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General Practitioners and HIV

In the primary care setting, General Practitioners (GPs) play a vital role in the prevention of transmission of the Human Immunodeficiency Virus (HIV), and the provision of care to people living with HIV (PLHIV), specifically in early diagnosis and management.

This resource will address the following:

PREVENTION
- Pre-exposure prophylaxis (PrEP)
- Post-exposure prophylaxis (PEP)
- Treatment as Prevention (TaSP)

DIAGNOSIS
- Testing

MANAGEMENT
- GP shared care arrangements for PLHIV
- Becoming accredited to prescribe antireretroviral therapy (ART)

Is HIV still a concern… the numbers
- At the end of 2017, 27,545 people were estimated to be living with HIV in Australia.
- Prevalence highest in men who have sex with men (MSM).
- HIV prevalence has increased by 14% between 2016 and 2017 for those who only risky behaviour was heterosexual contact

HIV throughout the life-span

HIV infection is now considered a manageable chronic disease. Newly diagnosed PLHIV who adhere to ART have a similar life expectancy as the general population. ART vastly improves the lifespan of PLHIV because of its effectiveness and as a result, the mean age of the HIV-positive population has increased quite dramatically since 1986.

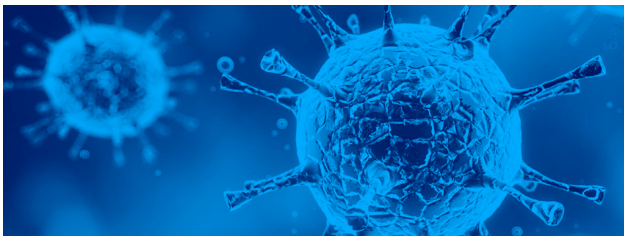
The health needs of the aging HIV positive population are similar to those of the general aging population. However, special attention is required for their relatively higher susceptibility to co-morbidities, such as malignancies and cardiovascular disease. PLHIV will continue to need comprehensive general practice care to age successfully.

Breaking HIV down

The Virus

HIV is a single-stranded ribonucleic acid (RNA) virus. It has an outer envelope that surrounds two copies of single-stranded RNA as well as a number of viral proteins. The HIV replication commences when the envelope 120 glycoprotein (gp 120) attaches to CD4 receptors expressed on the surface of lymphocytes.

Attachment allows fusion of the membranes of virus and cell at viral entry. The RNA is converted to deoxyribonucleic acid (DNA) which migrates to the cell nucleus and integrates as proviral DNA into the host cell DNA.



Natural History

Following infection with HIV, there is a period of high level viraemia associated with immunosuppression as measured by a reduction in the CD4 lymphocyte count. A host immune response then develops, partially controlling viral replication, but is unable to clear HIV from the body.

The majority of PLHIV develop a mononucleosis-like HIV seroconversion illness characterised by fever, pharyngitis, lymphadenopathy, rash, splenomegaly and aseptic meningitis. Others may either be asymptomatic or have subclinical illness. Symptoms of acute infection resolve as the immune system mounts an antiviral response that causes the viral load to decrease markedly. Simultaneously, there is a rebound increase in CD4 cell count to near baseline levels and the virus enters a period of clinical latency, although very high levels of replication continues, especially in lymphoid tissue.

The plasma HIV RNA plateaus to a level of viraemia known as the virological 'set point'. If left untreated, there is a gradual decline in CD4 cell count, with a median loss of 80 cells/uL per year. However, starting antiretroviral therapy causes a decrease in viral load which will reverse this decline in CD4 cells. Therefore, earlier treatment can potentially protect the individual's CD4 cell count. It also diminishes the size of the latent pool of HIV infected CD4 cells by reducing the number of infected CD4 cells.

If untreated, progression to AIDS, marked by the development of opportunistic infections or specific malignancies, occurs a median of 10 years after initial infection with HIV. At this time the CD4 cell count has usually fallen below 200 cells/μL and the person becomes severely immunocompromised (Figure 1).

Transmission

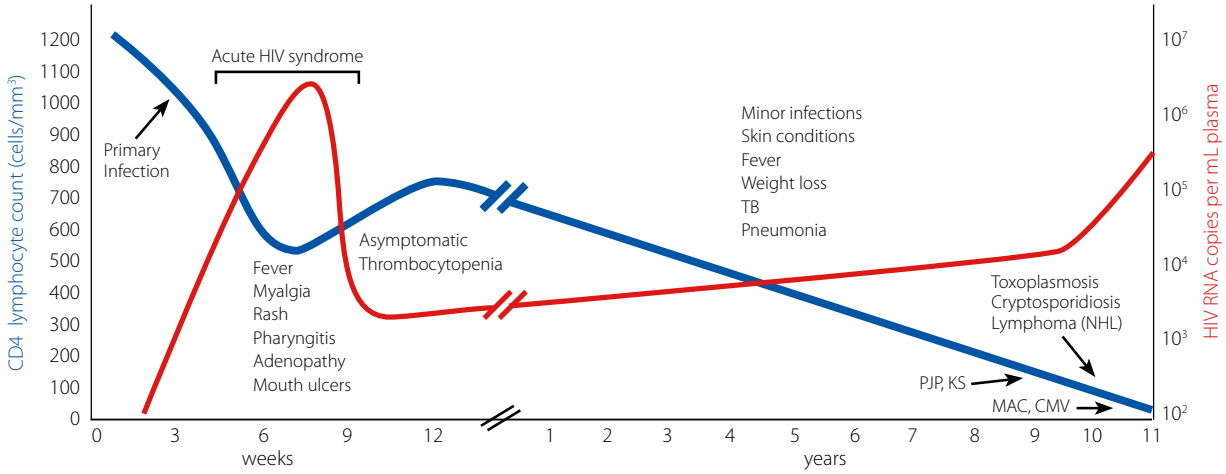
In Australia, transmission most commonly occurs in MSM (63% of the 2017 notifications), whereas in developing countries, especially in Africa, HIV is predominantly acquired through heterosexual contact (Table 1).

