Congenital, perinatal and neonatal infections

Some infections are more serious in pregnancy than in the non-pregnant state because of the potential for vertical transmission. Infection can pass vertically from mother to fetus/neonate in several ways:

- Across the placenta - infections include *Toxoplasma gondii, Treponema pallidum, Listeria monocytogenes, Plasmodium falciparum* (malaria), rubella and cytomegalovirus (CMV).
- Ascending maternal infection and chorioamnionitis causing fetal infection, usually subsequent to prolonged rupture of membranes.
- Perinatal infection acquired during birth via the haematogenous or genital route. These include human immunodeficiency virus (HIV), herpes zoster virus (HZV), hepatitis B virus (HBV) and .
- Postnatal infection transmitted via breast-feeding.

Pre-pregnancy or routine antenatal screening can determine the presence or susceptibility to *some* of these infections, enabling appropriate management to prevent adverse fetal or perinatal outcomes. Always try to consider the possibility of congenital infection when reviewing an unwell pregnant woman.

Screening programmes vary throughout the UK. See the links for the UK regional screening programmes under 'Further reading & references', below.

Whilst infections can occur in utero, birth represents an abrupt transition from a highly protected environment to exposure to a vast array of new pathogens ex utero. Parturition also places the baby in direct contact with maternal blood or genital secretions and infections may result, especially if there was prolonged or early rupture of membranes.

At birth, an infant's immune system remains immature. Some protection is provided by maternal antibodies (IgG) crossing the placenta. This process is less complete in the premature baby, especially if markedly premature. If a mother develops a new infection close to the time of birth, she may remain infectious and will not yet have produced any protective IgG, placing the infant at risk of a more severe form of the disease, as in the case of neonatal varicella. The current definitions are:[1]

- Perinatal period - liveborn baby from 20 weeks of gestation to 7 completed days following the time of birth.
- Neonatal period - liveborn baby from 20 weeks of gestation to 27 completed days, sometimes subdivided into early neonatal (birth to 6 completed days) and late neonatal (day 7 to day 27 completed days).

Within the UK and the Crown Dependencies, infection accounted for 3.9% of stillbirths and 8.7% of neonatal deaths in 2019.[1]

Congenital infections

Rubella

See the separate Rubella and Pregnancy article.

HIV

See the separate Congenital HIV and Childhood AIDS article.

CMV

See the separate Cytomegalovirus article.

Chickenpox[2]

See also the separate Chickenpox article.

- Varicella infection of the newborn may result from maternal infection near the time of delivery or immediately postpartum, or from contact with a person other than the mother with chickenpox or shingles during this time.
- The route of infection may be transplacental, ascending vaginal or direct contact with lesions during or after delivery.

- If maternal infection occurs 1-4 weeks before delivery, up to 50% of babies are infected and approximately 23% develop clinical varicella, despite high titres of passively acquired maternal antibody.
- Severe chickenpox is most likely to occur if the infant is born within 7 days of onset of the mother's rash or if the mother develops the rash up to 7 days after delivery.

Hepatitis B

See the separate Hepatitis B article.

Hepatitis C

See the separate Hepatitis C article.

Group B streptococci (GBS) [3]

- Approximately 50% of women are carriers of GBS. Bacteria are found in the vagina and in the urine. Infection has been associated with preterm delivery, and ascending infection following rupture of membranes may result in fetal infection.
- Maternal carriage of GBS is associated with a higher risk of chorioamnionitis and neonatal disease.
- Neonatal GBS disease occurs at a rate of 1 in 700-800 births.
- Neonatal sepsis with associated mortality of 6% occurs in 0.5-3.7/1,000 live births. It can be prevented with intrapartum penicillin in high-risk cases.

- There are guidelines for preventing neonatal GBS infection:[3]
    - Routine bacteriological screening of all pregnant women for antenatal GBS carriage is not recommended.
    - Intrapartum antibiotic prophylaxis (IAP), usually in the form of high-dose intravenous (IV) benzylpenicillin or ampicillin, should be offered to women with GBS bacteriuria identified during the current pregnancy.
    - IAP should be offered if GBS is detected on a vaginal swab (taken at 35-37 weeks, or 3-5 weeks before the anticipated delivery date) in the current pregnancy.
    - IAP should be offered to women with a previous baby with neonatal GBS disease.
    - Antibiotic prophylaxis specific for GBS is not required for women undergoing planned caesarean section in the absence of labour and with intact membranes.
    - Immediate induction of labour and IAP should be offered to all women known to be colonised with GBS with prelabour rupture of membranes at 37 weeks of gestation or more.
    - Women presenting in established preterm labour with intact membranes with no other risk factors for GBS should not routinely be offered IAP unless they are known to be colonised with GBS.
    - If chorioamnionitis is suspected, broad-spectrum antibiotic therapy including an agent active against GBS should replace GBS-specific IAP and induction of labour should be considered.

