual men, but part of the increase is due to immigration to the UK from countries where prevalence is higher, for example Eastern Europe. The prevalence of syphilis in pregnant women has been estimated at approximately 68 per million with regional variation, highest in north-east London.
Clinical features
Primary syphilis may present as a painless genital ulcer 3–6 weeks after the infection is acquired (condylomata lata)
Secondary manifestations occur 6 weeks to six months after infection and present as a maculopapular rash or lesions affecting the mucous membranes. Ultimately, 20 per cent of untreated patients will develop symptomatic cardiovascular tertiary syphilis and 5–10 per cent will develop symptomatic neurosyphilis.

In pregnant women with early untreated (primary or secondary) syphilis, 70–100 per cent of infants will be infected and approximately 25 per cent will be stillborn.
Mother-to-child transmission of syphilis in pregnancy is associated with fetal growth restriction (FGR), fetal hydrops, congenital syphilis (which may cause long-term disability), stillbirth, preterm birth and neonatal death. The risk of congenital transmission declines with increasing duration of maternal syphilis prior to pregnancy. Adequate treatment with benzathine penicillin markedly improves the outcome for the fetus.
Hutchinson Teeth appear in late Congenital Syphilis
Congenital Syphilis in a Newborn
syphilis: congenital
Screening

Because treatment is so effective, routine antenatal screening for all pregnant women is recommended.

- Non-treponemal tests detect non-specific treponemal antibodies and include the Venereal Diseases Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests.

- Treponemal tests detect specific treponemal antibodies and include enzyme immunoassays (EIA), *T. pallidum* haemagglutination assay (TPHA) and the fluorescent treponemal antibody-absorbed test (FTA-abs).
EIAs are over 98 per cent sensitive and over 99 per cent specific. Non-treponemal tests, on the other hand, may result in false negatives, particularly in very early or late syphilis, in patients with reinfection or those who are HIV positive. The VDRL may be falsely positive in women with lupus. Therefore, positive results should be interpreted with caution and the pregnant woman should be referred for expert assessment and diagnosis in a genitourinary medicine clinic.

None of these serological tests will detect syphilis in its incubation stage, which may last for an average of 25 days.
Management

The initial step is

• To confirm the diagnosis
• To test for any other sexually transmitted diseases
• Once a diagnosis of syphilis is confirmed
• Genitourinary medicine clinic will institute
• Appropriate contact tracing of sexual partners.
• Older children may also need to be screened for congenital infection.

Parenteral penicillin has a 98 per cent success rate for preventing congenital syphilis.
If a woman is not treated during pregnancy her baby should be treated after delivery. An infected baby may be born without signs or symptoms of disease but if not treated immediately, may develop serious problems within a few weeks. Untreated babies often develop developmental delay, have seizures or die.
Toxoplasmosis

**Infective organism**
Toxoplasma gondii is a protozoan parasite found in cat faeces, soil or uncooked meat. Infection occurs by ingestion of the parasite from undercooked meat or from unwashed hands.

**Prevalence**
The prevalence varies in different countries. It is 16 per 1000 in France but in the UK it is estimated to be less than two per 1000 pregnancies.
A fetus may contract toxoplasmosis through the placental connection with its infected mother.

The mother may be infected by:
- Improper handling of cat litter
- Handling or ingesting contaminated meat
Screening

UK National Screening Committee recently reported that screening for toxoplasmosis should not be offered routinely.

Appropriate preventative measure such as avoiding eating rare or raw meat, avoiding handling cats and cat litter, and wearing gloves and washing hands when gardening or handling soil.
Clinical features

The initial infection may be relatively asymptomatic, or may be a glandular fever-like illness. Parasitaemia usually occurs within 3 weeks of infection.

