Human Immunodeficiency Virus Infections

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HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS

Etiology[1,2]

- The human immunodeficiency virus (HIV) has been shown to be the causative agent of acquired immunodeficiency syndrome (AIDS).
- Infection with HIV results in the progressive destruction of CD4+ T lymphocytes. These cells are crucial to the normal function of the human immune system.
- Persons with HIV infection and subsequent immune suppression are, therefore, at risk of developing a variety of clinical AIDS-defining conditions, including opportunistic infections (e.g., *Pneumocystis jiroveci* [formerly *Pneumocystis carinii*] pneumonia, disseminated *Mycobacterium avium* complex [MAC] disease), primary neurologic disease (e.g., AIDS dementia) and malignancy (e.g., lymphoma, Kaposi sarcoma) (see *Table 3* for AIDS-defining conditions).

Epidemiology[3,4]

- The HIV/AIDS epidemic is a complex one, with differing rates of infection in specific at-risk populations. The number of Canadians living with HIV infection continues to increase. There has been a 20% rise in the number of positive HIV test reports in Canada in the last 5 years (2000–2004).
- In 2004, men who have sex with men (MSM) still represented the largest number and proportion of positive HIV test reports; however, the heterosexual exposure category represents a growing number and proportion of positive HIV tests, surpassing injection drug use (IDU) as the second largest exposure category.
- Persons migrating to Canada from countries where HIV is endemic also represent an increasing proportion of the positive HIV test reports in the last 3 years. These reports are included in the heterosexual exposure category.
- Women represent an increasing proportion of those with positive HIV test reports, as well as reported AIDS cases in Canada. Over 25% of the positive HIV test reports in 2004 were in women, compared to less than 10% prior to 1995. The largest rise in this group is seen among those aged 15–19 years. Heterosexual exposure and IDU are the two major risk behaviours for HIV infection in women.
- Aboriginal peoples make up a growing percentage of positive HIV test reports and reported AIDS cases. IDU continues to be a key mode of HIV transmission in the Aboriginal community. Nearly 50% of all positive HIV test reports among Aboriginal Canadians were in women (less than 20% of positive HIV test reports among caucasian Canadians were in women). Aboriginal peoples test positive for HIV at a younger age compared to non-Aboriginal persons.[4,5]
- Canadians of African ancestry also make up a growing percentage of positive HIV reports and reported AIDS cases. Heterosexual exposure accounts for more than 80% of positive HIV test reports in this group. Approximately 50% of positive HIV test reports in this group are in women.
- Approximately 30% of people living with HIV infection are unaware of their HIV status. These persons — representing the “hidden epidemic” — are particularly important, because they have not yet taken advantage of services for clinical assessment, counselling and therapy. They present for medical attention later in the course of their illness and may unknowingly continue to transmit the infection.

- Although the limited data available suggest that HIV prevalence is currently low among Canadian youth, sexual risk behaviour and sexually transmitted infection (STI) data clearly indicate that the potential for HIV transmission remains significant among young Canadians. Data from targeted studies show that street-involved youth, youth who inject drugs and young MSM are particularly vulnerable to HIV infection.
- Rates of HIV infection in Canadian provincial and federal prisons appear to be much higher than in the general population. It is likely that most HIV-positive inmates were engaged in high-risk behaviour prior to imprisonment; however, there is evidence to indicate that some inmates continue to engage in high-risk behaviour after incarceration, including needle-sharing, tattooing and unprotected sex. There is great potential for HIV transmission among inmates, with possible transmission later to the spouses/partners of those released.[6]
- In Canada, blood donors have been screened and tested for HIV infection since 1985. This has resulted in a marked decline in the proportion of transfusion-associated HIV infections. The current estimated risk of infection from blood and blood products is exceedingly low in Canada (approximately one per million units of blood).
- The risk of acquiring HIV infection from a single sexual contact with an HIV-infected person is variable; risk increases with number of exposures and higher viral load in the source person.[7–9] While oral sex is a lower-risk activity than unprotected anal or vaginal intercourse, repeated exposures may increase the risk.[4]
- **Sexual transmission (infectiousness or susceptibility) of HIV is enhanced by the presence of other STIs,[10–12] including ulcerative genital infections (e.g., syphilis, genital herpes) and non-ulcerative genital infections (e.g., chlamydia, gonorrhea, trichomoniasis).[13–17] Bacterial vaginosis, although not strictly considered an STI, may also increase sexual transmission of HIV.[18–21]**
- The median time from acquiring HIV infection to the diagnosis of AIDS now exceeds 10 years. There has been a marked decline in the number of persons diagnosed with AIDS in Canada. The use of highly active antiretroviral therapy (HAART) is the major factor responsible for this decline.
- The use of HAART has dramatically changed the face of the HIV epidemic.[22] The increased lifespan of persons living with this chronic disease may be leading to a more relaxed attitude and less caution in persons at risk of transmitting and acquiring this infection.[23–25]
- The success of HAART in transforming HIV infection into a chronic disease has increased the total burden of care. This has resulted in an increased incidence of adverse effects from therapy and greater difficulty with long-term adherence to HAART.
- Widespread use of HAART, including issues of non-adherence, has also increased the potential for transmission of drug-resistant virus.