Modes of transmission and increased risks of transmission

i. **Concurrent sexually transmissible infection (STI)** - also likely to increase risk of HIV infection. An STI can be a marker of recent or past risk, and genital inflammation itself may place the individual at higher risk of HIV infection.
ii. **Injecting drug use (IDU)** - uncommon in Australia, accounting for 3% of newly acquired HIV infections in 2017 but is particularly prevalent in parts of Europe, Asia and the USA.
iii. **Blood products** - largely occurred before the introduction of antibody screening in 1985 in Australia and was responsible for the high incidence of HIV among multiply transfused people, such as those with haemophilia. It is now exceedingly rare in countries where blood is screened.
iv. **Needlestick injury** - occurs in 0.3% of exposures from individuals with HIV infection where prophylaxis is not used.
v. **Perinatal transmission** - occurs in 20–45% of infants born to mothers with HIV, but this rate can be reduced to less than 5% with the administration of antiretroviral therapy during pregnancy, labour and after delivery, and other interventions such as avoidance of breast feeding. Indeed, from 2013 to 2017, the rate has reduced to 1% of newborns in Australia.

Figure 1: HIV Natural History

The various stages of untreated HIV infection depicting the development of different opportunistic infections with advanced immunodeficiency.



mac: mycobacterium avium complex, **cmv:** cytomegalovirus, **ks:** kaposi sarcoma, **pjp:** pneumocystis jirovecii pneumonia, **tb:** tuberculosis

UNDECTABLE = UNTRANSMITTABLE

Importantly, recently published studies have shown that no transmission has occurred from a partner with undetectable viral load within both homosexual and heterosexual couples, where undetectable viral load is defined as less than 200 copies /ml for 6 months and is achieved by taking ART daily as prescribed. Treatment is therefore very effective at reducing HIV transmission, which is known as 'treatment as prevention (TaSP)'.

Please refer to ***ASHM Undetectable = Untransmittable: A guide for clinicians*** to discuss for further details. https://www.ashm.org.au/products/product/UequalsU

COULD IT BE HIV?

Be alert in the context of flu-like illness, with symptoms such as:

- Glandular fever-like illness that is Epstein-Barr virus (EBV) seronegative
- Flu-like symptoms outside usual influenza season (e.g. myalgia, arthralgia, headache, malaise)
- Fever for more than three days
- Maculopapular rash
- Meningeal involvement
- Transient neurological syndromes (e.g. Guillain-Barré syndrome, neuropathies)
- Recent evidence of STIs or genital ulcers

Signs and Symptoms

- Signs and symptoms of acute HIV infection can present as early as three days or as late as 10 weeks following transmission.
- Onset of symptoms often coincides with the appearance of HIV antibodies although the enzyme linked immunosorbent assay (ELISA) may be HIV antibody negative for up to three weeks after onset of symptoms.
- Duration of the seroconversion illness is most commonly 4 to 14 days but may be longer.

Approximately 50 to 90% of PLHIV report signs or symptoms suggestive of primary HIV infection at the time of seroconversion. PLHIV who experience a severe symptomatic primary HIV infection appear to have more rapidly progressive HIV disease than those who do not.

While no single symptom distinguishes acute HIV infection from other acute viral illnesses, there are some factors that should alert the clinician to the possibility of acute HIV infection in the context of.

Please refer to ***ASHM Decision Making in HIV Tool*** for further referral and assessment suggestions. https://www.ashm.org.au/resources/hiv-resources-list/

Co-infection with Hepatitis B (HBV) or Hepatitis C (HCV)

Multiple blood-borne viral infections in the same individual can alter the natural history (course/progression) of disease. HBV has no adverse effect on HIV or the development of

Table 1: Exposure and transmission risk/exposure with knownHIV positive source

Type of exposure with known HIV positive source	Estimated risk of HIV transmission/exposure [a]
Receptive anal intercourse - ejaculation - withdrawal	 1/70 1/155
Contaminated injecting equipment	1/125
Insertive anal intercourse (IAI) uncircumcised	1/160
Insertive anal intercourse (IAI) circumcised	1/900
Receptive vaginal intercourse (RVI)	1/1250
Insertive vaginal intercourse (IVI)	1/2500
Receptive or insertive oral intercourse	Unable to estimate risk - extremely low
Needlestick injury (NSI) or other sharps exposure	1/440
Mucous membrane and non-intact skin exposure	<1/1000

[a] These estimates are based on prospective studies, not cross-sectional data or figures derived from modelling.

AIDS, but HIV does influence HBV and can be associated with accelerated development of cirrhosis and liver failure. Drugs that are effective against both HBV and HIV are available now and should be used for treatment.