Listeria monocytogenes

See the separate Listeriosis article.

Syphilis[4]

See also the separate Syphilis article.

- In many parts of the world, particularly sub-Saharan Africa, congenital syphilis is a significant public health problem. Although it is rare in most affluent countries there has been a slight resurgence recently in several European countries.
- Congenital syphilis is estimated to occur in 25-75% of exposed infants.
- At birth, infection manifests as neonatal rhinitis, osteitis, and skin bullae. Hutchinson's triad (abnormal teeth, interstitial keratitis and sensorineural deafness) arises later in untreated children.
- Maternal infection is usually detected by antenatal screening using a non-treponemal test (eg, VDRL) but note there is a risk of false positive results (due to concomitant infection or autoimmune disease) and confirmation with a specific treponemal test (eg, FTA-ABS) is required.
- Treatment is with parenteral benzylpenicillin.

C. trachomatis

C. trachomatis can be vertically transmitted at the time of delivery from mothers to infants. Approximately 50-70% of infants born to mothers with untreated genital chlamydial infection will become infected, with 30-50% developing conjunctivitis and 10-20% developing pneumonia.[5]

See also the separate Chlamydial Genital Infection and Ophthalmia Neonatorum articles.

Gonorrhoea

Gonorrhoea is usually asymptomatic in pregnancy. Gonococcal cervicitis is associated with chorioamnionitis and increased risk of premature labour. 40% of untreated maternal cases cause ophthalmia neonatorum - presenting with purulent discharge, lid swelling and corneal hazing within four days of birth.

See also the separate Gonorrhoea article.

Toxoplasmosis

About 75% of pregnant women are susceptible but seroconversion during pregnancy is uncommon. A third of infants become infected if their mother becomes infected during pregnancy, especially in later pregnancy (but the severity of disease decreases). There is very little good evidence that prenatal education reduces the risk of congenital infection.[6]

See also the separate Toxoplasmosis article.

Malaria

See the separate Malaria in Pregnancy article.

Screening

Routine antenatal screening tests in the UK completed prior to 16 weeks of gestation:[7]

Test	Purpose	Action
Hepatitis B surface antigen	To determine chronic carriers.	If positive, administer hepatitis B immune globulin and vaccine to the infant at birth (prevents carriage in 95%).
Syphilis	To detect active infection.	If reactive, treat with penicillin and consult a GUM specialist.
HIV antibody	To enable measures to be taken to reduce vertical transmission.	If positive, antiretroviral treatment for both mother and infant reduces vertical transmission rates significantly. Refer to a GUM/HIV specialist.
Urine culture	Treatment of asymptomatic urinary tract infection is thought to reduce adverse pregnancy outcomes (premature labour) and risk of maternal pyelonephritis.	If culture shows asymptomatic bacteriuria, treat with antibiotics and repeat culture to ensure fully treated.

Surveillance indicates that rates of maternal infection are variable across the country with high concentrations in particular geographical areas. Based on data from women receiving antenatal care in London between 2000-2007, prevalence of HIV infection was 3/1,000, of hepatitis B 11/1,000, of syphilis 4/1,000 and of rubella susceptibility 39/1,000.[8] Uptake of screening amongst this group of pregnant women was between 95-97%.

Currently there are no tests recommended nationally for antenatal screening of CMV, toxoplasma, parvovirus or GBS.

Do not forget that acute maternal infection may occur after screening - in resource-rich settings such as the UK and America, a significant proportion of perinatal transmission of HIV occurs due to infection acquired during pregnancy.[9]

Neonatal infections

Serious acute neonatal infections

- The incidence of serious acute infections in neonates is around 2/1,000 live births but the figure rises to 8-9/1,000 in small babies weighing just 1,000 to 2,000 grams and 26/1,000 in those of less than 1,000 grams. GBS is the most frequent cause of severe early-onset neonatal infection in neonates and occurs in 0.5/1,000 UK births.
- Of early-onset neonatal sepsis, 85% presents in the first 24 hours, 5% between 24 and 48 hours, and the remaining 10% over the subsequent four days. Early-onset infections include GBS, *Escherichia coli*, *Haemophilus influenzae*, and *Listeria monocytogenes* and are most likely to have been acquired transplacentally, by ascending or intrapartum infection.
- Diagnosis is complicated by the lack of clear clinical features of infection and very poor localising features. The lack of an effective immune response in the neonate means that infection can spread, rapidly causing significant damage to organs.