Infection during the first trimester of pregnancy is most likely to cause severe fetal damage (85 per cent), but only 10 per cent of infections are transmitted to the fetus at this gestation. In the third trimester 85 percent of infections are transmitted, but the risk of fetal damage decreases to around 10 per cent.
Severely infected infants may have ventriculomegaly or microcephaly, chorioretinitis and cerebral calcification. These features may be detected on ultrasound scan. The majority of infected infants are asymptomatic at birth but develop sequelae several years later.
A = Normal posterior pole of the right eye.
B = Superior periphery of the right eye, showing the retinochoroidal scar with central atrophy and pigmented margins.
C = Posterior pole of the left eye, showing a large and predominately pigmented retinochoroidal scar involving the macula. Retinal hemorrhages are seen in the superior margin of the lesion, indicating presence of a choroidal neovascular membrane.

**Figure 1** - Color fundus photographs of the mother 14 months after delivering the offspring with congenital toxoplasmosis; the patient had been treated for recurrent toxoplasmic retinochoroiditis in her left eye 12 months before
Management

The diagnosis of primary infection with toxoplasmosis during pregnancy is made by the Sabin-Feldman dye test. Enzyme-linked immunosorbant assays are available for IgM antibody. However, IgM may persist for months or even years, so often serial testing for rising titres is necessary.

If suspicion of congenital toxoplasmosis has arisen because of an abnormal ultrasound scan of the fetus, an amniocentesis can be performed. Polymerase chain reaction (PCR) analysis of amniotic fluid is highly accurate for the identification of *T. gondii*.
Spiramycin treatment can be used in pregnancy (a 3-week course of 2–3 g per day). This reduces the incidence of transplacental infection but has not been shown to definitively reduce the incidence of clinical congenital disease. If toxoplasmosis is found to be the cause of abnormalities detected on ultrasound scan of the fetus, then termination of pregnancy can be offered.
Cytomegalovirus

Infective organism

Cytomegalovirus (CMV) is a DNA herpes virus. It is transmitted by respiratory droplet transmission and is excreted in the urine.

Prevalence

The incidence of infection in pregnancy is estimated to be around 1–2 per cent of pregnancies. Of those infected, approximately 30 per cent will transmit the viral infection to the fetus and of these approximately 30 per cent of the fetuses will be affected by the virus.
How Many Babies Are Affected by Congenital CMV Infection?

- 1000 pregnancies that lead to live birth
- 600 women who have CMV before pregnancy
  - 594 CMV-negative babies
  - 6 CMV-positive babies
  - 1 to 2 babies with permanent problems
- 400 women who do not have CMV before pregnancy
  - 7 women get CMV
  - 393 women who do not get CMV
  - 2 CMV-positive babies
Clinical features

Primary infection often produces no symptoms or mild non-specific flu-like symptoms in the mother. The main features seen in an affected fetus are FGR, microcephaly, ventriculomegaly, ascites or hydrops. Some fetuses which are infected may not show any features on ultrasound, but may later be found to have neurological damage such as blindness, deafness or developmental delay. The neonate can also be anaemic and thrombocytopenic, with hepatosplenomegaly, jaundice and a purpural rash.
Congenital Cytomegalovirus
congenital cmv
Management

A serological diagnosis can be made by demonstrating the development of CMV antibodies in a seronegative woman, who initially develops CMV IgM antibody, and subsequently IgG antibody. Virology labs usually keep the initial sample taken at booking, so if infection is suspected a sample taken at the time of presentation can be compared with the initial booking sample to determine whether seroconversion has occurred. Since IgM can be secreted for several months, it is not sufficient to simply demonstrate IgM in a sample at the time of presentation; it has to be a new finding in a woman who was negative for IgM at the time of booking.
If there is a suspicion that the fetus may be infected, amniotic fluid can be tested for the virus by PCR. Since the virus is excreted in fetal urine it can be found in amniotic fluid. If abnormalities are detected on ultrasound and these are felt to be due to congenital CMV infection, termination of pregnancy should be offered.
Chickenpox

Infective organism
Chickenpox is caused by the varicella zoster virus (VZV), a herpes virus which is transmitted by droplet spread.

