

Pregnancy

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PREGNANCY

This chapter will highlight aspects of STI management particular to pregnancy, but details for each condition should be reviewed elsewhere in these guidelines.

A lower threshold of screening for sexually transmitted infections (STIs) should exist in pregnancy, as there are significant potential complications for both the pregnancy outcome (gestational age at delivery and type of delivery) and the health of the newborn, due to the risk of vertical transmission.

As such, the following recommendations are presented.

- At the first prenatal visit, all pregnant women should be:
 - Offered HIV counselling and testing.
 - Screened for hepatitis B surface antigen (HBsAg).
 - Screened for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.
 - Screened for syphilis.
- All pregnant women should be evaluated for STI risk factors prior to and during pregnancy. Risk factors are described in the *Primary Care and Sexually Transmitted Infections* chapter. Any woman with ongoing risk factors for STI acquisition during pregnancy should be considered for rescreening each trimester.
- If an STI is diagnosed in pregnancy, treatment specific to the disease should be initiated, taking the pregnancy into consideration (see below).
- Due to the potential for decreased efficacy of treatments in pregnancy, follow-up after treatment of STIs for both the patient and her sexual partner(s) is important to ensure therapeutic success.

Antimicrobial Therapy in Pregnancy

- Special attention is required to safely treat STIs in pregnancy.
- **Always consult with an experienced colleague if you are unclear about a medication risk in pregnancy.** Data or risks associated with antimicrobials are beyond the scope of this document. The Motherisk Clinic at the Hospital for Sick Children in Toronto is an excellent resource and can be accessed at www.motherisk.org or by calling (416) 813-6780.

- **The following is an incomplete list of drugs that are relatively or absolutely contraindicated in pregnancy:**

- Erythromycin estolate
- Sulfamethoxazole
- Fluoroquinolones
- Podophyllin/podophyllotoxin/5-fluoro-uracil/imiquimod (not licensed for use in pregnancy)
- Doxycycline/tetracycline/minocycline
- Gamma benzene hexachloride/lindane
- Interferons
- Ribavirin



Specific Issues Related to Obstetric and Gynecologic Circumstances

STI and pregnancy termination

Women presenting for surgical or medical termination of pregnancy should ideally be screened for STIs prior to termination. When feasible, screening for chlamydia and gonorrhoea and subsequent treatment are appropriate pre-procedure.



When screening is not feasible, prophylaxis pre-procedure with single-dose **azithromycin** (1 g PO [A-I]) or **doxycycline** 100 mg PO bid x 7 days for *C. trachomatis* coverage is recommended.¹

Although bacterial vaginosis (BV) is thought to contribute to postoperative infection, a recent randomized clinical trial of treatment with metronidazole prior to surgery in documented cases of BV did not improve outcome.² Further study is required in this area.

Artificial insemination and STI risk

STI risk with donor insemination is reduced with current Canadian practices of serologic screening for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis. It is recommended that donor semen be stored until repeat donor serology at 6 months is negative for HIV. Initial and repeat screening of donor semen should include *N. gonorrhoeae* and *C. trachomatis* testing.³ Antibiotic use at the time of embryo transfer to reduce iatrogenic pelvic inflammatory disease from *C. trachomatis* has not been studied in a controlled fashion.⁴ However, a recent survey in the U.K. indicates that *C. trachomatis* prophylaxis is used in half of embryo transfers in that country.⁵

Chlamydial Infections

There are variable reports in the literature, but no consistent association exists between poor pregnancy outcome (i.e., preterm birth or preterm prolonged rupture of membranes) and *C. trachomatis* cervicitis.⁶ Vertical transmission occurs in 50% of infants born vaginally to infected mothers. Vertical transmission can occur with cesarean section where membranes are intact. Of those neonates who acquire infection, at least 20% develop conjunctivitis, and 20% develop pneumonia.^{7,8} Although provincial guidelines may vary, general national recommendations are to screen for *C. trachomatis* early in pregnancy. Repeat screening should be performed in the third trimester for women at continuing risk for STI acquisition. (See *Chlamydial Infections* chapter for a full discussion of *C. trachomatis* diagnosis and management.)