If a baby needs antibiotic treatment it should be given as soon as possible and always within one hour of the decision to treat.[10]

Serious neonatal infections

These include:

- Sepsis:
    - In the early neonatal period, the most common organisms causing sepsis are *E. coli* and GBS. Later, coagulase-negative staphylococci (frequently meticillin-resistant) predominate.
    - Blind treatment is with a penicillin plus gentamicin or cefotaxime/cefuroxime. Vancomycin plus gentamicin is used in late-onset sepsis if meticillin-resistant *Staphylococcus aureus* (MRSA) is found or suspected.
- Meningitis:
    - Typical signs found in older children or adults are not present in a small infant. There may possibly be a bulging fontanelle but this is unreliable and features such as Kernig's sign and neck stiffness are of no value.
    - There may be depressed consciousness or convulsions.
    - If there is any doubt, a lumbar puncture should be performed, as failure to treat meningitis has such serious consequences.
    - The implicated organisms are totally different in the neonate from older patients. GBS and *E. coli* are responsible for around two thirds of cases.
- Pneumonia:
    - This may be acquired through aspiration of the micro-organisms during the delivery process.
    - Infection causes pulmonary changes with infiltration, and destruction of bronchopulmonary tissue. Fibrinous exudation into the alveoli leads to inhibition of pulmonary surfactant function and respiratory failure with a presentation very similar to respiratory distress syndrome (RDS).
    - Differentiating RDS from infection in a premature baby can be very difficult. Segmental or lobar atelectasis, seen on CXR, may occur in both.

- Urinary tract infection:
    - Symptoms are similar to the nonspecific ones of other serious acute infections.
    - Diagnosis is by examination of a urine sample, if necessary obtained by suprapubic bladder aspiration.
    - Treatment should start immediately in the ill child, purely on clinical suspicion.
    - Use IV cefotaxime or an aminoglycoside with careful monitoring of blood levels.
    - After successful treatment, the urinary tract should be checked for congenital abnormalities.

Clinical indicators of possible early-onset neonatal infection [10]

Red flags

- Respiratory distress starting more than four hours after birth.
- Seizures.
- The need for mechanical ventilation in a term baby.
- Signs of shock.

Other possible indicators

These include:

- Altered behaviour or responsiveness.
- Altered muscle tone - eg, floppiness.
- Feeding difficulties.
- Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension.
- Abnormal heart rate (bradycardia or tachycardia).
- Signs of respiratory distress.
- Hypoxia - eg, central cyanosis or reduced oxygen saturation level.

- Jaundice within 24 hours of birth.
- Apnoea.
- Signs of neonatal encephalopathy.
- The need for cardiopulmonary resuscitation.
- The need for mechanical ventilation in a preterm baby.
- Persistent fetal circulation (persistent pulmonary hypertension).
- Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors.
- Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation.
- Oliguria persisting beyond 24 hours after birth.
- Altered glucose homeostasis (hypoglycaemia or hyperglycaemia).
- Metabolic acidosis (base deficit of 10 mmol/L or greater).
- Local signs of infection - eg, affecting the skin or eye.

In those under 4 weeks old, temperature should be taken by an electronic thermometer in the axilla. A fever of 38°C or more in this age group indicates high risk of serious illness - see Further Reading, below.

Biomarkers, a low threshold for suspicion and risk scoring are used to identify sepsis as early as possible.[11] Inborn errors of metabolism or congenital abnormalities of the cardiovascular or respiratory systems may present in a similar manner to infection.

Investigations should include:

- FBC. White count is very nonspecific and platelets are often low in infection.
- Inflammatory biomarkers - eg, C-reactive protein, procalcitonin.
- Blood cultures.
- Urine culture.
- Ear, nose and throat swabs.

- Swabs from any obvious sites of infection.
- Lumbar puncture - should be used quite readily.
- CXR with respiratory signs.
- U&Es.
- Blood gases.

Serious neonatal infection has a bad prognostic implication for neurodevelopment and delay is common.[12] This is especially so if the infant is premature. The inflammatory mediators may have an important role in neurotoxicity. There may also have been hypoxia. Oxygen therapy has to be monitored very carefully in infants, especially if premature, as excessive oxygen can cause retrolental fibroplasia. Any baby that has received an aminoglycoside should have hearing assessed. See the separate Premature Babies and their Problems article.