Individuals with HIV and HCV co-infection typically have higher HCV viral loads and a more rapid course to end-stage liver disease. Since March 2016, HCV treatment (with cure rates above 90%) has been available in Australia through the PBS listing of the Direct Acting Antivirals (DAA) for all those living with HCV over 18 years old. The DAA treatment cure rates are the same for those co-infected with HIV/HCV as those mono-infected with HCV.

Initial HIV ART regimens that are recommended for most PLHIV with HCV/HIV coinfection are the same as those recommended for individuals without HCV infection. When treatment for both HIV and HCV is indicated, the ART and HCV treatment regimens should be selected with special consideration for potential drug-drug interactions and overlapping toxicities, as these may cause liver-associated complications that may affect the treatment of HIV in PLHIV with coinfection.

Please refer to ***ASHM Decision Making in HCV Tool*** and ***HCV Treatments Quick Reference Tool*** for further referral and assessment suggestions. https://www.ashm.org.au/resources/hcv-resources-list/

Prevention of HIV Transmission

The use of pre-exposure prophylaxis (PrEP) for the prevention of HIV infection largely lies in the primary care setting. Post-exposure prophylaxis (PEP) is also an effective strategy for the prevention of HIV infection.

Non biochemical

The use of condoms for anal or vaginal sex, and the use of new (clean) injecting equipment remain effective as a non-biochemical means of preventing the transmission of HIV.

Biochemical

Post-Exposure Prophylaxis (PEP)

There is evidence from a number of studies that a course of antiretroviral therapy, commenced within 72 hours of high-risk exposure to HIV and continued for 28 days from first exposure can reduce the risk of HIV infection.

Exposure to HIV can occur in:

i. **Occupational settings -** e.g. needlestick injury
ii. **Non-occupational settings** ie. sexual contact (e.g. through unprotected sex or condom breakage
iii. **Other means -** sharing of injecting equipment.

PEP involves:

- Taking a combination of antiretroviral medication (either a 2-drug regimen of Tenofovir and Emtricitabine, or Tenofovir and Lamivudine; or a 3-drug regimen where Dolutegravir, Raltegravir or Rilpivirine is added to the 2 drug regimen) for 28 days
- Commenced as soon as possible after and within 72 hours of a high-risk exposure to HIV
- To determine whether PEP is to be prescribed, a case-by-case comprehensive assessment of HIV transmission risk is carried out; based on
  - The nature of the exposure with its estimated risk per exposure
  - The HIV status of the source individual or the risk that the source individual is HIV positive, if their status is unknown
  - Factors associated with the source or exposed individual

Clinicians inexperienced in PEP initiation should always refer to and adhere with the most recent PEP protocols and seek appropriate advice from experts if required about administration of PEP.

It is important that clinicians respond to PEP presentations in a non-judgemental way, using non-stigmatising language, as there have been documented cases where people did not re-present for PEP due to a previous negative experience and then later seroconverted.

Please refer to ***ASHM Post-exposure Prophylaxis for HIV: Australian National Guidelines*** and ***ASHM PEP*** page for further information, including National Procedure Flowchart
http://www.pep.guidelines.org.au/
https://www.ashm.org.au/HIV/hiv-management/PEP/

Pre-exposure prophylaxis (PrEP)

PrEP involves:

- Taking HIV antiretrovirals (co-formulated tenofovir and emtricitabine) prior to potential HIV exposure.
- Is highly effective in preventing sexual transmission of HIV when used with optimal medication adherence.

Accessing PrEP:

1. **Medicare eligible –** through any GP using using Pharmaceutical Benefits Scheme (PBS) scripts at a subsidised cost.
2. **Medicare ineligible -** any GP to access PrEP but will be required to legally import PrEP using the Therapeutic Goods Administration (TGA) Personal Importation Scheme (PIS) or pay full price with a private script.

Who should be considered for PrEP:
All people at risk of HIV infection should be considered for daily PrEP, including:

- Men who have sex with men (MSM)
- Transgender people who have sex with men
- Heterosexual men and women in some circumstances
- People who inject drugs (PWID)

In the most recent guidelines, on-demand PrEP is recommended as an alternative option *only* for cis-gender MSM, who are HBV non-infected, because its' efficacy is yet to be determined in all other populations at risk of HIV infection.

For more information on prescribing on-demand PrEP, please see page 32-39 in ***ASHM PrEP Clinical Guidelines (last updated September 2019)*** https://ashm.org.au/resources/hiv-resources-list/

Assessment of the risk of HIV infection is determined by the clinician after obtaining a full sexual and drug-use history from a person, based on the PrEP suitability criteria for different groups (MSM, transgender & gender diverse, heterosexual and PWID) as per the ASHM PrEP Guidelines (Sept 2019).

PrEP recommendation is based on a person's past, or future, risk of HIV infection over 3 months. Clinicians are also encouraged to use a case-by-case approach as some people who do not meet the suitability criteria may still benefit from PrEP.

People who have been started on nPEP may transition to PrEP with clinician guidance. Close monitoring over 2-8 weeks for HIV seroconversion should be carried out for those with recent high-risk HIV exposure but outside the 72-hour window for nPEP, and who have been started on PrEP.