Prevention

- Persons presenting with concerns about HIV infection provide an important opportunity for education and encouragement for the consistent practice of risk reduction. These practices include sexual abstinence, reduced number of sexual partners, proper use of barrier methods and risk reduction with IDU.
- Persons with known risk behaviour(s) should be offered HIV testing, counselling and diagnosis.
- At the time of diagnostic testing for HIV, review and monitor prevention practices.
- Identify barriers to prevention practices and the means to overcome them.
- Discuss the potential use of HAART to not only improve prognosis, but also reduce infectiousness.[26]
- Discuss prompt treatment of any STI to reduce the risk of transmitting or acquiring HIV.[27–31]

Pre- and Post-Test Counselling[32]

- Counselling should be age-appropriate and individualized to the person being tested.
- Testing should be done only after informed consent has been obtained.

Pre-test counselling

- Clarify:
  - The confidentiality of HIV testing, reporting and record handling.
  - The testing options available (i.e., nominal, non-nominal, anonymous) (see *Laboratory diagnosis*, below).
  - That the test is for antibodies to HIV, not a direct test for the HIV virus or for AIDS.
  - That the majority of persons produce detectable antibodies within 3 months.
  - That an initial positive screening test is automatically followed by a confirmatory test (same blood sample) to rule out a false-positive test. This may mean a delay in the availability of the test result.
  - That the results should not be provided to the patient until confirmatory test results are available.
  - That the test results should be provided in person.
  - That returning for results is preferred, as it provides an opportunity to provide proper post-test counselling.
  - That a negative test may mean the person is not infected, or that it is too soon to detect antibodies.
  - That a positive test means the person is infected with HIV and is infectious to others through unprotected sexual contact, blood, breast milk or tissue/organ donation.
  - That an indeterminate confirmatory test result means that testing should be repeated in 3 months or additional testing performed (e.g., qualitative HIV polymerase chain reaction [PCR], serum p24 antigen; please consult your local laboratory regarding test availability).
  - That HIV is not casually transmitted through sweat, saliva, urine, feces or tears (unless there is visible blood in any of these).

Pre-test counselling (continued)

  - That transmission risks are as follows:
    - Unprotected sexual contact: anal sex (high risk), vaginal sex (high risk), oral sex (low risk).
    - Direct blood-to-blood contact.
    - Sharing needles or syringes (including IDU, tattooing, piercing with shared/unclean equipment).
    - Transmission from mother to child during pregnancy, at birth or via breast milk.
    - Receiving blood or blood products in Canada before November 1985 (elsewhere risk will vary depending on testing of donated blood).
- Discuss:
  - Specific risk behaviours, sexual and otherwise.
  - Availability of therapy to decrease the risk of mother-to-child transmission if the person is pregnant (decreased by ≥ 80%).
  - Whether future testing will be necessary.
  - Risk-reduction behaviours (see *Primary Care and Sexually Transmitted Infections* chapter):
    - Practice sexual abstinence (will eliminate risk).
    - Ensure consistent use of latex or polyurethane condoms.
    - Avoid casual/anonymous/unprotected sex.
    - Avoid sharing needles, syringes or other IDU equipment.
- Explore:
  - Psychological implications of testing.
  - Coping mechanisms to deal with either result; availability of support systems (personal, community, medical).
- Explain:
  - The need to return for test results and schedule a post-test counselling visit.
  - Public health notification for follow-up if the test is positive and the patient fails to return for results.
  - Post-test counselling procedures.
  - Partner notification and reporting requirements for HIV infection (depends on jurisdiction and availability of anonymous testing).
  - With a positive result, the need for full clinical and laboratory assessments and for discussion regarding antiretroviral therapy and prophylaxis for opportunistic infections.