Prevalence
In the UK 90 per cent of adults are immune to chickenpox. However, contact with chickenpox is common in pregnancy and approximately one in 200 women will contract chickenpox during their pregnancy.
Clinical features
Non-immune pregnant women are more vulnerable to chickenpox and may develop a serious pneumonia, hepatitis or encephalitis. It can occasionally be fatal with the mortality rate being approximately five times higher in pregnant women than in non-pregnant adults. Pneumonia occurs in about 10 per cent of women with chickenpox and seems more severe at later gestations. It may also cause the fetal varicella syndrome (FVS) or varicella infection of the newborn.
Management
Women should be asked whether they have had chickenpox at the initial booking visit.

Testing for immunity
If a woman reports that she has been in contact with chickenpox, she should have a blood test for confirmation of VZV immunity, by testing for VZV IgG. This can usually be performed within 24–48 hours and the virology laboratory may be able to use serum stored from booking antenatal bloods. At least 80–90 per cent of women tested will have VZ IgG and can be reassured.
Management of the non-immune woman exposed to chickenpox
If the pregnant woman is not immune to VZV and she has had a significant exposure, she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. VZIG is effective when given up to 10 days after contact and may prevent or attenuate the disease. Women who have had exposure to chickenpox (regardless of whether or not they have received VZIG) should be asked to notify their doctor or midwife early if a rash develops.
Management of chickenpox in pregnancy

Women with chickenpox should avoid contact with susceptible individuals; that is, other pregnant women and neonates, until the lesions have crusted over. This is usually about 5 days after the onset of the rash.

Oral aciclovir 800 mg five times per day for 7 days be prescribed for pregnant women with chickenpox if they present within 24 hours of the onset of the rash and if they are more than 20 weeks gestation. Aciclovir should be used cautiously before 20 weeks gestation.
VZIG has no therapeutic benefit once chickenpox has developed. The maternal risks are bleeding, thrombocytopenia, disseminated intravascular coagulopathy and hepatitis. There is a high risk of varicella infection of the newborn with significant morbidity and mortality. Supportive treatment and intravenous aciclovir is therefore desirable, allowing resolution of the rash and transfer of protective antibodies from the mother to the fetus. However, delivery may be required in women to facilitate assisted ventilation in cases where varicella pneumonia is complicated by respiratory failure.
The fetus
Spontaneous miscarriage does not appear to be increased if chickenpox occurs in the first trimester.
FVS is characterized by one or more of the following:
• skin scarring in a dermatomal distribution;
• eye defects (microphthalmia, chorioretinitis, cataracts);
• hypoplasia of the limbs;
• neurological abnormalities (microcephaly, cortical atrophy, developmental delay and dysfunction of bowel and bladder sphincters).
This only occurs in a minority of infected fetuses (approximately 1 per cent). FVS has been reported to complicate maternal chickenpox that occurs as early as 3 weeks and up to 28 weeks of gestation. The risk appears to be lower in the first trimester (0.55 per cent). No case of FVS has been reported when maternal infection has occurred after 28 weeks.
Maternal infection around the time of delivery
If maternal infection occurs at term, there is a significant risk of varicella of the newborn. Elective delivery should normally be avoided until 5–7 days after the onset of maternal rash to allow for the passive transfer of antibodies from mother to child.

Neonatal ophthalmic examination should be organized after birth.
If birth occurs within the 7-day period following the onset of the maternal rash, or if the mother develops the chickenpox rash within the 7-day period after birth, the neonate should be given VZIG.
Contact with shingles

Following the primary infection, the virus remains dormant in sensory nerve root ganglia but can be reactivated to cause a vesicular erythematous skin rash in a dermatomal distribution known as herpes zoster or shingles. The risk of a pregnant woman acquiring infection from an individual with herpes zoster in non-exposed sites (for example, thoracolumbar) is remote.