The occasional HIV-infected patient

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INTRODUCTION

HIV infection is an increasingly common diagnosis in rural and urban family practice. About 75 000 Canadians live with HIV/AIDS, 21% of whom are not aware of their HIV diagnosis.[1] As capable purveyors of patient-centred care and skilled managers of chronic disease, family physicians should play an integral role in the care of the HIV-positive patient.

Family physicians are often the front-line agents for the screening and diagnosis of HIV infection and must provide necessary counselling and support to patients with a new diagnosis. In areas where access to an infectious disease specialist may be difficult, family physicians can initiate a timely investigation for these patients. Also, as the disease has become simpler to manage in recent years and as life expectancies approach normal, long-term care of HIV infection is becoming similar to that of many other chronic diseases: family physicians will play a more central role in care over the patient's lifespan.

DIAGNOSIS

The traditional "targeted" approach of identifying only high risk individuals is increasingly being replaced by a model of "routine" or "opt-out" screening.[2] The routine screening approach will be familiar to physicians who care for pregnant patients.[3] Family physicians are encouraged to review recent guidelines for full details on screening recommendations.[4,5] Brief but appropriate history-taking can identify at-risk populations, including sexually active adults (including, but not limited to, men who have sex with men) and intravenous drug users. The "window" period of up to 3 months between an initial exposure and HIV test positivity should be described, although, in most cases, current fourth-generation HIV tests can detect acute infection within about 6 weeks of exposure.[6] Explicit oral or written consent for an HIV test is no longer necessary. Testing for other sexually transmitted infections should be strongly considered.

Should a test give a positive result, a family physician is likely the best health care professional to relay this news and initiate investigation. The most critical message for patients with newly diagnosed HIV infection is that, given appropriate treatment, affected people have a life expectancy no different from that of the rest of the population[7] and that medication can often consist of a single tablet once daily.[8] It is vital to also inform the patient (and subsequently document in your chart) that nondisclosure of HIV-positive status to a sexual partner is a potential criminal offence.

The initial and follow-up tests that should be ordered by a family physician are listed in Table 1.

TREATMENT

There are few reasons to delay treatment of HIV infection. All major guidelines now strongly recommend initiating antiretroviral therapy soon after diagnosis, regardless of the patient's CD4 count.[9,10] Early initiation of antiretroviral therapy has been associated with significant benefit in terms of reduced morbidity and mortality, even for patients

with CD4 counts greater than 500/μL, and also substantially reduces the risk of transmission to HIV-negative partners.[13,14]

If faced with a long wait time for in-person consultation, even family physicians without extensive experience with this infection should consider e-consultation with an HIV infection care provider and then initiate an initial treatment regimen. Typically, genotypic resistance testing is used to guide treatment selection. If a genotype is not available or if the practitioner is not experienced with interpreting a genotype, we recommend starting treatment with darunavir, 800 mg once daily, ritonavir, 100 mg once daily, and tenofovir disoproxil fumarate–emtricitabine (coformulated in 1 tablet), 300 mg/200 mg once daily, in the absence of known liver or renal disease. This combination of medications can be used successfully in nearly all patients and is accessible via most (if not all) provincial and federal drug formularies. Common side effects of this regimen include diarrhea, nausea, headache and rash. Severe side effects, including renal or hepatic toxicity or Stevens–Johnson syndrome, are rare. Inexperienced practitioners should review the use of these medications with a pharmacist.

The out-of-pocket cost of these medications can be prohibitive. We recommend consultation with a local AIDS service organization to discuss options for patient coverage. Pharmaceutical companies often consider compassionate release of medications for those who cannot pay or are in the process of organizing other private or provincial coverage.

After antiretroviral therapy has been started, repeat blood testing, including viral load and creatinine and liver transaminase levels, should be done after 2–8 weeks of treatment and every 3–4 months thereafter until the patient has attained an undetectable viral load for 2 years. Once genotype information is available, family physicians can consider switching to a simplified regimen with the guidance of an HIV infection care specialist.

Table 1: Initial and follow-up laboratory investigations in HIV-infected patients[9–12]

Investigation*	Follow-up
General	
Complete blood count, differential, platelet count	Every 3–6 mo
Renal and liver tests: creatinine, estimated glomerular filtration rate, phosphate, urine albumin to creatinine ratio, urinalysis, aspartate aminotransferase, alanine aminotransferase, bilirubin, international normalized ratio	Every 3–6 mo
Lipids, blood glucose	Every 6–12 mo
Pregnancy test	Where appropriate
Mantoux test, chest radiography	Where appropriate
HIV-specific	
HIV diagnostic test: CD4 T-lymphocyte panel	Every 3–6 mo; optional if CD4 count consistently > 500/μL and viral load undetectable
HIV viral load	Every 3–6 mo
HIV genotype for resistance testing	At initiation of antiretroviral therapy and if regimen failure is suspected
HLA-B5701 testing	
Other	
Serologic testing for hepatitis A and B	Only as required to determine immune status
Serologic testing for hepatitis C	As required for screening at-risk patients
Cytomegalovirus IgG	
Toxoplasma IgG	
Sexually transmitted infection screening: gonorrhea and chlamydia (urine nucleic acid amplification test and swabs as required), syphilis	As required for screening at-risk patients

*All performed at baseline.