Treatment

Table 1. Treatment for *C. trachomatis* during pregnancy

- **Amoxicillin** 500 mg PO tid for 7 days [A-I]
OR
- **Erythromycin** base 500 mg PO qid for 7 days [A-I]
OR
- **Azithromycin** 1 g PO in a single dose if poor compliance is expected [A-I]

Note:

Doxycycline and quinolones are contraindicated in pregnancy and in lactating women. Erythromycin estolate is contraindicated in pregnancy due to associated hepatotoxicity and cholestatic hepatitis. Amoxicillin and erythromycin are effective; however, compliance with erythromycin may be difficult due to gastrointestinal side effects.⁹ Azithromycin appears to be safe and effective.¹⁰⁻¹²

Sexual partners should be treated and undergo follow-up testing to ensure cure. Condoms or abstinence are recommended during treatment and until follow-up tests are negative. Repeat polymerase chain reaction (PCR) chlamydial testing may be positive due to the presence of persistent DNA from killed organisms for up to 4 weeks after the completion of treatment.¹³ Repeat testing should therefore be by PCR, as it is most sensitive, at 3–4 weeks post-treatment, or by culture if time does not allow for a 3 week waiting period. All pregnant women should be retested following treatment to ensure cure.

Gonococcal Infections

Infection with *N. gonorrhoeae* in pregnancy is associated with endometritis, pelvic sepsis, ophthalmia neonatorum and systemic neonatal infection.¹⁴ Although gonococcal infection is relatively uncommon in many clinical practices, it is still suggested that all pregnant women be screened in early pregnancy due to the adverse consequences of an untreated infection.

Those infected should be treated with a recommended or alternate cephalosporin.¹⁵ Women with a penicillin allergy or those who cannot tolerate a cephalosporin should be administered a single 2 g dose of spectinomycin IM.¹⁶ A diagnosis of *N. gonorrhoeae* is strongly associated with co-infection of *C. trachomatis*.¹⁷ Treatment for both STIs is recommended when *N. gonorrhoeae* is diagnosed,¹⁸ unless testing for *C. trachomatis* is negative. In pregnant women, a test of cure is recommended. (See *Gonococcal Infections* chapter for a full discussion of *N. gonorrhoeae* diagnosis and management.)

Treatment

Table 2. Treatment for *N. gonorrhoeae* during pregnancy

Preferred	Alternative
<ul style="list-style-type: none">• Cefixime 400 mg PO in a single dose [A-I]	<ul style="list-style-type: none">• Ceftriaxone 125 mg IM in a single dose [A-I] OR <ul style="list-style-type: none">• Spectinomycin 2 g IM in a single dose (available only through SAP) [A-I]

SAP=Special Access Program

All sexual partners of patients who have *N. gonorrhoeae* infection should be evaluated and treated for both *N. gonorrhoeae* and *C. trachomatis* infections. Patients and contacts should abstain from unprotected intercourse until treatment of both partners is complete (i.e., after completion of a multiple-dose treatment or for 7 days after single-dose therapy). In pregnancy, a test of cure in both partners is recommended.

Syphilis

Infectious syphilis in pregnancy, defined as primary, secondary or early latent infection (typically the first year after infection), can lead to fetal infection with stillbirth, preterm birth, congenital abnormalities and active disease at delivery. Transmission occurs transplacentally (as early as 14 weeks and throughout pregnancy) or at the time of delivery. Untreated primary or secondary syphilis carries a transmission risk of up to 100%, while early latent infection has a 40% transmission risk.¹⁹ Treated syphilis has a transmission rate of 1.8%.²⁰ In a small Canadian study, 1 of 98 treated women had a child with congenital syphilis, whereas 4 of 9 women not treated in pregnancy had infants with congenital syphilis.²¹ Breastfeeding by mothers with primary or secondary lesions of syphilis carries a theoretical risk of transmission of syphilis to the baby.

Given the resurgence of syphilis in Canada, universal screening of all pregnant women continues to be important and remains the standard of care in most jurisdictions.

Screening should ideally be performed in the first trimester and repeated at 28-32 weeks and again at delivery in women at high risk of acquiring syphilis or in areas experiencing heterosexual outbreaks of syphilis.