Before starting PrEP, a person must have a negative fourth generation HIV antigen/antibody test result documented at the time of evaluation for PrEP and must also be free from any clinical signs or symptoms of acute HIV infection.

Other assessments at baseline include

i. Renal function
ii. Sexually transmitted infections (STIs)
iii. Hepatitis A, B and C status
iv. Bone health, and
v. Pregnancy

Initial and ongoing prescriptions for PrEP should offer a 90-day medication supply. Supply can vary based on use and other situations.

- Laboratory and clinical follow-up schedules are outlined in the ***ASHM PrEP Clinical Guidelines (last updated September 2019***. See Table 7.1. https://ashm.org.au/resources/hiv-resources-list/
- For an assessment and evaluation tool, please see ***ASHM Decision Making in PrEP*** https://ashm.org.au/resources/hiv-resources-list/decision-making-in-prep/
- For more information, please see www.ashm.org.au/HIV/PrEP

Testing

Regular testing of those at risk is a strategic role for GPs in the early diagnosis of HIV and in reducing transmission

HIV and STI testing should be raised routinely and incorporated into regular health checks for all those at risk but especially for those in higher risk groups.

The fourth generation HIV antibody test, now accompanied in Australia by a test for HIV p24 antigen, is the most accurate test available to clinicians with its extremely high sensitivity and specificity (Table 2). False positives can still occur in very low-prevalence populations, but these can soon be clarified by supplementary HIV Western blot testing.

When HIV testing is indicated:
Sexual contact: MSM, transgender and gender diverse people who have sex with men, multiple or change of partners, sexual partners of the previous groups of people

- Recreational drug use: PWID, Methamphetamine-related illness, injecting partners of the previous groups of people
- People from high-prevalence countries; or travelled to high prevalence countries and engaged in high risk exposure
- A health-care worker conducting exposure-prone procedures or certain health-care settings, e.g. high prevalence of HIV, unsafe injections/transfusions.
- Contact tracing
- Mental health conditions associated with risk taking behaviour
- Pregnant women (+ retesting if ongoing risk during pregnancy)
- Blood transfusion, or blood/other tissue-derived products before 1985 in Australia, or from high risk overseas locations
- A specific request to a health-care service for an HIV test
- A reactive or inconclusive result on an HIV point-of-care test, HIV self-test or an HIV test performed overseas
- In the context of Post-Exposure Prophylaxis (PEP), subject to national and jurisdictional guidelines and policy
- As part of an initial and ongoing assessment for Pre-Exposure Prophylaxis (PrEP) or in the management of a person taking PrEP
- The presence of any symptom or diagnosis which could be indicative of HIV infection (an indicator condition*)

For the latest guidance on HIV testing please see the National HIV Testing Policy available at: www.testingportal.ashm.org.au/hiv

The Window Period

- Defined as the period after which it is certain that the person being tested for an infection will not seroconvert following exposure to that infection.
- The window period for HIV testing is still officially quoted as three months since the time of exposure, though the majority of individuals will seroconvert within six weeks of acquiring HIV infection.
- Some individuals take longer than six weeks to seroconvert, hence, the policy regarding the three-month window period

Rapid HIV Testing or Point-of-Care Testing (PoCT)

In December 2012, the Therapeutic Goods Association (TGA) approved the first point-of-care test for use in preliminary HIV screening in Australia. The point-of-care tests, also known as rapid tests, allow for on-the-spot HIV screening, with results delivered at the same appointment.

Although PoCT may have a longer window period than conventional tests, it is considered a way to increase HIV testing among high risk groups who may have barriers accessing the conventional test. Such barriers include: the need to attend a health service to access a test, time taken for test results to be available, poor access to health care providers, stigma and the risk of discrimination.

The sample tested is either finger prick capillary blood or mouth (oral) fluid and results usually appear (usually available) within 10-30 mins, which increases HIV testing among high risk populations, increases the number of people who receive their test results and decreases the number of undiagnosed HIV cases.

The TGA has set out strict conditions for their use, to ensure quality of care.

Reactive results must be followed up with a venous blood sample, sent to a diagnostic laboratory for confirmatory testing.

Refer to the latest National Testing Policy.

Informed consent for testing and conveying HIV test results

As for all pathology testing, informed consent is required for HIV testing, except for rare occasions when a legal order is made for compulsory testing or in emergency settings.

Informed consent for HIV testing means that the person being tested agrees to be tested on the basis of understanding the HIV testing procedures, the reasons for testing and is able to assess the personal implications.

For some people with a heightened awareness of HIV, routine HIV testing may be a behavioural norm. For others with little understanding of HIV or their potential risk of exposure, HIV testing may be novel, frightening and perceived as highly stigmatising.