Skin infections

Skin infections with S. *aureus* are common. Periumbilical skin infections present a special risk because of the possibility of bacteria passing up the umbilical vein, causing thrombophlebitis and even an hepatic abscess. Infection appears as:

- Pustules - singly or in multiples, without associated redness, almost anywhere on the skin. They can cause a problem in the axillae or groin but rarely spread. They should be treated with antiseptic powder to prevent cross infection.
- Bullous impetigo is less common but potentially far more serious. This presents as large pus-filled blisters that burst to form scabs. Where large areas of skin are involved, the condition is known as scalded skin syndrome. Treatment is with flucloxacillin, IV if necessary, and fluid replacement.
- Paronychia is infection of the nail fold and often involves more than one finger. It may produce pus. Treatment is with an anti-staphylococcal cream.
- Acute mastitis is strictly an infection of subcutaneous tissue, presenting with swelling, inflammation and fever. Treatment is with flucloxacillin and drainage of the abscess if needed.

MRSA is an increasing problem. These organisms may be transmitted perinatally from the mother's skin or genital tract or nosocomially, particularly among premature or sick infants, or acquired in the community after discharge from hospital.[13]

Conjunctivitis

See the separate Ophthalmia Neonatorum article.

Oral thrush

- *Candida albicans* is a common commensal but infection may affect the tongue and the rest of the mouth. It can spread to the gastrointestinal tract, causing diarrhoea and vomiting.
- It presents as a large number of firmly adherent, small, white plaques that may interfere with feeding by making the mouth sore.
- If the lesions are scraped with a tongue spatula, they will readily shift if they are only milk curds but thrush will be adherent.
- Treatment with a topical antifungal such as miconazole may be needed.[14]

Viral infections

HSV

See also the separate Encephalitis and Meningoencephalitis article.

- Neonatal HSV infection is rare but devastating. It is acquired from the mother during vaginal delivery and the virus initially mainly infects the eye, skin or mouth.
- Neonatal HSV infection most often presents with seizures, vesicular rash or critical illness.[15] Systemic infection may cause meningoencephalitis with jaundice and hepatosplenomegaly, and sometimes coagulopathy.
- Diagnosis is by viral culture and treatment is with IV aciclovir.
- Neonates with HSV infection acquired perinatally have a 65% mortality rate (untreated), reduced to 25% with treatment.

- Elective caesarean section can reduce the risk of infant exposure to infected secretions during birth and has become the standard of care for women with symptomatic lesions. However, most neonatal infections occur with asymptomatic mothers, who are subclinically shedding virus.
- Studies suggest that giving pregnant women with primary genital herpes infection or recurrences, aciclovir from 36 weeks of gestation prevents recurrence and reduces the risk of peripartum HSV shedding, thereby reducing the need for caesarean section.
- The best strategy for detecting pregnant women at risk of peripartum HSV shedding remains controversial and screening is not currently recommended.[16]

Varicella-zoster virus (VZV)

See also the separate Chickenpox article.

- Maternal infection in the perinatal period carries a risk of severe neonatal varicella, with a mortality rate of 30%. Approximately a quarter of neonates will develop clinical chickenpox if their mother develops chickenpox or shingles in the month before delivery.
- However, the highest risk of severe neonatal illness is where the mother develops infection from five days before delivery to two days afterwards.
- Babies of mothers developing perinatal chickenpox from a week before to a week after birth should receive varicella-zoster immune globulin (VZIG), as it prevents clinically apparent chickenpox in approximately half of neonates born to mothers with chickenpox around the time of delivery and reduces the severity where the disease is not prevented.[2] [17]
- If the baby has developed the varicella rash, VZIG is not helpful and treatment for neonatal chickenpox should be started with aciclovir.

Enteroviruses

- Echovirus infection often presents with gastroenteritis but can affect any system, with symptoms that range from slight illness to severe sepsis. Usually, no treatment is required.

- However, enterovirus infections in neonates can cause severe disease characterised by meningoencephalitis, myocarditis, pneumonitis, and/or hepatitis and coagulopathy.[18]

Tuberculosis (TB)

TB can be acquired from the mother very early in life and may present at around six weeks of life with unwillingness to feed, excessive weight loss, slight fever and hepatosplenomegaly.[19] CXR is required. Obtaining samples such as sputum is impractical in babies. Remember this possibility in those from high-risk groups. Treatment is with standard antituberculous drugs. If there has been TB in the family in the previous six months, BCG is given at 3 days - see the separate UK Immunisation Schedule article.

Further reading

- Viral rash in pregnancy; UK Health Security Agency.
- Population Screening Programmes (England); GOV.UK
- Screening Scotland
- Screening for Life; Public Health Wales
- Health Screening Programmes (Northern Ireland)
- Fever in under 5s: assessment and initial management; NICE Guidance (last updated November 2021)

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