REGULAR LABORATORY INVESTIGATIONS

For patients taking antiretroviral therapy and for those in whom virologic suppression has been attained for greater than 2 years, blood testing can be done every 6 months by the family physician.[9] Determination of viral load (to ensure ongoing suppression), a complete blood count, urinalysis, and measurement of creatinine and liver transaminase levels should be ordered at least every 6 months. In cases of virologic failure, where viral load rises, resistance to antiretroviral therapy or nonadherence should be considered, and further expert advice should be sought.

DRUG INTERACTIONS

HIV treatments can interact with commonly prescribed medications. Comprehensive drug interaction lists are available.[10,15] Careful drug interaction checks should be performed for all medications, including over-the-counter options. Although this list is not intended to be comprehensive, we suggest the family physician should be aware of the following interactions:

- Absorption issues: because HIV integrase inhibitors (elvitegravir and dolutegravir) bind with

polyvalent cations, these medications cannot be taken simultaneously with supplements, including antacids. As well, certain HIV medications (rilpivirine, atazanavir) cannot be coadministered with proton pump inhibitors, which reduce absorption.

- Mechanisms mediated by cytochrome P450: many antiretrovirals (including regimens containing ritonavir or cobicistat, and efavirenz) interact with commonly prescribed medications via P450-mediated mechanisms. Common medications to watch for include statins, methadone, clarithromycin,[16] α-blockers, estradiol-containing contraceptives, erectile dysfunction medications and St. John's wort.[10,15]
- Other: 1 commonly prescribed antiretroviral, dolutegravir, inhibits renal elimination of metformin. Management strategies include the use of an alternative orally administered hypoglycemic or reduction of the metformin dosage, with monitoring for loss of treatment effect and adverse effects.[15]

SPECIAL CONSIDERATIONS

Opportunistic infections

Patients with a CD4 count less than 200/μL are at high risk for contracting an AIDS-defining illness (which includes opportunistic infections as well as other, rare conditions, such as Kaposi sarcoma and wasting syndrome). It is important to screen for and provide prophylaxis against opportunistic infections. For example, patients may present with ongoing shortness of breath and indolent cough; this suggests *Pneumocystis jiroveci* pneumonia, and the case may warrant discussion with an expert. Table 2 highlights relevant therapies for prophylaxis of opportunistic infections; treatment of these infections requires consultation with an expert. For *P. jiroveci* pneumonia prophylaxis, single-strength trimethoprim–sulfamethoxazole tablets may be associated with fewer adverse effects than double-strength tablets, although hypersensitivity reactions are still common. A telephone or in-person consultation with an expert in HIV infection care is warranted in the case of any patient who is unwell and has a CD4 count less than 200/μL.

Neurosyphilis

The diagnosis of syphilis in the presence of HIV infection may necessitate investigation for neurosyphilis by means of lumbar puncture. More specifically, if an HIV-infected patient has neurologic symptoms or signs, late latent syphilis, a CD4 count less than 350/μL or syphilis rapid plasma reagin of 1:32 dilutions or greater, or suboptimal decline in titres after penicillin treatment, lumbar puncture is warranted.[17]

Early infection/seroconversion

Patients with acute HIV infection may present with influenza-like symptoms within a few weeks of exposure to the virus. Appropriate and rapid identification of patients at high risk may present an opportunity to provide an early diagnosis and treatment and may significantly reduce future morbidity.[13,14]

VACCINATIONS

Immunocompetent (CD4 count > 200/μL) patients should be vaccinated with all available agents (Table 3). Family physicians should not neglect other recommended vaccines appropriate to any high-risk patient groups.

Table 2: Treatment for opportunistic infections in HIV-infected patients[10,11]

Infection	Medication	Treatment threshold, CD4 count
Pneumocystis jiroveci pneumonia	Trimethoprim–sulfamethoxazole (single- or double-strength), 400/80 mg or 800/160 mg daily	< 200/μL
Toxoplasma gondii	Trimethoprim–sulfamethoxazole (double-strength), 800/160 mg daily	< 200/μL
Mycobacterium avium complex	Azithromycin, 1200 mg weekly	< 50/μL

Table 3: Recommended vaccinations in HIV-infected patients[11]

Vaccine	Timing
Hepatitis A	Baseline (if not immune)
Hepatitis B (typically higher dosage, 40 μg)	Baseline (if not immune)
Influenza	Yearly
Tetanus–diphtheria/tetanus–diphtheria–pertussis	Every 10 yr
Live vaccines as required (measles–mumps–rubella, shingles)	Baseline if CD4 count > 200/μL
Human papillomavirus (preferably 9-valent)	Baseline
Pneumococcal conjugate (PCV 13)	Baseline
Pneumococcal polysaccharide (PCV 23)	8 wk after PCV 13, then second dose in 5 yr

OTHER PREVENTIVE CARE

Malignant disease may develop in people with HIV infection at about 4 times the rate among the average population.[18,19] Cervical cancer screening guidelines differ, and most HIV-infected females will require a normal Papanicolaou test result for 3 serial years before transitioning to a Papanicolaou test every 3 years. In centres that can offer it, anal Papanicolaou tests for men who have sex with men with warts due to human papillomavirus are supported by evidence.[18] Colon and breast cancer screening remain the same as for noninfected people. Those with HIV infection are also at increased cardiovascular risk, and family physicians are the best advocates for aggressive treatment of hypertension and hyperlipidemia and for smoking cessation.[9,10]

CONCLUSION

Screening and management of HIV-infected people are increasingly within the scope of the primary care practitioner. In resource-limited settings, the family physician can initiate basic investigation and management of such patients while awaiting specialist consultation.

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