If initial screening is done using non-treponemal tests (NTTs) such as VDRL or RPR in women considered to be at high-risk, a treponemal test should be added to initial testing.

The introduction of treponemal tests for IgG/IgM antibodies, such as the treponemal enzyme immunoassay (EIA), may provide a more sensitive screening test for syphilis. Although EIA is highly sensitive, the test can lack specificity therefore if the treponemal-specific ELISA is positive, confirmation by a second treponemal-specific test is required (e.g. FTA-ABS, MHA-TP or TP-PA).

Where initial screening is done using NTT only and serology is positive, treponemal-specific testing is required to confirm the diagnosis (e.g. FTA-ABS, MHA-TP or TP-PA).

Biological false-positive results are possible with non-treponemal and treponemal tests in pregnancy, but they are more common with non-treponemal results.

Any woman delivering a stillborn infant at ≥ 20 weeks gestation should be screened for syphilis. For details on specific tests, see *Syphilis* chapter.

Diagnostic considerations

Pregnant women with confirmed syphilis should be considered infected unless an adequate treatment history is documented and sequential serologic antibody titers have declined. In some cases, titers will not decline to undetectable levels even after successful treatment and may remain positive at low levels, such as 1:1 or 1:2, indefinitely.

Treatment

Penicillin is effective for preventing maternal transmission to the fetus and for treating fetal infection. Treatment during pregnancy should consist of the penicillin regimen appropriate for the presenting stage. Penicillin alternatives have not been proven effective for the treatment of syphilis during pregnancy. Pregnant women who have a history of significant penicillin allergy should be desensitized and then treated with penicillin.

Table 3. Treatment for syphilis during pregnancy

Stage	Preferred treatment ^ψ	Alternative treatment for penicillin-allergic patients
<ul style="list-style-type: none"> • Primary • Secondary • Early latent (<1 year duration) 	<p>Benzathine penicillin G 2.4 million units IM weekly for 1-2 doses ^{ψ‡*20} <i>[B-II (single dose); C-III (2 doses)]</i> (available only through SAP)</p>	<p>There is no satisfactory alternative to penicillin for the treatment of syphilis in pregnancy; insufficient data exist to recommend ceftriaxone in pregnancy</p> <p>Strongly consider penicillin desensitization followed by treatment with penicillin <i>[A-III]</i></p>
<ul style="list-style-type: none"> • Late latent syphilis • Latent syphilis of unknown duration 	<p>Benzathine penicillin G 2.4 million units IM weekly for 3 doses²²<i>[B-II]</i> (available only through SAP)</p>	<p>There is no satisfactory alternative to penicillin for the treatment of syphilis in pregnancy; insufficient data exist to recommend ceftriaxone in pregnancy</p> <p>Strongly consider penicillin desensitization followed by treatment with penicillin <i>[A-III]</i></p>

SAP=Special Access Program

^ψ Reports from some jurisdictions have indicated inappropriate use of short-acting benzylpenicillin (Penicillin G) (IM) for the treatment of infectious syphilis rather than long-acting Benzathine penicillin G (Bicillin-LA). Practitioners, pharmacists and purchasing agents should be aware of the similar names of these two products to prevent and avoid inappropriate and inadequate treatment. Long-acting benzathine penicillin achieves detectable serum levels of penicillin for 2-4 weeks in non-pregnant adults and is required to adequately treat infectious syphilis; short acting penicillin agents are not adequate for achieving cure.²³

* Some experts recommend 3 weekly doses (total of 7.2 million units) of benzathine penicillin G in HIV-infected individuals.

‡ Given the complexity of accurately staging early syphilis, some experts recommend that primary, secondary and early latent cases in pregnancy be treated with two doses of benzathine penicillin G 2.4 million units 1 week apart; the efficacy of this regimen in preventing fetal syphilis is not known.²⁴

In the second half of pregnancy, management and counselling may be facilitated by a sonographic fetal evaluation for congenital syphilis, but this should not delay therapy.

