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Title	Infections in pregnancy
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Infections in pregnancy

Summary

- Infections in pregnancy represent a challenging and often underappreciated area of concern for many specialists and general practitioners and can cause serious sequelae.
 - Antenatal status should be highlighted on pathology request forms, as this serves to alert the laboratory of the need to store serum for an extended period. Prior antenatal specimens can be forwarded to other laboratories to enable testing in parallel with the more recent sample.
 - Women with a confirmed, potentially vertically transmissible infection should be referred to a specialist with expertise in the management of perinatal infections.
 - Cytomegalovirus infection is the most common congenital infection. Women who care for young children are at greater risk of exposure to the virus. Preventive steps including hand hygiene and avoiding contact with children's urine, mucous and saliva are recommended for all pregnant women.
 - The incidence of parvovirus B19 infection in pregnancy is unknown. This infection is highly contagious and may result in fetal loss; particularly in the first half of pregnancy, pregnant women should avoid contact with adults or children who may have an infection.
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Infections in pregnancy represent a challenging and often underappreciated area of concern for many specialists and general practitioners and may cause serious sequelae. However, given that ambiguous laboratory findings without specific symptoms may lead to unnecessary anxiety, interpretation and judgement are required for appropriate investigation and management. This narrative review provides an update on a 2002 article highlighting infections that can affect the fetus or neonate;¹ viral hepatitis, human immunodeficiency virus (HIV) infection, tuberculosis and carriage of group B streptococcus have been reviewed elsewhere.²⁻¹⁰

Methods

We used PubMed to search original and review articles published between 1980 and 2018, as well as specialist society publications and guidelines, to formulate an evidence-based overview of the topics as applied to clinical practice.

Pre-pregnancy testing and counselling

Patients who seek pre-conception advice from a practitioner offer an opportunity to address preventive health topics (Box 1). In addition, online information is readily available from a number of sites.^{13,14}

If possible, the assessment of varicella and rubella immune status and vaccination of non-immune women should occur before conception (Box 2). As both rubella and varicella are live vaccines, pregnancy should be avoided for 4 weeks after these immunisations.¹⁸ Women who are found to be non-immune at antenatal screening should be offered vaccination post partum.

Influenza vaccination is recommended and free for all pregnant women regardless of gestation, for women planning pregnancy and for those who are breastfeeding; pertussis vaccination is recommended between 28 and 32 weeks gestation.^{18,19} Vaccination confers ongoing protection to the baby for up to 6 months after birth.

Routine antenatal screening

Routine screening should occur as early as possible and include the tests outlined in Box 2 — the clinical practice guidelines were updated in 2018.²⁰ Additional testing should be carefully considered, acknowledging the risk and ramifications of false positive results in pregnancy.²¹ Antenatal screening should be highlighted as such on request forms so that laboratories can identify samples that should be stored for a year from receipt.

Management of infection in pregnant women

Possible or confirmed exposure

Prompt assessment of possible exposure is key. Once the woman's susceptibility is determined, the nature of the exposure can be assessed and diagnosis confirmed in the contact. Assessment for infection may continue for many weeks and should be done in consultation with laboratories and specialists. In all cases, the possibility of false positive or false negative test results should be discussed.

Presentation with symptoms and proven infection

Infections in pregnancy usually present in the same way as in the non-pregnant patient. An assessment of clinical symptoms and potential exposures in the context of a full medical history is followed by targeted diagnostic tests and screening for potential complications. Box 3 summarises the differential diagnoses and suggested investigations for clinical presentations.

The best serological evidence of recent primary infection is an IgG seroconversion (ie, a change from a negative to a positive IgG), which may be demonstrated in acute and convalescent sera over 2–3 weeks.¹ A significant increase in IgG level between the two serum specimens tested in parallel by the same laboratory also suggests recent infection. Prior antenatal specimens can be forwarded to other laboratories to enable testing in parallel with the more recent sample. Although IgM may be due to recent infection, non-specific, false positive or persisting IgM levels occur.¹ Microbiologists at the testing laboratory can assist in guiding and interpreting serology (online Supporting information, case study 1).

Fetal effects depend on the type of infection and the timing of infection in gestation.^{1,2} Women with a confirmed, potentially vertically transmissible infection should be referred to a specialist with expertise in the management of perinatal infections. Expert counselling and workup are essential before decisions about termination of pregnancy or administration of drugs for fetal benefit.¹ In pregnancies complicated by possible congenital infection, neonates may need prompt paediatric review for time-critical investigation and treatment.