Post-test counselling[33,34]

- If the test result is **negative**:
  - Interpret as:
    - No infection or "window period" with infection, but no detectable antibodies. Retesting may be required 3 months after last potential exposure to allow for detection of an antibody response. Retesting 6 months after last potential exposure may be required for those presenting with late clinical signs and symptoms of HIV infection or in persons with an impaired immune response.
    - In the case of sexual assault (see *Sexual Abuse in Peripubertal and Prepubertal Children* and *Sexual Assault in Postpubertal Adolescents and Adults* chapters) and occupational exposure (see *Occupational transmission*, below) baseline testing should be performed, followed by additional testing at 6 weeks, 12 weeks and 6 months.
  - Reinforce risk reduction:
    - Avoid high-risk behaviours.
    - Avoid needle/syringe sharing.
    - Use lubricated latex or polyurethane condoms with sexual activity.
- If test is **positive**:
  - Interpret as:
    - Infected with HIV, not diagnostic of AIDS.
    - Explain that a confirmatory test to rule out a false-positive test has been performed.
  - Consider a first priority:
    - Dealing with the issues important to the infected person.
    - Discussing coping and support systems.
    - Discussing and assisting in the partner-notification process (by the infected person or the local public health unit).
    - Providing specific guidance about avoiding HIV transmission:
      - Protect others from sexual secretions, blood and other bodily fluids.
      - Avoid donating blood, organs, tissue, sperm or breast milk.
      - Be aware of infectivity (reinforce mechanisms of transmission, including high- and low-risk behaviours).
  - Discuss disclosure issues:
    - Persons with HIV infection should be informed of the medico-legal requirement to disclose their HIV status to a potential sexual or drug-injecting partner. This is particularly important if they will be engaging in high-risk behaviour(s).[35–37]
    - Persons with HIV infection should inform their family physician and consider informing other health care providers (e.g., dentist).
    - Disclosure in the workplace is usually not mandatory but should be individualized (e.g., where the person with HIV infection has direct patient-care responsibilities).
    - Disclosure to friends or family is not essential but might be considered if there is potential for a positive outcome (e.g., positive family support).
    - Discuss benefits of treatment and follow-up.

Positive post-test counselling (continued)

- Deal with soon:
  - Further medical support, immune testing, HIV viral load testing, CD4 count and counselling are required.
  - Discuss use of laboratory testing to make therapeutic decisions.
- Discuss medical care:
  - Screen for hepatitis B virus (HBV) infection and immunity (see *Hepatitis B Virus Infections* chapter). Screen for hepatitis A virus (HAV) immunity in injection drug users, MSM, individuals with chronic liver disease and hemophiliacs.
  - Screen for hepatitis C virus (HCV) infection.
  - Screen for syphilis and other STIs.
  - Screen for tuberculosis.
  - Refer where required (e.g., HIV specialist).
  - Discuss health-enhancing lifestyle modifications, empowerment.
  - Discuss issues of confidentiality in the health care system, community, at school or at work.
  - Discuss avoidance of activities that increase transmission risk of toxoplasmosis and enteric pathogens.

Transmission

- Transmission of HIV infection occurs essentially through specific exposure to blood and/or body fluids from an HIV-infected person. The most concerning types of exposure include sexual exposure, parenteral blood exposure through IDU or blood transfusion, perinatal mother-to-child transmission and occupational exposure in the health care setting. Strategies for prevention should be aimed at risk reduction in these areas. A high viral load in the infected person increases the potential for transmission.[38]

Sexual transmission

- This is the major route of HIV transmission.[39]
- Sexual activities can be divided according to risk.[40] This ranges from touching and hugging, which carry no risk, to penile-anal and penile-vaginal intercourse without a condom, which carries a high risk. Providers should be aware of and counsel patients according to the implications that specific behaviours can have on the transmission of other blood-borne pathogens and STIs.
- Persons should be counselled that:
  - Only sexual abstinence and “no-risk” activities are guaranteed to prevent transmission.
  - Low-risk activities are preferable to high-risk activities.
  - Male and female condoms made of latex or polyurethane are an effective barrier for preventing HIV transmission. Correct and consistent use of condoms can reduce but not eliminate the risk of HIV transmission.[41–44]
  - The presence of another STI in either the source or the exposed person, particularly ulcerative lesions such as syphilis or genital herpes, increases the potential for sexual transmission of HIV.
- Infected individuals should be strongly urged to inform past, present and future sexual partners about their known HIV-positive status.

- Ongoing counselling and discussion about sexual behaviour is appropriate.

Parenteral transmission

- Risk of parenteral HIV transmission can be divided according to risk.[40] This ranges from the use of sterilized injection equipment, which is considered no-risk, to the use of shared needles, which is considered high-risk. Providers should be aware of and counsel patients according to the implications that specific behaviours can have on the transmission of other blood-borne pathogens.
- Active injection drug users should be encouraged to discontinue drug use by using addiction-treatment services and should be counselled on the health risks associated with IDU.
- If the individual is not ready, willing or able to discontinue IDU, harm-reduction strategies should be stressed, including not sharing injecting equipment and adopting safer modes of drug use.
- Access to sterile injecting equipment, such as needle-exchange programs, should be discussed and encouraged.