Sonographic signs of fetal syphilis (i.e., hepatomegaly, ascites and hydrops) indicate a greater risk for fetal treatment failure; such cases should be managed in consultation with obstetric specialists.²⁵

Women treated for syphilis during the second half of pregnancy are at risk for premature labour and/or fetal distress if the treatment precipitates the Jarisch-Herxheimer reaction; this includes fever, uterine irritability and contractions. It is estimated to occur in 40% of patients with primary or secondary syphilis, begins on average within 10 hours of treatment and resolves within 24 hours.²⁶ These women should be advised to seek obstetric attention after treatment if they notice any contractions or decrease in fetal movements. Some centers admit and conduct fetal monitoring at the time of treatment. Although stillbirth is a rare complication of treatment, concern about this complication should not delay necessary treatment.

All patients who have syphilis should be offered testing for HIV infection. In the case of suspected congenital syphilis, consult a colleague with experience in this area.

Women who are treated for syphilis during pregnancy and babies born to women who were treated for syphilis during pregnancy require close monitoring of serologic tests and other follow-up. Refer to the syphilis chapter for recommendations on follow-up and monitoring as well as indications for treatment of infants born to mothers treated for syphilis during pregnancy.

Trichomoniasis

Vaginal trichomoniasis has been associated with adverse pregnancy outcomes, particularly premature rupture of the membranes, preterm delivery and low birthweight. However, data have not indicated that treating asymptomatic trichomoniasis during pregnancy lessens the risk of adverse pregnancy outcomes. In fact, treatment of asymptomatic trichomoniasis with metronidazole 2 g x 2 doses has been shown to increase preterm birth in a placebo-controlled trial.²⁷ For this reason, screening of all pregnant women cannot be recommended. Women who are symptomatic with trichomoniasis, however, should be treated to ameliorate symptoms and minimize the risk of sexual transmission as described below.^{28–30} Women may be treated with 2 g of metronidazole orally in a single dose. Marginally better cure rates have been found with 7 day treatment (as per treatment recommendations, below).³⁰ Multiple studies and meta-analyses have not demonstrated a consistent association between metronidazole use during pregnancy and adverse fetal effects — it is therefore considered safe in pregnancy.^{31–33}

Diagnostic considerations

Diagnosis of vaginal trichomoniasis is usually performed by microscopy of vaginal secretions (wet mount), but this method has a sensitivity of only about 60–70%.

Microscopy and culture performed rapidly from time of sample collection is the most sensitive available method of diagnosis.

Treatment

Table 4. Treatment for trichomoniasis during pregnancy

Preferred	Alternative
Metronidazole 2 g PO in a single dose [A-I]	Metronidazole 500 mg PO bid for 7 days [A-I]

Topical therapy is ineffective for cure compared to oral metronidazole (<50% with intravaginal treatment³⁴). Treatment of sexual partner(s) is essential for cure.

Abstinence during treatment is recommended to avoid reinfection. Retesting in pregnancy is necessary only for those who remain symptomatic after treatment.

Bacterial Vaginosis

Bacterial vaginosis in pregnancy has been associated with adverse outcomes, including premature rupture of membranes, preterm labour, preterm birth and postpartum endometritis. There is evidence to support screening and treatment at 12–16 weeks in high-risk pregnancies (i.e., previous preterm labour/delivery or preterm premature rupture of membranes). If the patient is symptomatic or at high risk, test for BV and treat as below. Treatment of BV in such cases may reduce the risk of prematurity, low birthweight and preterm premature rupture of membranes.^{35–38} In low-risk and asymptomatic women, screening is not recommended, as it has not been shown to affect adverse outcomes in well-designed randomized, controlled trials.^{35,36} If symptoms suggest BV, testing is appropriate, and positive results warrant treatment for symptom resolution.

Treatment

Table 5. Treatment for bacterial vaginosis during pregnancy

Preferred	Alternative
Metronidazole 500 mg PO bid for 7 days [A-I]	Clindamycin 300 mg PO bid for 7 days [A-I]

Systemic rather than topical treatment is recommended in pregnancy, as vaginal treatment has not been shown to decrease the risk of adverse pregnancy outcomes.