Cytomegalovirus infection

Cytomegalovirus (CMV) infection is the most common intrauterine infection causing fetal and neonatal complications^{22,23} (Box 4). Congenital CMV affects nearly 1% of live births, and 40–50% of Australian women are at risk of primary CMV infection in pregnancy.²² Congenital infection can occur from primary infection or, less commonly, re-infection by different CMV strains or re-activation of dormant CMV.^{22,23} Further data are needed to evaluate hyperimmune gamma globulin and antivirals, and as vaccination remains on the horizon, there is no therapeutic intervention of proven benefit for pregnant women with CMV and routine screening is not recommended.²³

Maternal infection is typically asymptomatic but may cause a mild influenza-like illness and a hepatitis.⁴² CMV is present in the blood and shed in saliva, urine (notably that of young children), genital secretions and breast milk.^{1,2,21,43,44} Transplacental viral transmission occurs in 30–40% of primary infections and in 1–2% of non-primary infections.^{2,22,23} Fetal infection is more common in later gestation but is generally less severe.^{22,23}

Symptomatic infection occurs in 10–15% of infected neonates at birth,²² associated with growth restriction, chorioretinitis, sensorineural hearing loss, microcephaly, brain malformations, hepatosplenomegaly, hepatitis, jaundice and thrombocytopaenia.^{22,23,45} In this context, 40–60% of infected neonates develop long term complications, particularly hearing

impairment and neurodevelopmental difficulties.^{23,46} Even if symptom-free at birth, 10–15% of neonates develop long term complications, particularly delayed onset hearing impairment,⁴⁶ manifesting as late as adolescence (online Supporting information, case study 2) — congenital CMV is the cause of 10–20% of hearing impairment in 0–18-year-olds.^{46,47} Prompt assessment of neonates and consideration of therapy may improve outcomes.^{22,23,46}

Maternal IgG seroconversion is diagnostic of primary CMV infection and should be sought if this is suspected; IgM is present in primary infection, but can also be produced in non-primary infections and false positives are common.^{2,22,23,44} IgG avidity testing is an important diagnostic tool to detect primary infection as only low to moderate avidity IgG antibodies are produced in the first 12 weeks after primary infection.^{2,22,23,44} Maternal blood or urine polymerase chain reaction (PCR) does not correlate well with timing of infection or neonatal outcomes.⁴⁴ Amniotic fluid PCR for further investigation of maternal primary CMV or fetal abnormalities compatible with CMV on imaging is the gold standard for diagnosis of intrauterine infection and carries a low risk of miscarriage; the sensitivity is increased after 21 weeks gestation and 6 weeks after infection, though it may be done earlier for practical reasons.^{23,44} The input of a maternal fetal medicine unit should be sought early, and carefully considered counselling should be offered.^{2,23,43}

Toxoplasmosis

Toxoplasma gondii is a protozoan parasite that reproduces in the intestine of cats and for which humans are an intermediary host.⁴⁸ Seroprevalence in Australian women of childbearing age is 20–30% and it is widely variable in women born overseas.^{49,50} Congenital toxoplasmosis is uncommon and affects around 0.017% of live births in Australia (Box 4).²⁹ Routine antenatal screening is not recommended in low prevalence countries, including Australia.^{28,51,52}

Maternal infection may go unnoticed or produce influenza-like symptoms.^{28,52} The risk of fetal infection increases from 5–15% in the first trimester to 70–80% in the third trimester, but infection in early pregnancy is associated with more severe pathology.^{26–28,30} Fetal infection may cause growth restriction, microcephaly, intracranial calcifications, hydrocephalus, hepatosplenomegaly and fetal death.^{51,53,54} Later complications include hearing loss, developmental delay, and up to a third of infected children will develop chorioretinitis that manifests as late as 12 years of age in more than half of children infected.^{26,51,53,54}