Perinatal mother-to-child transmission

- The HIV prevalence rate among pregnant women is approximately 3–5/10,000 in Canada.
- Transmission of HIV infection from the HIV-positive mother to her infant may occur in utero, during childbirth or after childbirth through breastfeeding. Preventing this mode of transmission can, therefore, be achieved by identifying HIV-infected women who are pregnant and using strategies to minimize the risk of mother-to-child transmission.[45]
- Antiretroviral therapy can dramatically reduce perinatal transmission of HIV.
- In all Canadian provinces and territories, HIV testing of pregnant women remains the choice of the woman. Guidelines and/or recommendations for HIV testing of pregnant women have been developed in each province and territory to encourage informed decision-making.
- **All pregnant women should be offered confidential HIV testing and counselling as part of routine prenatal care.**
- In some provinces and territories (Alberta, Newfoundland and Labrador, Northwest Territories, Nunavut), an "opt-out" policy treats HIV screening as a routine prenatal screening test. The pregnant woman is informed that testing will be done, but consent is implied unless she specifically refuses.[4]
- Women who present in labour who have not had prenatal HIV testing or who have been engaging in high-risk behavior after initial negative prenatal HIV testing should be offered expedited or rapid HIV testing.[45]
- HIV-positive women of childbearing age should be counselled about the risk of mother-to-child transmission. They should also be given complete information regarding contraceptive and reproductive options, as well as the availability of therapy to decrease the risk of transmission to the child (see *Pregnancy* chapter).
- **In North America, breastfeeding is contraindicated for HIV-infected mothers.**

Occupational transmission[46]

- Transmission of HIV infection in the workplace (occupational exposure) is primarily concerned with the potential for transmission from patient to health care personnel. The potential for transmission from health care personnel to patient and from one health care person to another is not within the scope of this section.
- Occupational exposure to HIV infection may occur in several instances:
  - Percutaneous injury with a sharp object potentially contaminated with blood or other bodily fluid.
  - Mucous membrane exposure to blood or other bodily fluid.
  - Skin exposure to blood or other bodily fluid.
- The average risk of HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% (3/1,000), and after a mucous membrane exposure, approximately 0.09% (0.9/1,000).[47,48] Although episodes of HIV transmission after non-intact skin exposure have been documented, the average risk for transmission by this route has not been precisely quantified but is estimated to be less than the risk for mucous membrane exposures.[49,50] The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified, but is probably considerably lower than for blood exposures.[51]
- The decision to initiate postexposure prophylaxis (PEP) for HIV infection is based on clinical judgment and should be a joint decision with the exposed health care worker.
- The choice of no PEP vs. a two- or three-drug PEP regimen is based on the index of suspicion after evaluating the following:
  - Source of exposure: the potential for HIV infection (e.g., high-risk activity or HIV-positive source).
  - Type of exposure: the potential for transmission of HIV infection (e.g., hollow-bore needle visibly contaminated with source patient's blood).[52,53]
- **PEP should be initiated as soon as possible, as it may be less effective if initiated more than 72 hours after exposure.**

Diagnosis

- The diagnosis of HIV infection is based primarily on a positive serologic test. Persons with HIV infection may be totally asymptomatic. Therefore, serologic testing is recommended when there is a high index of suspicion (e.g., high-risk behaviour and/or suspicious clinical symptoms and signs). Persons may also present with specific opportunistic infections or other conditions indicative of underlying immunosuppression.

Risk behaviours

- Multiple sexual partners.
- Unprotected sexual activity (i.e., no barrier [condom] protection).
- Sex with an HIV-infected partner.
- Receptive anal/vaginal intercourse.
- Sharing of IDU equipment.
- Acquisition of other STIs, such as HBV or syphilis.

Clinical diagnosis

- The time from initial HIV infection to clinical disease is highly variable, with a median time of approximately 10 years. However some HIV-infected persons experience more rapid progression of disease.
- The person with HIV infection may experience several stages:
  - Primary or acute HIV infection.
  - Chronic asymptomatic HIV infection.
  - Chronic symptomatic HIV infection.