This is also an opportunity to provide information and support around the testing procedure, to minimise the personal impact of diagnosis, to change health-related behaviour and to address

Table 2: Pathology tests for diagnosis of primary HIV infection

HIV antigen tests	
p24 antigen	p24 antigen may become positive within a few days of symptoms and be absent after two weeks.
Quantitative HIV RNA viral load by reverse transcriptase polymerase chain reaction (RT PCR)	HIV RNA viral load may become positive within a few days. However, the quantitative viral load assay is generally not recommended to diagnose acute HIV infection due to a reported low false-positive rate in the acute setting (usually indicated by low viral levels).
HIV antibody tests	
HIV antibodies (Enzyme immunoassay)	Enzyme immunoassay may take up to three weeks to become positive after onset of clinical signs and symptoms
HIV Ag/Ab Combo Test	The majority of labs use this test as the standard HIV antibody screening test. This is a combined p24 antigen plus HIV antibody test and so it will become positive before a test using HIV antibody alone in acute infection.
HIV antibodies (Western Blot)	Western Blot may take up to three weeks to become positive after onset of clinical signs and symptoms

Note: Other tests may be indicated and should be performed in conjunction with specialist centres and laboratories

the anxiety of the person being tested. The discussion process also allows the clinician to assess risk, to educate the person regarding risk of transmission, to obtain informed consent, and to follow up and arrange referrals as indicated (Table 3).

During the discussion process, information is exchanged, and concerns explored. Coping strategies are developed that may be used in the event of a positive result. While discussion does not need to proceed according to any formula, key information areas need to be covered during the consultation. Referring to a framework of key points ensures that the necessary information regarding blood-borne viruses is conveyed.

Formal counselling is frequently required in the management of a person who has tested positive, or in the situation where a person who tested negative is continuing to participate in high-risk behaviours for HIV. This counselling is usually specialised and requires referral to an appropriate service or practitioner (Table 4).

The discussion should be performed in a way that is relevant and appropriate to the person's gender, culture, behaviour, language, and their understanding of HIV testing and testing history. That is, the discussion that occurs with a high-risk man who has sex with men in a major city will differ from that which occurs with a pregnant Indigenous woman undergoing testing in a remote area of Australia.

Table 3:
Gaining informed consent: discussion points

Reason for testing and risk assessment
Timing of risk and option of post-exposure prophylaxis (PEP)
Need for other sexually transmissible infection (STI) and blood-borne virus testing
History of previous HIV testing
Confidentiality and privacy issues around testing
Natural history and transmission information (if appropriate)
Prevention of transmission and risk reduction through behaviour change
Implication of a positive test result, including availability of treatment
Implications of a negative test result
Explanation of the window period
General psychological assessment and assessment of social supports in the event of a positive result
Logistics of the test: time taken for results to become available and the method of delivery of results

All positive HIV test results should be given in person, however, the clinician ordering the test may consider delivery of HIV test results to PLHIV by telephone or by another mutually agreed method in some cases.

Key points of conveying a negative result

- Explain the negative test result and the window period (if relevant)
- Reinforce education regarding safer behaviours
- Consider vaccination – for hepatitis B and, if indicated, hepatitis A (in men who have sex with men) and human papillomavirus (HPV)
- Further discuss anxiety or risk behaviours
- Discuss testing for other STIs.

Table 4:
Conveying a confirmed positive test result: discussion points

First post-test consultation
Establish rapport and assess readiness for the result
Know referral pathways, both clinical and psycho-social
Give positive test result
Avoid information overload
Listen and respond to needs (the patient may be overwhelmed and hear little after being told the positive result)
Discuss the immediate implications and treatment options if patient ready for the information
Review immediate plans and support
Reassess support requirements and available services
Arrange other tests and the next appointment
Begin contact tracing process and discuss options available to facilitate this
Subsequent consultations
Treatment options, diet and exercise
Effect of diagnosis on relationships and prevention information
Issues of disclosure
Assessment of contact tracing process and difficulties encountered
Access to life insurance may be affected
Workplace implications
Impact of other issues (e.g. drug use, poverty, homelessness) on ability to access health care and treatments
Referral for on-going counselling, social worker, medical specialist as appropriate

Key points of conveying a positive result

- Ensure privacy and undertake the consultation in an area where you will not be interrupted.
- Discuss treatment options where appropriate
- The information and support may be provided over a number of consultations and discussion should include those points listed in Table 4.
- It is important to explain to someone who has recently acquired HIV infection that they are highly infectious during early infection due to high HIV viral loads in their blood and body fluids.

Indeterminate Results

- Occasionally, an equivocal or indeterminate result from HIV testing may occur.
- Can be a source of great anxiety
- Seek advice in interpreting indeterminate results from specialist HIV clinicians based in hospitals or public sexual health clinics or from pathology laboratory staff.
- In the case of HIV antibody testing, a positive ELISA and a single band on Western blot constitutes an indeterminate result.

Next steps

A person with an indeterminate result who has reported a recent high-risk exposure is regarded as being in the window period of infection and may require considerable support during this time to deal with anxiety. Further tests for viral antigens may be indicated to test for the presence of infection and should only be performed in consultation with a specialist clinician.

False positives

In populations of low seroprevalence of bloodborne viral infections, indeterminate results may be false positives. Factors such as pregnancy, past blood transfusions, intercurrent viral infections, autoimmune diseases and malignancies may play a role in indeterminate results. Upon re-testing at approximately two weeks, a second indeterminate result where there has been no progression at all in development of bands in the HIV Western blot is regarded as confirmation of negative status.

However, to be sure and to address absolutely the fears of the person being tested or the health care worker's doubts, HIV testing at approximately 12 weeks post-exposure should be performed.

Treatment

Following diagnosis, people living with HIV (PLHIV) will then need life-long antiretroviral therapy (ART), which may be provided by GPs with advanced training or HIV specialists.