Toxoplasma IgM may be present for a year or more, and false positive results occur (specificity 88–100%).⁵² IgG avidity testing should be interpreted according to laboratory-specific cut-offs.⁵² Women with suspected or proven toxoplasmosis should have monthly monitoring with ultrasound or magnetic resonance imaging.²⁶ Maternal infection or abnormal imaging findings suggestive of toxoplasmosis may be further investigated with amniotic fluid PCR, which has most diagnostic utility more than 5 weeks after infection and is not affected by prior treatment.⁵⁵ Spiramycin may be offered to reduce materno–fetal transmission and does not cross the placenta.^{28,51,52} Treatment with pyrimethamine, sulfadiazine and folinic acid, by contrast, may be offered as treatment after 18 weeks gestation to reduce the risk of serious neurological sequelae.^{28,30,51,56} The placenta can be sent for histopathology and *Toxoplasma* PCR. Neonatal testing includes serology with IgM and IgA as well as PCR on blood, cerebrospinal fluid, and urine.^{27,30,52} Infants should have ongoing developmental and hearing surveillance as well as ophthalmology review for several years, as chorioretinitis may be progressive.²⁸

Rubella

While vaccination has reduced the incidence of congenital rubella syndrome (CRS), vaccination rates are low in parts of Australia and internationally — the most recent notified case of CRS in Australia was in 2015 (Box 4).⁵⁷ Up to 5% of pregnant women are non-immune, although the protective antibody level is debatable,³⁴ and CRS in the context of reinfection has been reported.^{1,58} The World Health Organization has recommended an IgG level above 10 IU/mL to indicate immunity. Australian immunisation guidelines recommend repeat vaccination if standard assays do not demonstrate evidence of current immunity, and this should be assessed pre-conception for each pregnancy.¹⁸

Infections are often mild and non-specific. After an incubation period of 14–23 days, a cephalocaudal rash occurs in 75% of

patients and lasts 2–7 days; small joint arthralgia often occurs in adult women.²¹ Investigation should occur if a pregnant woman is symptomatic or has had contact with a person with confirmed rubella, irrespective of a previously positive rubella IgG.^{1,2,21} Maternal first trimester infection is associated with fetal microphthalmia, eye abnormalities, and sensorineural deafness in 80–90% of cases and, as such, termination of pregnancy may be considered.^{2,21} Neither rubella-specific nor pooled human immunoglobulin is effective in reducing CRS.^{59,60} Infection after 16 weeks gestation is unlikely to result in CRS and pregnancy may be monitored.^{1,21}

Varicella

Varicella, or chickenpox, is highly contagious and has an incubation period of 10–21 days;⁶¹ the period of infectivity is from 2 days before the rash appears until all lesions have crusted over. Clinical findings strongly suggest the diagnosis and this is confirmed by PCR and/or immunofluorescence of fluid or a swab from a moist lesion. Serology is useful in establishing risk in the antepartum period and, if negative, immunisation should be offered post partum.

Fetal infection occurs in 10–15% of maternal chickenpox, is usually transient and, if symptomatic, most commonly manifests as shingles in the infant.¹ Chickenpox in the first half of pregnancy is complicated by fetal varicella syndrome in about 1% of pregnancies, characterised by microcephaly, convulsions, dermatomal skin scarring and ipsilateral limb hypoplasia.^{35,36,61}

Pregnant women are at risk of disseminated infection and varicella pneumonia.^{2,21} Women should be evaluated if they have had significant exposure to varicella, such as a household contact with active chickenpox or herpes zoster, or face to face contact.² If there is no or uncertain history of past chickenpox and varicella serology is negative or unavailable within 96 hours of exposure, varicella zoster immunoglobulin should be given.^{2,35} Zoster immunoglobulin is more effective the earlier it is received, and is not effective after rash onset.^{1,2} If reviewed more than 96 hours after exposure, prophylaxis with oral acyclovir may be considered to reduce the risk of varicella pneumonia in women with underlying lung disease, smokers or women who are immunocompromised or in the second half of pregnancy.² Should illness ensue, acyclovir can reduce the severity if started less than 24 hours after the onset of rash. Complicated infection requires treatment with intravenous therapy.² Complicated chickenpox is characterised by respiratory, haemorrhagic or neurological complications, as well as ongoing new lesions or persistent fever after 6 days.²

