



Managing HIV in general practice

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Summary

As a consequence of advances in care, life expectancy has significantly increased for many people with HIV. In Australia, the focus of care has shifted from acute illness and palliative care to chronic disease management. Many people with HIV receive much of their medical care from general practitioners. It is therefore important to know which problems can be managed in general practice and when these patients should be referred.

Key words: adverse effects, AIDS, travel, vaccination.

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Introduction

In 2009 it was estimated that 20 171 people were living with HIV in Australia.¹ As overall HIV infection numbers increase and uptake of more effective and less toxic antiretroviral therapy becomes more widespread, this population is going to increase and live longer. As a consequence, it is likely that more general practitioners will become involved in the care of people living with HIV. An understanding of the standard care, general management and medication-related issues is important.

To become a community prescriber of antiretroviral therapy for HIV, general practitioners need to complete an accredited training course. Details of training courses are on the Australasian Society of HIV Medicine website (www.ashm.org.au).

Standard care of a person with HIV

The aim of antiretroviral therapy is to achieve long-term control of HIV replication, enabling recovery and improved functioning of the immune system. The goal is to suppress the plasma viral load to below 40 copies/mL, which is the lowest point of detection in most routine assays.

Initiating therapy

Current guidelines² advise starting treatment if there is an AIDS-defining illness or a CD4 count below 350 cells/microlitre. There is some research (based on cumulative observational cohort data) to support earlier treatment for people with CD4 counts above 350 cells/microlitre,³ but current opinion is divided on this.⁴

In certain circumstances, treatment is initiated regardless of the CD4 count⁵ including:

- pregnancy
- rapid decline of CD4 cell counts
- active or high risk of cardiovascular disease
- high risk of HIV transmission, for example in serodiscordant couples
- treatment of co-infection with hepatitis B or C is indicated
- HIV-associated nephropathy
- malignancy
- certain opportunistic infections.

Regular monitoring

Treatment with antiretroviral therapy is generally lifelong and requires a great deal of commitment from patients, who require continued monitoring and support. There may be enduring adverse effects from earlier antiretroviral therapy in treatment-experienced patients. However, newer antiretroviral therapies are better tolerated and have less toxicity.

Most people with HIV see their doctor every three months for review and routine blood testing (Table 1). General practitioners can play a pivotal role in helping patients to address problems with their general health, adherence to medications, adverse effects of treatment, psychosocial wellbeing, broader preventive health and sexual health.

Adherence to treatment

It is vitally important that patients achieve close to 100% adherence to treatment to maintain viral suppression and minimise any risk of acquiring resistance to their antiretroviral therapy. A number of strategies to promote adherence have been trialled.⁶ Increased alcohol use is a predictor for decreased adherence. State-based AIDS councils and People Living with HIV organisations have community and peer workers who are able to assist people with practical advice and counselling about HIV treatments (see Patient support organisation page 72).

Sexual health

Sexual health is an important issue in HIV management on many levels. The general practitioner should consider such issues as sexual behaviour and potential risk for HIV transmission as well as the risk of acquiring other sexually transmitted infections. Sexually active HIV-infected men who

Table 1

Routine laboratory testing for people with HIV ^{2,14}

Test	Recommendations
CD4 count and other T cell subsets	Every 3 months
HIV RNA (viral load)	2–8 weeks after starting antiretroviral drugs, then every 3 months
Complete blood count, biochemistry and liver function	Every 3 months
Fasting lipids	Every 6 months if borderline or abnormal, or annually if last measurement normal
Fasting glucose	Every 3 months if borderline or abnormal, or 6-monthly if last measurement normal
HIV resistance analysis – genotyping	At entry into care and at treatment failure (HIV RNA levels need to be >1000 copies/mL for testing)
Hepatitis B serology	At entry into care (If HBsAg positive, use tenofovir in regimen to treat both hepatitis B and HIV. If HBsAb negative, hepatitis B vaccination at 0, 1, 2 and 6 months using double dosage of vaccine)
Hepatitis C	Test if history of injecting drug use. Consider in male to male sexual transmission.
Urinalysis and urinary albumin creatinine ratio	Every 6 months to exclude HIV-associated nephropathy
Pregnancy testing	In women before starting on efavirenz
Sexual health check which may include: Pharyngeal swab – gonorrhoea NAAT/culture First void urine – chlamydia NAAT (in the presence of a urethral discharge, a swab for gonorrhoea culture would also be appropriate) Anal swab – gonorrhoea NAAT/culture and chlamydia NAAT Syphilis serology	Every 3–6 months depending on number of sexual partners and sexual behaviours
Pap smear	Annually
HLA-B*5701 testing for abacavir hypersensitivity	Before starting antiretroviral therapy