Initiating Antiretroviral Therapy

The Australian Antiretroviral Guidelines

Antiretroviral treatment guidelines based on expert opinion and available scientific evidence, have been developed to guide decisions about commencing and switching treatment. Australia adopts the United States Department of Health and Human Services guidelines and adds an Australian commentary where local issues are relevant. These guidelines are available via the ASHM website: https://arv.ashm.org.au/.

When to intiate

i. **As soon as possible -** The Australian Antiretroviral Guidelines recommend that ART should be initiated for all PLHIV, regardless of their CD4 T cell count. When the PLHIV feels ready to start needs to be considered also.

ii. Immediate initiation of ART is recommended in the following circumstances:
Prevention of onward transmission of HIV
Individuals >50 years
Rapid CD4 cell decline
Hepatitis B co-infection requiring treatment for HVB
Early HIV infection
HIV associated neurocognitive disorders
Malignancies requiring immunosuppressive
Chemotherapy or radiotherapy
Tuberculosis

Benefits of ART

- Reduces HIV-related morbidity and mortality at all stages of infection, improving the duration and quality of survival for PLHIV
- Suppresses the plasma viral load to levels below assay detection
- Prevents HIV transmission (treatment of PLHIV with ART reduces the risk of HIV transmission to a HIV negative sexual partner by 93% and reduces the risk of perinatal transmission to 0.1-0.5%)
- Improves CD4 cell counts
- Prevents or delays drug resistance
- Decreases immunological responses and inflammation responsible for cardiovascular and other end-organ damage reported in PLHIV.

Viral suppression below limits of detection is now achievable with the increasing numbers of ART drugs and drug classes, and usually takes 12-24 weeks of therapy to occur. Predictors of success include low baseline viremia, tolerability of the regimen, and excellent adherence to the regimen.

The decision to start ART should take both personal health benefits and risks, and transmission risk reduction into consideration. Clinicians should discuss the latest knowledge regarding ART initiation with PLHIV who are not on treatment.

The decision made by PLHIV to start ART should be fully informed and supported. When starting ART, PLHIV should be educated about the benefits and considerations regarding ART, and strategies to optimize adherence should be addressed. Advice regarding the decision can be obtained from an experienced antiretroviral HIV prescriber and resources listed at the end of this booklet.

How ART works

Antiretroviral drugs inhibit enzymes involved in viral replication inside the CD4 cell (usually reverse transcriptase, protease or integrase). PLHIV commencing treatment should be started on a combination of drugs from at least two different drug classes. Treatment regimens are developed at the individual level based on dosing requirements, toxicity profiles and co-morbidities.

Antiretroviral Medications

There are more than 25 individual ART medications in six major classes of HIV agents available in Australia in 2019:

- Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Protease inhibitors (PIs)
- Fusion inhibitors (FI)
- CCR5 antagonists
- Integrase strand transfer inhibitors (INSTIs)

Who can prescribe ART

Only an HIV s100 prescriber, sexual health physician or HIV specialist can initiate ART.

If you are interested in prescriber training or HIV management as a GP through shared care, please visit ***ASHM Training Page*** https://www.ashm.org.au/training/ for more information.

Adverse Effects of Antiretroviral Therapy

Newer ART regimens are much more tolerable and have far fewer adverse effects than older regimens. Adverse effects of antiretroviral therapy may be early (e.g. headache), persistent (e.g. diarrhoea) or long term (e.g. lipodystrophy). The individual should be supported through initial adverse effects, most of which are very common and usually short lived. Individualised therapy in which long-term adverse effects are avoided should be considered.

For further information, refer to https://arv.ashm.org.au/adverse-effects-of-antiretroviral-agents/.

Some adverse effects are life-threatening and necessitate immediate cessation of the medication and initiating of an alternative treatment without overlapping toxicities. These include acute hepatitis, severe rashes including the Stevens-Johnson syndrome (associated with the NNRTIs) and the abacavir hypersensitivity reaction. This reaction occurs within six weeks of starting abacavir and symptoms include fever, nausea, vomiting, diarrhoea and malaise, with or without rash, and is largely avoidable with HLA-B*5701 testing.

Lactic acidosis is a rare adverse effect associated with the nucleoside analogues, which may lead to multi-organ failure and death. Usually the antiretroviral prescriber will monitor very closely through this phase. If the primary care clinician is presented with this problem, the antiretroviral prescriber should be consulted.

Non-life-threatening adverse effects e.g. urolithiasis with atazanavir [ATV], renal tubulopathy with tenofovir disoproxil fumarate [TDF]) are managed by substituting another ART agent for the presumed causative agent without interrupting ART. Other chronic non-life-threatening adverse effects (e.g. dyslipidaemia) can be addressed either by switching the potentially causative agent for another agent, or by managing the adverse effect with additional pharmacological or nonpharmacological intervention. Management strategies must be individualised for each person.

Adherence Issues

Although newer ART medications have a higher barrier to resistance and are more forgiving compared to older medications, adherence is still very important and needs to be addressed at every monitoring visit.

Suboptimal adherence to the ART therapy may lead to virologic failure and drug resistance, opportunistic infections, and increased morbidity and mortality. Drug resistance limits future options of effective ART regimens, as unfortunately, there is often significant cross-resistance within the same class of antiretroviral drugs and resistance to one drug may undermine response to subsequent regimens.