Primary/acute HIV infection

- This is the period from initial infection to development of the full serum antibody profile (i.e., seroconversion).[54–56]
  - High levels of viral replication and plasma viremia.
  - Shedding from mucosal sites.
  - No detectable antibody.
  - Depressed CD4 count.
- Although some patients in this stage are asymptomatic, up to 90% may be symptomatic (i.e., the acute retroviral syndrome).[57] Symptoms generally appear 2–4 weeks after initial infection and are often nonspecific or mild. They are usually self-limited, lasting 1–2 weeks, but may last several months.
- The spectrum of symptoms may include an acute mononucleosis-like illness, fever and skin rash. Meningoencephalitis or aseptic meningitis may occur. Less commonly, AIDS-defining conditions such as *Pneumocystis jiroveci* (formerly *carinii*) pneumonia or oroesophageal candidiasis may occur.

Table 1. Symptoms of acute HIV infection

Symptoms	Frequency
Fever (mean temperature 39.4°C [102.9°F])	>80%
Arthralgia or myalgia, rash, lymphadenopathy, sore throat, fatigue, headache	40–80%
Oral ulcers and/or genital ulcers, >5 kg weight loss, nausea, vomiting or diarrhea	10–40%

- If initial HIV serologic tests are negative or indeterminate, additional testing can be considered. Please consult appropriate resources or colleagues experienced in this area.
- A high index of suspicion in the person with a nonspecific febrile illness and a history of high-risk behaviour is key to making the diagnosis.
- **Although the treatment of primary or acute HIV infection is considered optional at this time, these persons may be highly infectious.[58] Detection of primary HIV infection provides an opportunity for counselling and preventing further transmission.**

Chronic asymptomatic HIV infection

- This is the stage where viral replication and plasma viremia are more controlled by the immune response. There is a balance between ongoing viral replication and the host immune response represented by the level of CD4+ T cells.
  - Many persons fall into this category.
  - Generalized lymphadenopathy is frequently present.
  - Thrombocytopenia may be present.

Chronic symptomatic HIV infection

- This is the stage where viral replication depletes the CD4+ T cells to the level of profound immunosuppression.[59] See *Table 2* for signs and symptoms.

Table 2. Signs and symptoms of chronic symptomatic HIV infection

- Oral hairy leukoplakia
- Unexplained fever (>2 weeks)
- Fatigue or lethargy
- Unexplained weight loss (>10% body weight)
- Chronic diarrhea (>3 weeks)
- Unexplained lymphadenopathy (usually generalized)
- Cervical dysplasia
- Dyspnea and dry cough
- Loss of vision
- Recurrent or chronic mucocutaneous candidiasis (oral, esophageal, vaginal)
- Dysphagia (esophageal candidiasis)
- Red/purple nodular skin or mucosal lesions (Kaposi sarcoma)
- Encephalopathy
- Herpes zoster, especially if severe, multidermatomal or disseminated
- Increased frequency or severity of mucocutaneous herpes simplex virus infection
- Unexplained “anemia of chronic disease”

Table 3. AIDS-defining conditions[60,61]

(Require concurrent positive HIV serology to be diagnostic of AIDS)

- Bacterial pneumonia, recurrent
- Candidiasis (esophageal, bronchi, trachea or lungs)
- Cervical cancer, invasive
- Coccidioidomycosis (disseminated or extrapulmonary)
- Cryptococcosis (extrapulmonary)
- Cryptosporidiosis (chronic intestinal)
- Cytomegalovirus disease (other than liver, spleen, nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV-related (dementia)
- Herpes simplex virus (chronic ulcers or bronchitis, pneumonitis or esophagitis)
- Isosporiasis, chronic intestinal
- Kaposi sarcoma
- Lymphoma (Burkitt, immunoblastic, primary in brain)
- *Mycobacterium avium* complex or *M. kansasii* (disseminated or extrapulmonary)
- *Mycobacterium* of other species (disseminated or extrapulmonary)
- *Mycobacterium tuberculosis* (pulmonary, disseminated or extrapulmonary)
- *Pneumocystis jiroveci* (formerly *carinii*) pneumonia
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV

Laboratory diagnosis – HIV antibody testing

- Any physician or qualified health care provider may order an HIV test. (Check with your local laboratory for the availability of these tests.)
- Testing should be carried out only with the informed consent of the person being tested.
- HIV antibody testing should be offered to any person with identified risk behaviour who has clinical or laboratory clues suggestive of HIV infection, or who requests it.
- Explain clearly the nature of the test, and provide appropriate pre- and post-test counselling.
- Point-of-care rapid tests for HIV antibodies are now more widely available. All reactive screening tests using these kits require confirmatory testing (e.g., Western blot analysis).[62]
- CD4 count and viral load testing should not be used as screening or diagnostic tests.
- p24 antigen testing, although occasionally useful in diagnosis of primary or acute infection, is insensitive for screening purposes.