Also, clindamycin topical treatment has been associated with adverse outcomes in the newborn when used in pregnancy.^{40–42}

Based on multiple studies, most recently assessed by meta-analysis, the evidence supports the safety and lack of teratogenicity of systemic metronidazole use in pregnancy.^{31–33} Rescreening and re-treating may be advisable in women with high-risk pregnancies (i.e., previous preterm labour, delivery or preterm premature rupture of membranes).

It is important to note that clindamycin has been associated with increased risk of pseudomembranous colitis and should be used only when alternatives are not possible.

Vulvovaginal Candidiasis

Vulvovaginal candidiasis is a common occurrence in pregnancy. Management depends on the degree of symptomatology. Often *Candida* is difficult to eradicate in pregnancy, so the primary goal of therapy should be symptom control. To date, only topical “azole” treatments are recommended in pregnancy, and these should be monitored by a physician. Treatment for 7 days may be necessary in pregnancy to achieve resolution of symptoms.⁴³ Oral fluconazole is considered teratogenic in animal studies,⁴⁴ but in 226 cases of first-trimester exposure in humans there was no increased risk of complications.⁴⁵ There are reports, however, of women with chronic exposure in pregnancy who have had infants with skeletal malformation syndromes suggestive of fluconazole teratogenic effects.^{46,47} **Therefore, oral “azoles” are not recommended. The use of intravaginal boric acid is not recommended in pregnancy due to its teratogenic potential in animal studies.⁴⁸**

Treatment

Table 6. Treatment for vulvovaginal candidiasis during pregnancy

Butoconazole [A-I]	<ul style="list-style-type: none"> • 2% cream 5 g (butoconazole1-sustained release) in a single intravaginal application
Clotrimazole [A-I]	<ul style="list-style-type: none"> • 1% cream 5 g intravaginally per day for 7–14 days OR • 100 mg vaginal tablet, one tablet per day for 7 days OR • 100 mg vaginal tablet, two tablets per day for 3 days OR • 500 mg vaginal tablet, one tablet in a single application
Miconazole [A-I]	<ul style="list-style-type: none"> • 2% cream 5 g intravaginally per day for 7 days OR • 100 mg vaginal suppository, one suppository per day for 7 days OR • 200 mg vaginal suppository, one suppository per day for 3 days
Nystatin [A-I]	<ul style="list-style-type: none"> • 100,000 unit vaginal tablet, 1 tablet for 14 days
Terconazole [A-I]	<ul style="list-style-type: none"> • 0.4% cream 5 g intravaginally for 7 days OR • 0.8% cream 5 g intravaginally for 3 days OR • 80 mg vaginal suppository, one suppository per day for 3 days

Pubic Lice

Patients who have *P. pubis* (i.e., pubic lice) usually seek medical attention because of pruritus, lice or nits in their pubic hair. Pediculosis pubis is usually transmitted by sexual contact.⁴⁹ Treatment should be given in pregnancy as follows (see also *Ectoparasitic Infestations* chapter).

Treatment

Table 7. Treatment for pubic lice during pregnancy

- **Permethrin 1% cream rinse** applied to affected areas and washed off after 10 minutes [B-II]
- OR
- **Pyrethrins with piperonyl butoxide** applied to the affected area and washed off after 10 minutes [B-II]

Note: Lindane is contraindicated in pregnancy.

Follow-up

Patients should be evaluated after 1 week if symptoms persist. Re-treatment may be necessary if lice or eggs are observed at the hair-skin junction. Patients who do not respond to one of the recommended regimens should be re-treated with an alternative regimen. However, pruritus alone in the absence of persistent organisms warrants symptomatic treatment only.

Sexual partners within the last month should be treated. Patients should avoid sexual contact with their sexual partner(s) until patients and partners have been treated and re-evaluated to rule out persistent disease.

Scabies

The predominant symptom of scabies is pruritus. Sensitization to *Sarcoptes scabiei* must occur before pruritus begins. The first time a person is infected with *S. scabiei*, sensitization takes up to several weeks to develop. However, pruritus may occur within 24 hours after a subsequent reinfestation. Scabies in adults often is sexually acquired, although scabies in children is usually not (see *Ectoparasitic Infestations* chapter for more information on transmission). Pruritus may persist for several days or weeks after treatment.^{49–51}

Treatment

Table 8. Treatment for scabies during pregnancy

- **Permethrin cream (5%)** applied to all affected areas of the body from the neck down and washed off after 8–14 hours [B-II]

Note: Lindane and ivermectin are contraindicated in pregnant and lactating women.