Herpes simplex virus infection

Latent herpes simplex virus (HSV) types 1 and 2 infections are common.^{32,33,37} Primary infection occurs in 2–3% of pregnancies, although over half are subclinical (Box 4).³² Fetal HSV infection accounts for less than 5% of neonatal cases, more likely less than 20 weeks gestation and associated with miscarriage and congenital anomalies.³³ The risk of neonatal infection is high (50%) in women with primary HSV infection within 6 weeks before delivery, but low (<3%) when active recurrent genital HSV infection is present at delivery.³⁷ Women can be unaware of a prior primary infection, and HSV serology in conjunction with a lesion swab and PCR can help characterise episodes.³³ Acyclovir can be offered for active genital herpes to reduce the duration and severity of symptoms and suppressive therapy in the third trimester to reduce the chance of active lesions and viral shedding at delivery. Caesarean delivery is recommended if primary infection has occurred in the 6 weeks before labour onset to reduce the risk of neonatal disease.³² Reactivation is not a contraindication to vaginal delivery.^{2,32} Neonatal follow-up is essential.

Parvovirus B19 infection

Parvovirus B19 epidemics have been reported to occur in 2-yearly cycles (associated with school-aged children) and, during epidemics, around 10% of pregnant women may experience acute infection.⁶² Exposure results in infection of 50% of susceptible household contacts,⁶² and about 40% of Australian women are parvovirus B19 non-immune (Box 4).^{2,38,62}

Parvovirus B19 infection can be asymptomatic and classically causes the common childhood illness known as erythema infectiosum or fifth disease.^{2,21,40,62} Diagnosis in children is dependent on phlebotomy and is likely to be under-recognised. An acute symmetric arthropathy affecting the hands, wrists and lower limbs is more common in adults, particularly women.^{2,21,40,62} Once rash or arthralgia are present, people infected are typically no longer contagious.

Transplacental infection occurs across the three trimesters, with greatest risk to the fetus earlier in the pregnancy.^{1,62} There is no intervention to prevent fetal infection. With proven maternal infection before 20 weeks of gestation, there is a 10% excess spontaneous pregnancy loss and a 3% chance of hydrops fetalis, for which monitoring should occur via a maternal fetal medicine unit.^{2,62} Fetal hydrops may be due to fetal anaemia or cardiomyopathy, mediated by P antigen expressed on fetal cardiomyocytes and erythrocytes.⁶³⁻⁶⁶ Assessment of the middle cerebral artery using Doppler ultrasound to determine peak systolic velocity and fetal blood sampling may be required to determine the need for fetal blood transfusion⁶⁷ (Box 5).

Zika virus infection

The World Health Organization⁶⁸ and the Centers for Disease Control and Prevention⁶⁹ provide current advice on countries affected by Zika virus and travel. A mosquito vector (*Aedes aegypti*) is present in Australia, although no transmissions have occurred. The sexual transmission of Zika virus has been reported,⁷⁰ and while after infection virus RNA is detectable in semen for up to 281 days, infectious viral shedding seems to be limited to the first few weeks.⁷¹ Zika virus infection symptoms include self-limiting low grade fever, lethargy, headache, maculopapular rash, arthralgia, myalgia and conjunctivitis.⁷² Congenital Zika virus syndrome includes microcephaly; ventriculomegaly; abnormalities of thalami, brainstem, corpus callosum, vermis and eyes; and severe arthrogryposis.⁷³ A meta-analysis of antenatal Zika virus infection found a 0–10% rate of microcephaly.⁷⁴ Significant neurodevelopmental problems can present after birth.⁷⁵ There is no antiviral therapy at present, and specialist input should be sought for suspected cases.

Diagnosis is based on Zika virus IgM, seroconversion, or a fourfold rise in titre of Zika virus IgG.^{76,77} Cross-reactivity of IgG (and less so IgM) to other flaviviruses, including Murray Valley encephalitis, Kunjin virus and others, which are endemic in Australia,⁷⁸ is common and an important clinical history to include with laboratory requests. Providing details of dengue fever or vaccination for yellow fever or Japanese encephalitis, clinical symptoms and dates with respect to travel also assist when requesting serology.^{76,77} Sensitivity is imperfect and, thus, the advice to returned travellers wishing to become pregnant is to wait at least a month after return.⁷⁹ Positive test results should be sent to reference laboratories for confirmation. Zika virus may be detected by PCR early in the first week of infection in blood (sensitivity 80–100%) and in urine for up to a month (sensitivity 12–60%).^{70,76,77}