- There are three options for HIV testing and reporting in Canada: nominal, non-nominal or anonymous. The use and availability of these options varies across the provinces and territories. Your local public health authority will provide information on the options available in your region.[4]
  - **Nominal testing**: the HIV test is ordered using the name of the person being tested.
  - **Non-nominal testing**: the HIV test is ordered using a code or the initials of the person being tested. Only the person ordering the test knows the identity of the person being tested and is able to link the result to that person's health care record.
  - **Anonymous testing**: the HIV test is ordered using a unique non-identifying code. The person(s) ordering the test and providing the result (usually by telephone) do not know the identity of the person being tested. Only the person being tested knows the code, so the test result is not linked to that person's health care record. Although anonymous testing may encourage more persons to have testing, it is not available in all provinces and territories.
- A positive enzyme immunoassay (EIA) screening test requires confirmatory testing (e.g., Western blot analysis) using the same specimen.
- Repeat all initial positive HIV serologic tests using a second blood specimen to rule out laboratory error and confirm the diagnosis.

Management, Treatment and Follow-up[63,64]

- **This is an increasingly complex area, with rapid changes in optimal therapy as new research becomes available. Recommendations for a given person should be made in collaboration with a colleague experienced in HIV/AIDS. Your local public health authority will have a listing of these.**

Guiding principles

- Asymptomatic infected persons are usually followed at 3–6-month intervals if untreated.
- The follow-up interval may vary if antiretroviral therapy is provided or if the person is symptomatic.
- Routine monitoring of CD4 lymphocyte count and plasma HIV RNA viral load are key in assessing effectiveness of antiretroviral therapy.[65,66]

First visit after positive HIV test

- Conduct a medical history and complete physical examination, including genital and anal inspection.
- Order laboratory tests, including complete blood count with white cell differential, CD4 count, viral load, liver functions tests, creatinine kinase, blood glucose, amylase and lipase. Screen for HBV infection and immunity (see *Hepatitis B Virus Infections* chapter). Screen for HAV immunity in injection drug users, MSM and individuals with chronic liver disease and hemophilia. Screen for HCV infection. Screen for toxoplasma (IgG) and syphilis. Tests for other STIs, such as gonorrhea and chlamydia, should also be considered (see *Consideration for Other STIs*, below).
- For women, cervical screening for dysplasia and/or human papillomavirus (HPV) infection is recommended if not performed within the last 6–12 months. The anal Pap smear for men with a history of anal receptive intercourse and/or a history of anal warts is available only in certain centres.
- Baseline fasting lipids and glucose would be appropriate if considering starting antiretroviral therapy.

- **Tuberculin skin testing is essential. A negative test may not rule out latent or active tuberculosis.**[67]
  - If past exposure to *Mycobacterium tuberculosis* is indicated (induration ≥5 mm in diameter), the person should be assessed for active tuberculosis.
  - If active tuberculosis is excluded and the person has not previously received therapy to prevent or treat tuberculosis, isoniazid 300 mg once daily for 9–12 months is highly effective in preventing the development of active tuberculosis. Rifampin 600 mg daily or rifabutin 300 mg daily can be used for isoniazid-resistant strains or when isoniazid toxicity precludes isoniazid use.[68]
  - **Consultation with a colleague experienced in this area should be sought.**
- Immunization (e.g., HAV, HBV) should be discussed according to current guidelines.[69,70] Generally, there is no contraindication to the use of inactivated or component vaccines in HIV-positive persons. The routine childhood immunization schedule should be completed if indicated. Pneumococcal immunization (boosted once only after 5 years) and annual influenza immunization are recommended.
- Influenza and pneumococcal immunization have been associated with transient increases in plasma viral load levels. However, this does not appear to have any significant impact on disease progression, and the benefits are generally felt to outweigh the risks.
- Smoking cessation is an important issue, particularly in persons with other cardiovascular risk factors who will be starting antiretroviral therapy.

Follow-up visits

- Conduct a clinical assessment, including assessment for cardiovascular disease, lipodystrophy, lactic acidosis and diabetes mellitus.
- Conducting an annual anal inspection for the presence of HPV lesions, particularly in MSM, is encouraged.[71,72]
- Take the opportunity for risk-reduction counselling. Sexual and drug-use history should be discussed at each visit.
- If the patient is on therapy, assess adverse effects and adherence.
- CD4 counts and viral load testing should be performed every 3–6 months. Other laboratory tests, including complete blood count with white cell differential, liver function tests, creatinine kinase, amylase, lipase, fasting lipids and blood glucose should also be performed every 3–6 months, depending on drug therapy.
- There are two components to drug treatment: antiretroviral therapy and drugs to prevent or treat opportunistic infections.