Both sexual and close personal or household contacts within the preceding month should be examined and treated. Re-treat if symptoms persist or recur.

Genital Herpes Simplex Virus Infection

Counselling on the signs and symptoms of herpes simplex virus (HSV), as well as risk reduction behaviours to avoid contracting genital herpes, is important for all women who present for pregnancy care. There is currently no evidence to investigate or treat pregnant women who have no history of genital herpes and whose partners also have no history. However, without past history, these women are at risk of acquiring primary infection in pregnancy. Primary infection in pregnancy is associated with significant vertical transmission rates.

Women without a history of HSV should receive risk-reduction behaviour counselling to avoid contracting HSV. Both HSV-1 and HSV-2 can cause genital lesions, be vertically transmitted and lead to neonatal disease. Diagnosis of genital herpes can be complicated due to the common phenomenon of asymptomatic or subclinical disease. Diagnosis requires a careful assessment of clinical features, culture or PCR of genital sites and type-specific serology. Neonatal HSV is associated with significant morbidity and mortality, causing cutaneous, central nervous system and disseminated disease, such as pneumonitis and encephalitis.

Primary infection

If the mother is seronegative, she is at risk of primary infection with HSV-1 or -2 in pregnancy. If this occurs during the second half of pregnancy, a vertical transmission rate of 30–50% exists.^{52,53} A significant proportion of neonatal herpes cases are born to mothers with no recognized history of genital herpes.^{54,55} At present, there is no evidence that routine serotesting in pregnancy will be successful at decreasing the risk of neonatal herpes.

However, if a known serosusceptible pregnant woman is known to have a partner with oral or genital herpes, it is prudent to advise abstinence from oral and/or genital sexual contact. In addition, non-pregnancy data would suggest that suppressive therapy in the male partner with genital herpes would decrease the risk of sexual transmission, but this should not replace abstinence or judicious condom use.⁵⁶

Treatment

Table 9. Treatment for genital HSV during pregnancy

- **Acyclovir** 200 mg PO five times per day for 5–10 days [A-I]⁵⁷

Primary infection in pregnancy warrants acyclovir treatment and consideration of cesarean section for delivery, especially if infection is in the late third trimester. Such measures reduce, but do not eliminate, the risk of vertical transmission.⁵⁸ See *Genital Herpes Simplex Virus Infections* chapter for more information on treatment.

Recurrent HSV infection

In a woman with prior infection, the risk of vertical transmission is 2–4%. For those who have had an outbreak within the previous year, prophylaxis at 36 weeks' gestation until delivery with **acyclovir** 200 mg PO qid OR **acyclovir** 400 mg PO tid OR **valacyclovir** 500 mg PO bid is recommended. [A-I].^{57, 59-61} Transmission can occur at the time of delivery, with or without lesions, due to asymptomatic shedding.

Treatment with acyclovir reduces the risk of lesions and the risk of asymptomatic viral shedding, thereby reducing the cesarean section rate.^{57,62} See *Genital Herpes Simplex Virus Infections* chapter for more information on suppressive therapy.

If genital lesions or prodromal symptoms are present at the time of delivery, cesarean section is recommended.⁶² In the event of ruptured membranes, cesarean section is thought to confer protection, ideally if performed within less than 4 hours.^{63,64}

Genital Warts and Genital Human Papillomavirus Infection

Vertical transmission of genital human papillomavirus (HPV) types 6 and 11 can cause recurrent respiratory papillomatosis (RRP) in infants and children. Symptomatic perinatal transmission is infrequent and is usually clinically apparent within 2 years. When it occurs, it is associated with anogenital and vocal-cord lesions in the newborn. Although maternal HPV prevalence is high, HPV vertical transmission is low, and RRP is rare.⁶⁵⁻⁶⁷ The value of cesarean section for reducing/preventing transmission is unknown. Cesarean section is not recommended for the sole purpose of reducing transmission of HPV to the newborn. If the pelvic outlet is obstructed by warts, or if the warts are significant in number as to cause a bleeding complication with vaginal delivery, cesarean section may be warranted.