Syphilis

Syphilis is a treatable infection in pregnancy for which routine antenatal screening is recommended.^{2,3,80} Congenital syphilis can be prevented with penicillin treatment during pregnancy, reducing rates from around 5% to less than 0.6%.⁸¹ Neonates at risk of congenital syphilis (including those whose mothers have been treated during pregnancy) require urgent paediatric assessment and treatment.⁴ A syphilis outbreak predominantly affecting Indigenous young people in rural and remote areas of northern Australia has continued since 2011, with five neonatal deaths attributed to congenital syphilis (Box 4).⁸² New diagnoses of HIV, hepatitis B, hepatitis C, gonorrhoea and chlamydial infection are also more prevalent among Indigenous people.⁸³

Listeriosis

Pregnant women have an increased risk of listeriosis and should receive preventive advice (Box 1).⁸⁴⁻⁸⁶ Listeriosis can be associated with fetal death (particularly if infection occurs before the third trimester), premature delivery, and neonatal infection.^{85,87} Four cases of congenital listeriosis, one of which was linked to contaminated rockmelon as well as one fetal

loss, were reported in New South Wales in 2017.⁸⁸ Maternal infection may present with fever, influenza-like and gastrointestinal symptoms. Evaluation should include a recent dietary history and at least two sets of blood cultures, as a single set has a sensitivity of 50–60%.⁸⁷ Further guidance may be found in the regularly updated guidelines of the Australasian Society for Infectious Diseases.² Treatment is with intravenous ampicillin and gentamicin.^{2,85}

Conclusion

Routine and risk-based antenatal screening identifies some vertically transmissible infections that can be prevented or treated in pregnancy. Investigations that are not based on established screening recommendations or a defined plan of action may cause unnecessary anxiety and potentially harmful intervention. Prompt assessment and management can moderate adverse outcomes and reduce unnecessary intervention.

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[Insert Boxes]

[Box 1]

1 General advice to pregnant women to prevent infections*

Advice	Details	Reasoning
Protect from travel-related infections	Pre-travel consultation for any travel when planning pregnancy or pregnant	Prevention of infections, including Zika virus infection and toxoplasmosis
Wash hands with soap and water or alcoholic hand rub	Wash hands after: <ul style="list-style-type: none"> ■ using the toilet; ■ touching raw meat, raw eggs or unwashed fruit and vegetables; ■ preparing food and before eating; gardening or touching dirt or soil 	Prevention of toxoplasmosis, listeriosis, salmonellosis
Reduce contact with saliva and urine from babies and young children	<ul style="list-style-type: none"> ■ Kiss infants and young children on the cheek or head rather than on the lips ■ Wash hands after changing diapers 	Prevention of CMV
Avoid unpasteurised (raw) milk and derived foods	Do not eat (unless pasteurised) soft cheese (eg, feta, Brie, <i>queso fresco</i>)	Prevention of listeriosis
Avoid unwashed or pre-cut fruit and vegetables	<ul style="list-style-type: none"> ■ Eat freshly made salad ■ Do not eat sprouts 	Prevention of listeriosis
Do not touch or change dirty cat litter	If necessary to change cat litter, wear gloves and wash hands afterwards	Prevention of toxoplasmosis
Practice safe sex	<ul style="list-style-type: none"> ■ Protect yourself from STIs ■ Get tested for STIs if indicated 	Treatment and prevention of vertical STI transmission
Talk to your health care provider about vaccinations	Some vaccinations are recommended before pregnancy and some during pregnancy	Live vaccines before pregnancy; whooping cough and influenza during pregnancy
Avoid people who have an infection	Avoid contact with people who are symptomatic	Prevention of rubella, chickenpox, parvovirus B19 infection

CMV = cytomegalovirus; STI = sexually transmissible infection. * Adapted from the Centers for Disease Control and Prevention¹¹ and NSW Food Authority.¹²

[Box 2]