Antiretroviral therapy[73]

- **This is a rapidly evolving field, and any decision on specific therapy for a given person should be made in collaboration with a colleague experienced in HIV/AIDS.** Therapy should be individualized and based on factors such as efficacy, tolerability, potential adverse effects, convenience and drug-drug interactions. Specific details and recommendations for antiretroviral drug therapy are beyond the scope of this chapter.

- The antiretroviral drug classes licensed in Canada so far include the following:
  - Nucleoside reverse transcriptase inhibitors (NRTIs): e.g., zidovudine (AZT), lamivudine (3TC) and stavudine (d4T).
  - Nucleotide reverse transcriptase inhibitor (NtRTI): tenofovir.
  - Non-nucleoside reverse transcriptase inhibitors (NNRTIs): e.g., efavirenz and nevirapine.
  - Protease inhibitors (PIs): e.g., nelfinavir, saquinavir, ritonavir and atazanavir.
  - Fusion inhibitor: enfuvirtide/T20.
- Other types of investigational antiretroviral drugs are presently in development and clinical trials. Immune-based therapy to boost CD4 counts is still in clinical trials.
- Recommendations for antiretroviral therapy are based on clinical status, CD4 count, viral load and patient willingness to undertake therapy (see *Table 4*). It should be recognized that prolonged therapy is limited by drug toxicity, adherence issues, drug resistance and cost.
- Therapy, when indicated, includes at least three agents (e.g., two NRTIs plus one NNRTI or PI).
- The goal of therapy is to suppress viral replication to the point where plasma HIV RNA is undetectable, with minimal patient toxicity.
- **Monotherapy and dual therapy should be avoided, as this has been associated with the emergence of drug resistance.**
- Persons should be instructed to take medication regularly, as missed doses and under-dosing may promote drug resistance.
- Significant drug-drug interactions may occur with some antiretroviral drugs.
- Alteration of HAART is usually indicated if there is a failure to achieve or maintain control of viral replication or there is unacceptable toxicity. Resistance testing (genotyping or phenotyping) may be valuable in the selection of the initial or subsequent regimens.

Table 4. Guidelines for starting antiretroviral therapy for the person with chronic HIV infection

Clinical status	CD4 count	Viral load	Therapy
AIDS-defining illness or severe HIV symptoms	Any	Any	Yes
Asymptomatic	<0.2 x 10^9/L (<200/μL)	Any	Yes
Asymptomatic	0.2–0.35 x 10^9/L (200–350/μL)	Any	Offer
Asymptomatic	>0.35 x 10^9/L (>350/μL)	≥100,000 copies/mL	Defer or consider
Asymptomatic	>0.35 x 10^9/L (>350/μL)	<100,000 copies/mL	Defer

Prevention of opportunistic infections[74]

- HIV-infected persons are at increased risk of specific opportunistic infections, depending on their CD4 count.
- It is safe to discontinue prophylactic therapy once CD4 count has increased and remained above a certain level for 3–6 months.

Table 5. Prophylactic therapy for opportunistic infections

CD4 count	Opportunistic infection	Prophylactic therapy
<0.2 x 10^9/L (<200 cells/μL)	*Pneumocystis jiroveci* (formerly *carinii*) pneumonia	• Preferred: **trimethoprim-sulfamethoxazole** PO once daily or three times per week • Alternate: **dapsone** PO once daily, **atovaquone** PO once daily, **aerosolized pentamidine** once monthly Also indicated with oral candidiasis or prior *P. jiroveci*, regardless of CD4 count
<0.1 x 10^9/L (<100 cells/μL)	*Toxoplasma gondi*	• Same drugs as *P. jiroveci*, except for aerosolized pentamidine
<0.05 x 10^9/L (<50 cells/μL)	*Mycobacterium avium* complex	• Preferred: **azithromycin** PO once weekly • Alternate: **clarithromycin** PO twice daily, **rifabutin** PO once daily

- Cytomegalovirus disease:
  - Present guidelines do not recommend primary prophylaxis for cytomegalovirus (CMV) disease. However, persons with CD4 count <0.05 x 10^9/L (<50 cells/μL) are at highest risk of CMV disease. These persons should be aware of the symptoms of CMV disease, in particular CMV retinitis (e.g., visual distortions, floaters). A regular 4–6-monthly funduscopic examination performed by an ophthalmologist may be helpful in early detection of CMV retinitis.
- Other infections:
  - Treatment and prevention of bacterial, viral, parasitic and fungal infections should be individualized and response to therapy monitored.
  - In many instances, long-term suppressive therapy is required.