Suboptimal adherence may result from a complex treatment regimen, factors including depression, substance use and intolerable adverse effects, or health system issues including inadequate treatment education and difficult access to medication. Strategies to manage these issues must be implemented to improve adherence

Key components of medication-adherence counselling include:

1. Establish trust and bidirectional communication

2. Provide simple explanations and education

- Medication dosage and schedule
- Management of common adverse effects
- Relationship of adherence to the efficacy of treatment

3. Support adherence

- Tailor daily dose taking to a daily routine (e.g. with tooth brushing, or before bed)
- Identify reminders and devices to minimise forgotten doses
- Identify and address barriers to adherence

4. Monitor medication adherence in a non-judgemental manner

- Normalise occasional missed doses, while ensuring the importance of daily dosing for optimal protection is understood
- Reinforce success
- Identify factors interfering with adherence and address those factors

5. Assess adverse effects and plan on how to manage them

Monitoring and the Role of the GP

PLHIV require regular monitoring of their immune function and will need more intense monitoring after starting or changing antiretroviral medication (ART). Once stable, however, six-monthly reviews of HIV viral load and CD4 count are considered sufficient (see table 5). At these review visits adherence, adverse effects and possible drug interactions are also checked. Periodic biochemistry and urinalysis are performed to check for toxicity. The HIV prescriber will normally perform these tests. Frequently this will be a GP who has undertaken additional training.

To formalise the assessment and monitoring process for PLHIV, it is recommended that GPs implement a GP Management Plan (GPMP) for HIV. Please see the ***ASHM resource HIV Shared Care for GPs*** (www.ashm.org.au/HIV/hiv-management/hiv-shared-care-for-gps) for more details.

Close monitoring is required at the initial period of treatment, when adverse effects are more common, and modifications of treatment may be required. This period lasts about 3 months, which is the time needed for HIV blood levels to become undetectable. Low viral load will be associated with recovery of CD4 counts. The recovery process is slow and may take several years. Once stable on treatment, and HIV viral load is undetectable, frequency of monitoring can be reduced to every 3-6 months.

For those PLHIV who meet the requirements of "Undetectable = Untransmittable", intensive professional support may be needed to maintain their treatment adherence. See ***ASHM Undetectable = Untransmittable: A Guide for Clinicians to Discuss*** for more information: https://ashm.org.au/products/product/UequalsU.

Table 5: Assessment and monitoring of the patient with HIV infection

All visits

- History and symptom review
- Psychosocial assessment and support
- Patient education (e.g. transmission, treatment options)
- Health promotion (e.g. safe alcohol use, smoking cessation)

6 monthly review

- Weight, BMI, BP, waist circumference
- Full blood count
- Liver function tests
- Renal function
- CD4 cells count, HIV viral load
- STI screening including syphilis serology (depending on risk group)

Annual reviews

- Assessment of immunity to hepatitis A and B and vaccination if susceptible, hepatitis C antibody if at risk
- Influenza vaccination, (pneumococcal vaccination - see guidelines)

Annual reviews (continued)

- Cervical screening test (3 yearly)
- Fasting cholesterol (including HDL and LDL), triglycerides and glucose
- Urinalysis
- Cancer screening as per guidelines (colon, breast)
- Cardiovascular risk calculation
- Physical assessment for lipodystrophy (fat wasting, fat accumulation)
- Review risks for osteoporosis
- Refer for annual dental check
- Additional monitoring for PLHIV taking antiretroviral therapy
- Frequent review during the first month of treatment by prescriber
- Monitoring for severe adverse effects (e.g. hypersensitivity, CNS toxicity, neuropathy)
- Management of treatable adverse effects (e.g. nausea, diarrhoea
- Adherence monitoring and support
- Review possible drug interactions

Most other monitoring is in line with standard GP care, as detailed in the ***RACGP Red Book*** (https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/red-book) and the ***Immunisation Handbook*** (https://immunisationhandbook.health.gov.au/vaccination-for-special-risk-groups/vaccination-for-people-who-are-immunocompromised)

However the following should be considered:

i. **Cardiovascular disease :**more common in PLHIV, so risk factors, such as smoking, need to be managed.
ii. **Cancer screening:** follow standard guidelines for the general population. These checks will frequently need to be performed by the PLHIV's regular GP (who may be their HIV treatment provider) rather than by the HIV clinic.
iii. **Sexual health monitoring** will depend on risk factors. Men who have sex with men are advised to have frequent sexual health checks including comprehensive testing for chlamydia, gonorrhoea, syphilis and HCV.
iv. **Hepatitis A, B and C:** Vaccinate for hepatitis A and B if susceptible.
v. **Respiratory infections:** are more common in people with HIV, so it is recommended to provide annual influenza vaccinations and periodic pneumococcal vaccination (per guidelines).
vi. **Depression/anxiety and other mental health problems:** are more common in PLHIV. The GP is ideally placed to screen for and detect mental health problems, to provide early treatment and to refer if needed.

Legal responsibilities

This section refers to a number of key Australian laws and policies relating to privacy, confidentiality and duty of care. Although addressing some important questions, this information does not constitute legal advice. Practitioners who are uncertain about their statutory or common law obligations to PLHIV or to the local Health Department, including privacy and reporting obligations, are strongly advised to contact their local Health Department or applicable privacy office or to seek independent legal advice.