2 Recommended routine antenatal screening for infections in Australia

Test	Reasoning	Action/amplifying comments
Rubella IgG status	Antibody titre can decline after immunisation	If non-immune, give MMR vaccine ideally before pregnancy or wait until post partum*
Hepatitis B serology	Surface antigen to detect chronic carriers	Chronic carriers of hepatitis B virus should have an assessment of their liver function and viral load (ie, HBV DNA level and HBeAg status) performed, and be referred for specialist support. If positive, administer hepatitis B immunoglobulin to infant at birth in addition to vaccine
Hepatitis C serology†	Interventions that increase the risk of transmission to the baby can be avoided, including fetal scalp blood sampling, internal electronic fetal scalp electrode Curative treatment can be offered post partum for chronically infected women identified by screening	Hepatitis C positive women should have an assessment of liver function and viral load (ie, HCV RNA PCR). Specialist support and post partum follow-up and treatment are recommended
HIV serology (Ab and Ag)	Testing should be offered to all women regardless of risk factors	HIV positive women are recommended to receive specialist support; antiretroviral therapy for the mother significantly reduces vertical transmission
Syphilis serology	Women at high risk should also be tested in the third trimester and at delivery in addition to initial assessment in pregnancy	If positive on TPHA or TPPA, seek specialist support and treat with appropriate penicillin course. A postnatal paediatric review may be indicated
Varicella IgG‡	Check varicella antibodies, ideally when planning pregnancy, when there is no definite history of chickenpox	If non-immune, give varicella vaccine before pregnancy (delaying conception one month after vaccination) or post partum if already pregnant. Vaccination is contraindicated in pregnancy*
MCS urine	Anatomical changes increase the risk of urinary tract infection and pregnancy complications	Current guidelines suggest treating asymptomatic bacteriuria during pregnancy due to an increased risk of pyelonephritis and pre-term labour
HPV	Cervical screening (HPV DNA testing) is recommended at the first antenatal visit for any woman whose regular screening, according to cervical screening guidelines, would fall during the pregnancy	There is no evidence to suggest that cervical screening in pregnancy is harmful (a Cytobrush [CooperSurgical] should not be inserted into the cervix). If positive, referral for colposcopic examination should be made
Chlamydial infection, gonorrhoea,	Transmission to neonate and maternal complications (eg, pelvic inflammatory	Investigate high risk and symptomatic women

Ab = antibody; Ag = antigen; HBeAg = hepatitis B e antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HPV = human papilloma virus; MCS = microscopy, culture and sensitivities; MMR = measles, mumps, rubella; PCR = polymerase chain reaction; TPHA = *Treponema pallidum* haemagglutination assay; TPPA = *Treponema pallidum* particle agglutination. * There is no evidence that inadvertent administration of live vaccines during pregnancy adversely affects the fetus and is therefore not an indication for termination. † With new, effective HCV treatments, known chronic carriers should be offered treatment before conception. ‡ Varicella testing is not mentioned in the recently published *Pregnancy care guidelines*,¹⁵ although it remains in the recent Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) guidelines.¹⁶ NB: Routine screening for group B streptococcus at 35–37 weeks gestation with combination low vaginal with or without anorectal swab or a clinical risk factor-based approach are both acceptable strategies dependent on local health jurisdiction practices. Table adapted from the Department of Health¹⁷ and RANZCOG.¹⁶

[Box 3]

3 Differential diagnosis and investigation of a symptomatic infective illness during pregnancy*

Presentation	Possible diagnoses	Tests
Influenza or glandular fever-like illness (lethargy, fever, malaise, myalgia, with or without headache, with or without lymphadenopathy)	<ul style="list-style-type: none"> Primary CMV infection (can cause hepatitis and lymphocytosis) Primary toxoplasmosis (lymphadenopathy often prominent) Listeriosis (often associated with diarrhoea) Influenza and other viral infections 	<ul style="list-style-type: none"> IgG and IgM (paired sera and avidity if indicated) IgG and IgM (paired sera and avidity if indicated) Blood culture (faecal culture for <i>Listeria</i> requires special or non-routine selective media and the significance of faecal excretion in perinatal infection is uncertain) Respiratory viral swab, serology if appropriate
Maculopapular rash with or without fever, with or without arthritis or arthralgia	<ul style="list-style-type: none"> Rubella Parvovirus B19 infection Enterovirus infection 	<ul style="list-style-type: none"> IgG and IgM (paired sera) IgG and IgM (paired sera) Throat or rectal swab for PCR
Vesicular rash	<ul style="list-style-type: none"> Varicella Hand, foot and mouth disease (enterovirus, usually coxsackie virus) 	<ul style="list-style-type: none"> Characteristic rash allowing for a clinical diagnosis, but if in doubt, serology (IgG/IgM, paired sera) and/or vesicular fluid swab for PCR Throat and rectal swab for PCR
Genitourinary symptoms (frequency, dysuria, genital ulcer, vaginal discharge)	<ul style="list-style-type: none"> Urinary tract infection Chlamydial infection, gonorrhoea, trichomoniasis, bacterial vaginosis (may all be asymptomatic) Genital herpes Primary syphilis (chancre) 	<ul style="list-style-type: none"> Urine microscopy and culture First pass urine or vaginal swab (can be self-collected) for chlamydia and gonorrhoea PCR. Vaginal swab for gram stain, microscopy and culture for trichomoniasis and bacterial vaginosis. PCR also available for trichomoniasis Swab ulcer for herpes simplex virus PCR Syphilis serology interpreted in the context of clinical history. Ulcer swab for syphilis PCR
Intrapartum fever or fever in the setting of ruptured membranes or pre-term labour	<ul style="list-style-type: none"> Chorioamnionitis Urinary tract infection Obstructed labour 	<ul style="list-style-type: none"> High vaginal swab for gram stain, microscopy and culture Blood culture Urine microscopy and culture Clinical assessment