Consideration for Other STIs

- Persons with risk behaviours for HIV infection should be offered testing for other STIs.
  - Testing from appropriate sites for chlamydia and gonorrhea.
  - Serologic tests for syphilis.
  - Screening for HBV infection and immunity (see *Hepatitis B Virus Infections* chapter); screening for HAV immunity in injection drug users, MSM, individuals with chronic liver disease and hemophilia; screening for HCV infection.
  - Type-specific herpes simplex virus (HSV) serology (HSV-2 infection): if available, this may be useful in identifying persons who are potentially more at risk of acquiring or transmitting HIV infection. The increased risk of acquisition or transmission appears to be primarily during symptomatic genital HSV (active genital ulcers).[75–79] However, asymptomatic genital HSV may also be an important factor in HIV acquisition or transmission. Episodes of acute genital HSV have been shown to increase mucosal shedding and plasma levels of HIV.[80–83] Antiviral therapy and suppression of genital HSV reactivation may be an important strategy in minimizing HIV transmission in association with genital HSV infection.[84,85] If genital ulcers are present, see the *Genital Ulcer Disease* chapter for testing recommendations.
- Offer immunization for HBV and HAV if non-immune as per current guidelines.[69]
- Discuss HPV vaccine with women as per the recommendations outlined in the Canada Communicable Disease Report, Volume 33 ACS-2, (2007) *National Advisory Committee on Immunization (NACI) statement on Human papillomavirus vaccine*.

Reporting and Partner Notification

- HIV infection is reportable in all provinces and territories; such reporting may be nominal or non-nominal, depending on the jurisdiction.
- AIDS is reportable by physicians to local public health authorities in all provinces and territories.
- Partner notification must be undertaken in all cases of AIDS and HIV infection.
- Local public health authorities are available to assist with partner notification and help with appropriate referral for clinical evaluation, testing, treatment and health education. The treating physician is responsible for ensuring that partner notification is initiated.
- All children born to mothers who are or may be HIV-infected need to be evaluated (see *Pregnancy* chapter).
- All HIV-positive persons who have previously received or donated blood should be reported in confidence to the local Canadian Blood Services.

Special Considerations

- **The increased risk of cervical cancer in HIV-infected women is related to the degree of immunosuppression.[86] Pap smears should be performed at baseline and 6 months later, with subsequent Pap smears at least annually depending on the results of initial smears.[74,87]**
- **Anal HPV infection with subsequent epithelial changes of anal cancer and its precancerous lesions have been detected in HIV-infected persons, even in the absence of anal intercourse. These changes may be seen despite the use of HAART and immune restoration.[71,72]**
- In some centres, anal Pap smears and HPV detection are performed on a regular basis in HIV-positive MSM. Colposcopy and biopsy is performed if indicated. Aggressive therapy of high-grade lesions is warranted.
- It is important to ensure access to psychological counselling for all HIV-infected persons as needed.
- **It may be appropriate to provide non-occupational PEP to persons in certain situations (e.g., sexual assault) on a case-by-case basis.[88]**
- Some persons may develop acute symptoms, such as fever, arthralgia, myalgia, lymphadenopathy, worsening liver disease or encephalopathy within the first few weeks of starting HAART. This "immune reconstitution syndrome" is associated with the improved immune response to pre-existing co-infection (e.g., with HCV or *mycobacterium avium complex* [MAC]).
- All persons on HAART have the potential to develop a number of adverse effects. These include direct drug-related toxicity (e.g., pancreatitis, peripheral neuropathy, body-fat maldistribution [lipodystrophy] or metabolic abnormalities such as hyperglycemia or hyperlipidemia). Lactic acidosis and liver dysfunction may be more frequent with specific drugs.
- Many persons are also at increased risk of cardiovascular disease related to family history, risk factors such as smoking and drug-induced hyperlipidemia.
- Other issues, such as osteopenia, osteoporosis and hypogonadism, may also become problematic.
- Persons with HIV co-infection may experience a more rapid progression of HCV infection and HBV infection. HBV or HCV co-infection is a risk factor for severe hepatotoxicity during HAART.[89–93]
- HIV co-infection may alter the natural history of syphilis and neurosyphilis, including response to therapy.[94–97]
- Therapeutic drug monitoring is being used to assess therapeutic drug levels in some persons who are adherent but fail an appropriate regimen. This is not yet universally available.
- Discussion of sexual and other risk behaviours should be routinely performed at each visit. The medico-legal implications of infection transmission without disclosure should be reinforced. Referral to local public health authorities should be made in cases where risk behaviours are not being voluntarily controlled.