Table 1 adapted from references 2 and 14

HBsAg	hepatitis B surface antigen	HBsAb	hepatitis B surface antibody
NAAT	Nucleic Acid Amplification Testing		

have sex with men should be tested for syphilis and other sexually transmitted infections during their routine check-ups (Table 1). Surveillance conducted in inner Sydney since 2006 shows a consistent pattern of 50–55% of all infectious syphilis notifications occurring in HIV positive men who have sex with men.⁷

Other issues relating to sexual health include the effect of ill health, depression and antiretroviral therapies on an individual's

sexual functioning, for example erectile dysfunction, and the effect this may have on sexual relationships.

Mental health

Mental health problems, particularly depression and anxiety disorders, are common among people living with HIV.

HIV-positive men have high rates of major depression – a study of gay men in urban general practice revealed that 32% of

195 men with HIV had major depression compared to 20% of 314 men who did not have HIV. However, HIV status was not independently associated with major depression. Rather, socio-economic hardship, interpersonal isolation and personal withdrawal were the major factors linked to depression in males.⁸

HIV can cause dementia and there is evidence that cognitive impairment develops earlier among people with HIV.⁹ It impairs treatment compliance and adds to morbidity and mortality.

General practitioners are involved in the management of mental health problems, including pharmacotherapy, developing Medicare-funded mental health treatment plans with their patients and facilitating referral for psychological therapy.

Prophylaxis

Prophylaxis against *Pneumocystis jirovecii* pneumonia, usually trimethoprim with sulfamethoxazole, is recommended for patients with CD4 cell counts less than 200 cells/microlitre. Trimethoprim with sulfamethoxazole can also be used as prophylaxis against toxoplasmosis.

Patients with advanced immunodeficiency (CD4 cell count <50 cells/microlitre) should be considered for prophylaxis against *Mycobacterium avium* complex. Azithromycin is usually the best tolerated drug with fewest interactions.

Vaccinations

It is important for general practitioners to be familiar with recommendations around vaccinations (Table 2). This includes standard vaccinations, like influenza and pneumococcal, which

are offered to patients with chronic conditions, hepatitis A and hepatitis B (in those who are not immune), as well as vaccinations relevant for travel.

Doctors should be aware that if the CD4 count is below 350 cells/microlitre, people might not respond adequately to vaccination. There are also safety issues around live vaccines such as MMR (measles, mumps, rubella), BCG (Bacillus Calmette-Guérin) and yellow fever*. If in doubt, specific guidelines are given in the Immunisation Handbook 9th edition,¹⁰ or the treating HIV specialist can be contacted.

Travel

Some countries impose travel restrictions on people with HIV (<http://hivtravel.org>). Recently the USA has removed entry restrictions, which means that people living with HIV can now freely enter that country.

Chronic disease management

General practitioners are ideally placed to manage many of the complex issues facing the individual with HIV infection. A number of these problems are in fact familiar to general practitioners looking after people with any chronic condition.

* If travel to a yellow fever-endemic region by an immunocompromised person cannot be avoided, a medical exemption letter can be written. However, travel and quarantine regulations need to be checked.

Table 2

Vaccinations for people with HIV¹⁵

Vaccine	Recommendations
Hepatitis B	4 double dose injections, at 0, 1, 2 and 6 months
Influenza	Yearly
Pneumococcal	Should be given soon after HIV diagnosis. If CD4 count is <200 cells/microlitre when the vaccine is given, immunisation should be repeated when CD4 count is >200 cells/microlitre
Tetanus, diphtheria and pertussis	Repeat every 10 years
Hepatitis A virus	2 injections, at 0 and 6–12 months
Meningococcal oligosaccharide conjugate vaccine (tetraivalent)	Recommended for all who are travelling to the meningitis belt in sub-Saharan Africa during certain times of the year
Rabies, typhoid (polysaccharide vaccine), oral cholera (inactivated)	Recommended if travelling to an endemic region. Equally applicable as HIV seronegative persons.