CMV = cytomegalovirus; PCR = polymerase chain reaction. * Adapted from Gilbert.¹

[Box 4]

4 Incidence of congenital infection

Infection	Incidence
Syphilis ^{24,25}	<ul style="list-style-type: none">▪ 23 cases of congenital syphilis per 100 000 live births in Aboriginal and Torres Strait Islander populations in outbreak areas in northern Australia▪ Syphilis notification rates in the general population are 0.4–0.64 per 100 000 non-Indigenous women, and 19–35 per 100 000 Indigenous women (2005–2009)
Cytomegalovirus (CMV) infection ^{2,22}	<ul style="list-style-type: none">▪ 3.85 cases of congenital CMV infection per 100 000 live births in Australia▪ Maternal infection occurs in approximately 1% of pregnancies▪ 40–50% of maternal infections are primary and associated with increased risk of transmission to the fetus▪ Overall, 10–15% of infections are symptomatic in the fetus or child
Toxoplasmosis ^{26–30}	<ul style="list-style-type: none">▪ 1.7 cases of congenital toxoplasmosis per 100 000 live births in Australia▪ Fetal infection occurs in 5–15% of pregnancies in the first trimester and 70–80% in the third trimester
Herpes simplex virus (HSV) infection ^{2,31–33}	<ul style="list-style-type: none">▪ Rare — 186 cases of neonatal HSV infection reported between 1993 and 2016▪ Fetal transmission accounts for < 5% of infections▪ Primary infection occurs in 2–3% of pregnancies (half subclinical)▪ Intrapartum transmission to the neonate occurs in 50% of primary infections and < 3% of recurrent episodes of genital HSV infection
Rubella ^{31,34}	<ul style="list-style-type: none">▪ Rare — 59 cases of congenital rubella reported in Australia between 1993 and 2016▪ Up to 5% of pregnant women are non-immune▪ Fetal infection occurs in 80–90% of first trimester infections
Varicella ^{31,35–37}	<ul style="list-style-type: none">▪ Rare — 27 cases of neonatal varicella and two cases of congenital varicella reported in Australia between 1993 and 2016▪ Fetal infection occurs in about 1% of cases of maternal varicella in the first half of pregnancy
Listeriosis ²	<ul style="list-style-type: none">▪ Rare — 0.3 cases per 100 000 general population
Parvovirus B19 infection ^{2,38–40}	<ul style="list-style-type: none">▪ Incidence in pregnancy in Australia is unclear▪ Approximately 40% of pregnant women are non-immune and 50% of exposures lead to infection in susceptible individuals▪ One-third of maternal infections are transmitted to the fetus, and 5–10% of acute infection in pregnancy results in fetal loss
Zika virus infection ^{31,41}	<ul style="list-style-type: none">▪ No known cases of congenital Zika virus infection have been identified in Australia to date▪ In endemic areas, the rate of fetal transmission in infected women is approximately 10% and 1.7% of fetuses demonstrated microcephaly

[Box 5; kei_mja18.00676_gr]

5 Approach to parvovirus B19 infection

[Box 5 foot]

MCA PSV = middle cerebral artery peak systolic velocity. * IgM is detectable within 1–3 weeks of exposure and usually persists for 2–3 months.

† MCA PSV can be reliably used to assess fetal anaemia from 16 to 34 weeks gestation.

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