Genital warts may proliferate, reappear and become friable in pregnancy. Women should be reassured that this growth usually regresses postpartum. In general, the practice is to defer treatment due to poor response to therapy in pregnancy. If treatment is desired, the following options are appropriate. Weekly treatment may be required.

Treatment

Table 10. Treatment for genital HPV during pregnancy

- TCA trichloroacetic acid (85%) [B-II]
- Cryotherapy (liquid nitrogen) [B-II]
- CO₂ laser [B-II]
- Surgical excision [B-II]

Note: Imiquimod, podophyllin, podofilox, podophyllotoxin, 5-fluoro-uracil and interferon are contraindicated in pregnancy.

Hepatitis A Virus Infection

Vertical transmission of hepatitis A virus is not described. An infected woman can infect her newborn through the usual fecal/oral routes of transmission. Immunization and/or gammaglobulin treatment in pregnancy is safe and may confer some protection for the newborn.⁶⁸

If a pregnant woman is infected, consider prophylaxis with vaccine and/or gammaglobulin for household contacts. Household contacts should consider receiving hepatitis A vaccine. **If a pregnant woman is a contact of an infected person, there is no contraindication to the use of gammaglobulin or hepatitis A vaccine in pregnancy [B-II].**

Hepatitis B Virus Infection

Mothers who are acutely infected with HBV, or are carriers, can transmit the virus to their infant. Transmission appears to occur at time of delivery, but not transplacentally. Depending on the stage of maternal infection, the vertical transmission risk of hepatitis B can be as high as 90% in the absence of intervention at the time of delivery.⁶⁹ Ninety-five percent of cases can be prevented with the use of hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine administered at birth to the neonate, followed by two additional vaccine doses at 1 and 6 months.⁷⁰ **The first dose of hepatitis B vaccine should be administered within 12 hours of birth and HBIG immediately after birth (efficacy decreases sharply after 48 hours).**⁷¹

If a woman is newly identified to be HBsAg-positive in pregnancy, she warrants further investigation. Consideration should be given to testing for HIV, hepatitis B e antigen, hepatitis B core antibody (anti-HBc IgM and IgG), HBV DNA, hepatitis A IgM and hepatitis C antibodies. If she is found to be positive for any of these, an evaluation of liver transaminases and function is warranted (see *Hepatitis B Virus Infections* chapter).

If the mother is infectious at time of delivery, document the diagnosis on prenatal forms and plan for administering HBIG and the first dose of hepatitis B vaccine to the neonate immediately after birth. The second and third dose of the vaccine should be given to the infant 1 and 6 months after the first dose. Special attention is required to complete the three-dose schedule, since long-term exposure is possible and there may be difficulty in reaching the family for the third dose. A follow-up hepatitis B surface antibody at 1–2 months after completion of HBV vaccine series to document adequate immune response is recommended (see *Hepatitis B Virus Infections* chapter and *Canadian Immunization Guide*⁷¹). Breastfeeding is safe if the neonate is treated.

If the mother is a contact of an infected person or is at risk of acquiring hepatitis B, there is no contraindication to HBIG or HBV vaccine in pregnancy [A-I].

Hepatitis C Virus Infection

Approximately 0.8% of the Canadian population is infected with hepatitis C.⁷² **Persons with hepatitis C should be referred to health care professionals with experience in the treatment of hepatitis C.** Pregnancy does not appear to have an effect on the progression of hepatitis C.

Hepatitis C in pregnancy may be associated with increased rates of cholestasis.⁷³

The risk of vertical transmission is estimated to be 7.9%.⁷⁴ It is not yet known if cesarean section reduces the vertical transmission of HCV, as it has not been adequately studied to date.⁷⁵

Breastfeeding is considered to be safe unless nipples are cracked or bleeding. Although HCV RNA has been identified in breast milk,⁷⁶ breastfeeding is still considered safe. Assessment of and education to reduce risk behaviour is important in pregnancy.