Management plans can assist in a number of ways by clarifying the issues for both the patient and doctor. They enhance communication and can facilitate appropriate referral to allied health practitioners and counsellors.

Cardiovascular disease

HIV is recognised to increase the risk of cardiovascular disease. Some antiretrovirals have been found to further add to this risk. Heart disease has been associated with abacavir use in an observational cohort. The protease inhibitor class and efavirenz are associated with lipid dysfunction. The HIV specialist may in some circumstances switch antiretroviral therapy to minimise this risk.

It is also important to manage other cardiovascular risk factors and lifestyle modification. Smoking cessation,¹¹ and improving diet and exercise should be encouraged. Drugs to reduce cholesterol can be used but caution should be taken due to potential drug interactions. Blood pressure should be managed according to current guidelines.

Diabetes

Abnormalities in glucose metabolism are common in patients on antiretroviral therapy. The aetiology is multifactorial and may involve antiretroviral drugs, patient factors (age, body mass index, family history) and perhaps even HIV infection itself. Antiretroviral treatment may lead to glucose abnormalities indirectly through their effects on body composition (peripheral lipoatrophy and central lipohypertrophy).

Current guidelines² suggest screening for diabetes before antiretroviral therapy is initiated, then at 3–6 months and annually after that. Recommendations for monitoring the microvascular complications of diabetes in patients with HIV are the same as for the general population.

The benefits of lifestyle modification in patients with HIV have not been evaluated. However in a small randomised trial of HIV patients with metabolic syndrome, intensive lifestyle changes were associated with significantly reduced HbA1c.¹²

Neurological conditions

Painful peripheral neuropathy can develop as a consequence of HIV infection or as an adverse effect of some antiretroviral therapies such as didanosine and stavudine. Treatment options for painful symptoms include gabapentin, tricyclic antidepressants or narcotic analgesia.

Efavirenz can cause sleep disturbance, anxiety and depression. Most symptoms diminish or disappear within 2–4 weeks of the first dose. Advise the patient to expect adverse effects and that they will probably settle. A short course of benzodiazepines can assist with the unsettling symptoms in the first two weeks. A shorter-acting drug with fewer metabolites is preferred, such as oxazepam, lorazepam or temazepam.

Osteopenia and osteoporosis

These conditions can be associated with androgen deficiency, low body weight and the use of tenofovir. As the cohort of people living with HIV ages, these conditions will become more prevalent.¹³ Consider assessing fracture risk (see www.garvan.org.au/bone-fracture-risk or www.shef.ac.uk/FRAX), and bone mineral density after any fracture following minimal trauma. Encourage weight-bearing exercise and ensure adequate intake of calcium and vitamin D. Hormone replacement may be considered in hypoandrogenous states. Diagnosed osteoporosis should be actively treated. There are no known interactions between bisphosphonates and drugs used to treat HIV.

Renal disease

HIV can cause nephropathy. Contact an HIV specialist should any concerns arise.

Liver disease

Eleven percent of people living with HIV in Australia are co-infected with hepatitis C, 6% with hepatitis B, and 1% have both hepatitis C and hepatitis B. It should be remembered that antiretroviral use (that is, nevirapine and darunavir) can be associated with hepatotoxicity. Transaminase elevation can occur with most antiretroviral therapy. Exclusion of other causes of liver disease and monitoring of liver function are required. Consider alcohol intake as well. Atazanavir commonly causes hyperbilirubinaemia for which no action is required.

Gastrointestinal intolerance

The protease inhibitors lopinavir/ritonavir, fosamprenavir and ritonavir are associated with diarrhoea. Psyllium, loperamide or diphenoxylate/atropine can be trialled to relieve symptoms.

Lipodystrophy

Some antiretroviral drugs have been implicated in the development of redistribution of fat. Lipoatrophy (loss of fat from face and limbs) causes psychological distress. An injectable poly-L-lactic acid is available on the Pharmaceutical Benefits Scheme for the treatment of severe facial lipoatrophy. Practitioners who are trained and registered to perform this procedure are listed at www.lipoatrophy.com.au.

Effects to look out for that may be related to medications

Haematology

Zidovudine and other antiretrovirals are associated with a benign increase in mean cell volume. This is not harmful, but other causes need to be considered and excluded. Zidovudine can also cause life-threatening haemolytic anaemia and bone marrow suppression.

HIV infection causes thrombocytopenia which can respond to antiretroviral therapy.

Drug interactions

Antiretrovirals interact with a wide range of drugs so check for potential interactions before adding a new drug – start low, go slow and monitor the patient closely. If a patient presents with an adverse event, check if they have recently started any new drugs.

It is important to be familiar with some of the potential drug interactions with antiretroviral therapy (see www.hiv-druginteractions.org). Common medications that interact are St John's wort (with protease inhibitors, efavirenz, etravirine, nevirapine and maraviroc) and fluticasone (with ritonavir). Ritonavir, commonly used to pharmacologically boost protease inhibitors, is a potent inhibitor of cytochrome P450 enzymes and has the potential to interact with many common medications. For example, ritonavir can increase the risk of Cushing's syndrome in patients taking inhaled corticosteroids. Conversely, nevirapine and efavirenz are potent inducers of cytochrome P450 *in vivo* and will reduce concentrations of drugs such as methadone and the combined oral contraceptive pill. Warfarin concentrations can increase or decrease with efavirenz and need to be closely monitored.

With statins, there is a potential for interactions through CYP3A4. When prescribing them, use the lowest starting dose and carefully monitor for adverse effects.

The solubility of atazanavir decreases as pH increases. If used concomitantly, proton pump inhibitors should not exceed a dose equivalent to omeprazole 20 mg daily and should be administered at least 12 hours before atazanavir. Proton pump inhibitors should not be given to treatment-experienced patients already taking atazanavir as plasma concentrations of atazanavir may be reduced and loss of efficacy and viral resistance can occur.

All protease inhibitors increase the concentration of phosphodiesterase type 5 inhibitors (for example sildenafil). If needed, start with the lowest dose of the erectile dysfunction drug and monitor for adverse effects.

Conclusion

The treatment of HIV infection continues to evolve and people with HIV are living longer. General practitioners are likely to need to become more involved in providing care to people with HIV using their skills to manage the problems associated with chronic medical conditions.

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Further reading

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 91)

1. Ritonavir can increase the risk of Cushing's syndrome in patients taking inhaled corticosteroids.
2. Vaccination may not be effective in patients who have a CD4 count below 350 cells/microlitre.

Dental notes

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Doctors treating patients with HIV should be cognisant of the oral problems that occur in these patients. While their immunological status is reasonable, the majority of these patients will not develop the classically recognised oral manifestations of HIV disease, such as florid pseudomembranous candidosis, Kaposi's sarcoma or oral hairy leukoplakia. However, the patients are likely to have oral problems associated with their long-term treatment.

A recent study assessed the long-term use of highly active antiretroviral therapy (HAART) on the oral health of HIV-infected patients. The multiple logistical regression analysis, controlling for duration of HIV infection, CD4 count, smoking habits and alcohol consumption, showed patients have a greater risk of developing oral lesions with long-term use than with short-term use of HAART.¹

Patients with HIV can develop profound oral dryness with a resultant increase in traumatic mucosal ulceration and pain, as well as an increased likelihood of developing dental caries. Furthermore, these patients have an increased risk of periodontal disease, dental decay, oral infections and poor healing after periodontal treatment or extraction. It is advisable for the treating clinician to discuss with the patient the potential dental adverse effects of the long-term use of HAART. Early referral to a dentist for appropriate management is important, particularly for the establishment of an effective dental preventive program. The key to oral health management would be six-monthly reviews by a general or special-needs dentist with an interest and training in the dental management of patients with HIV.

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Patient support organisation

NAPWA, National Association of People living With HIV/AIDS

NAPWA is Australia's national peak organisation representing people living with HIV. Its website has a range of resources and links to its member organisations in every state and territory.

NAPWA promotes access to the latest treatments for those who need them. It produces educational resources, provides training in HIV medicine for community workers, and

collaborates with healthcare professionals, researchers, government and pharmaceutical companies.

Contact

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There are member organisations in every state and territory. Contact the national office for up-to-date details.