Current treatments available for HCV infection are contraindicated in pregnancy (i.e., interferon-alpha and ribavirin, combination therapies of pegylated interferon-alpha 2a and 2b plus ribavirin). Although not well studied, interferon-alpha does not appear to have an adverse affect on the human embryo or fetus, but it is associated with increased rates of preterm delivery and intrauterine growth restriction. Animal studies have shown an increased rate of fetal loss.⁷⁷ If interferon is to be used in pregnancy, the potential benefits of its use should clearly outweigh possible hazards.⁷⁸⁻⁸⁰ Because there are no large studies of ribavirin use during human pregnancy and ribavirin is highly teratogenic in animal studies, its use during pregnancy is absolutely contraindicated.⁸¹ Ribavirin has been given Pregnancy Category X by the U.S. Food and Drug Administration.



It is mandatory that women and/or their male partners who have received ribavirin as part of a combination treatment for HCV infection both use a highly effective method of birth control to prevent pregnancy during ribavirin therapy and for 6 months afterward.

Canadian guidelines for the management of hepatitis C in pregnancy are detailed elsewhere.⁷⁴

Human Immunodeficiency Virus Infection

All women should be offered HIV antibody testing with appropriate counselling and informed consent at their first prenatal visit. A diagnosis of HIV and pregnancy presents a need for complex care and requires consultation with experts in the area as soon as possible. Initiation of antiretroviral therapy in HIV-infected pregnant women is critical for the reduction of vertical transmission; this typically consists of combination antiretroviral therapy, also known as highly active antiretroviral therapy (HAART). Effective suppression of viral load in pregnancy prior to delivery, along with intrapartum and 6 weeks of neonatal antiretroviral therapy, reduces vertical transmission from 25% to less than 1%.⁸²

If the mother is found to be HIV-positive on confirmatory testing (see *Human Immunodeficiency Virus Infections* chapter), consultation should be made with a specialist in HIV pregnancy care. The best care and greatest chance for viral suppression is with early management. If the pregnancy is to be continued, HAART should be initiated either immediately or at 14–18 weeks' gestation, depending on CD4 counts and viral load. Women should be counselled regarding the potential side effects of antiretroviral therapy, the importance of strict compliance and need for close monitoring. At a minimum, monthly complete blood count, aspartate aminotransferase, alanine aminotransferase, amylase, bilirubin, creatinine, serum lactate, glucose, CD4 count and viral load are recommended. Specific guidelines are found elsewhere.⁸²

Specific antiretroviral drugs that are contraindicated in pregnancy include the following:

- Efavirenz
- Delavirdine
- Hydroxyurea
- Nevirapine (the initiation of continuous nevirapine in pregnancy is not currently recommended due to its potential toxicities: rash, severe hepatitis, Stevens-Johnson syndrome)

If a woman presents in pregnancy already taking nevirapine and tolerating it well, continuation may be considered. One-time maternal dosing of nevirapine used in the high-risk setting at the time of delivery is still appropriate.

Because of the complexity associated with the use of antiretroviral drugs in pregnancy, all HIV-positive pregnant women should be managed in cooperation with an HIV specialist.

If HIV viral load is undetectable at the time of delivery, vaginal delivery is usually recommended, unless cesarean section is required for obstetric reasons. With a viral load greater than 1,000 copies/mL, a cesarean section is usually recommended to reduce the risk of vertical transmission.^{83–87} Additionally, all infected women should receive IV zidovudine from the onset of labour until delivery or before a cesarean section is started. **Breastfeeding is contraindicated, as HIV can be transmitted through breast milk.**

Women who are diagnosed HIV-positive late in pregnancy or in labour are at very high risk for perinatal transmission of infection. Further management should be in cooperation with both adult and pediatric HIV specialists, who may recommend one or more of the following: intrapartum prophylaxis options with IV zidovudine, cesarean section, single-dose nevirapine to the woman in labour and single-dose nevirapine to the infant, and 6 weeks of oral antiretroviral therapy to the infant.⁸²

Note that these guidelines are under constant revision, and each case should be managed with an expert in the area. For more detailed information, please see the Canadian guidelines for management of HIV-affected pregnancy, labour and delivery, and postpartum period.⁸²