For further information, refer to: https://hivlegal.ashm.org.au/

Provision of Information to a Patient

The provision of information, and the exchange of information between a health care provider and a patient, are key elements in any treatment or procedure. This process of engagement between a patient and clinician and any agreement about treatment is often called informed consent. The aim of such discussion is to enable a patient to consider the information that is provided in order to facilitate his or her decision making.

Further, a health care practitioner should advise a person who is found to have acquired HIV of what the law may demand of him or her. Each state and territory's body of law deals with this area differently so please refer to the appropriate guidelines.

Confidentiality

Health practitioners will be well aware of their duty to maintain the confidentiality of PLHIV. This duty is now reinforced by Commonwealth and State privacy laws. Practitioners should seek legal advice if they have questions regarding their duty of confidentiality.

Notification of Third Parties

Health care practitioners may become aware a PLHIV has placed one or more people at risk of contracting HIV. In such instances the health care practitioner may wish to encourage the PLHIV to discuss the matter with those who may be at risk of infection because of an exposure with this person. Alternatively, the health care practitioner may advise that the PLHIV bring his or her partner/s or contact/s in so they may be counselled.

There will be the occasional PLHIV whom the health care practitioner sincerely believes may have transmitted the infection to others and who refuses to cooperate. In such cases, depending on the jurisdiction, there may not be an immediate legal obligation to notify, however, the practitioner will need to weigh up the relative ethical issues. In the very rare instance where the practitioner believes a PLHIV is intentionally placing others at risk, the obligation to notify becomes more compelling.

Contact Tracing

Contact tracing is the practice whereby a medical professional or the relevant governmental agency traces all the contacts of a person who has, or is suspected of having, an infectious disease. Faced with an outbreak, public health officials can use contact tracing to identify people at risk of infection and people or places contributing to the spread of the disease.
Every State & Territory manages contact tracing differently. Please contact your local health authority for more information.

Australasian Contact Tracing Manual available at: http://www.contacttracing.ashm.org.au/

Anti-discrimination

Anti-discrimination provisions exist in every Australian jurisdiction, which make it illegal to discriminate against someone on the basis of having HIV. In each jurisdiction, discrimination is prohibited either on the basis of disability or

impairment and it includes blood-borne viruses. Please visit your jurisdiction's Anti-Discrimination Commission for more information.

To raise awareness of the systemic barriers, stigma and discrimination and to increase access to the health system by people at risk of or with HBV, HCV or HIV, ASHM has set up a website 'Removing Barriers?' as well as an online learning module for health professionals to develop their knowledge to recognise and address stigma and discrimination.

Visit ***Removing Barriers*** website:
https://removingbarriers.ashm.org.au/

By international standards, Australia has very good outcomes in terms of HIV care, but there is much more that can be done. Of particular importance is the prevention of HIV transmission and infection, the need to regularly test those at risk, early diagnosis and initiation of ART, supporting PLHIV to start and remain on treatment, and manage their age-specific health needs. These are key roles for the GP.

Contacts

ASHM T: 02 8204 0700 E: ashm@ashm.org.au W: www.ashm.org.au	**Australasian Chapter of Sexual Health Medicine (AChSHM)** T: 02 9256 5484 W: www.racp.edu.au
Australian College of Rural and Remote Medicine T: 07 3105 8200 W: www.acrrm.org.au	**Australasian Society for Infectious Diseases** T: 02 8315 2152 W: www.asid.net.au
Australian Government National Health and Medical Research Council T: 1300 064 672 W: www.nhmrc.gov.au	**Australian Sexual Health and HIV Nurses Association (ASHHNA)** W: www.ashhna.org.au
Gastroenterological Society of Australia (GESA) T: 1300 766 176 W: www.gesa.org.au	**National Serology Reference Laboratory (NRL)** T: 03 9418 1111 W: www.nrl.gov.au
Royal Australian College of General Practitioners (RACGP) T: Freecall* 1800 472 247 W: www.racgp.org.au	**Royal Australian College of Physicians (RACP)** T: 02 9256 5444 or Freecall* 1300 697 227 W: www.racp.edu.au
Australian College of Nursing T: Freecall* 1800 061 660 W: www.acn.edu.au	**Royal College of Pathologists of Australasia** T: 02 8356 5858 W: www.rcpa.edu.au

List of Support Services

National:
- Australian Federation of AIDS Organisations (AFAO): https://www.afao.org.au
- National Association of People with HIV Australia: http://napwha.org.au/
- Australian Injecting & Illicit Drug Users League (AIVL): http://aivl.org.au/
- Scarlet Alliance, Australian Sex Workers Association: http://www.scarletalliance.org.au/
- Femfatales/Living Well Women With HIV: https://www.womenlivingwell.org.au/

NSW:
- AIDS Council of NSW (ACON): https://www.acon.org.au/
- Bobby Goldsmith Foundation: https://www.bgf.org.au/
- Positive Life NSW: https://www.positivelife.org.au/
- Positive Heterosexual Service: https://pozhet.org.au/
- Multicultural HIV and Hepatitis Health Services: http://www.mhahs.org.au

Australian Capital Territory:
- AIDS Action Council of the ACT: https://www.aidsaction.org.au/

Northern Territory:
- Northern Territory AIDS and Hepatitis Council: https://www.ntahc.org.au/about-us

Queensland:
- Queensland Positive People: https://www.qpp.org.au/
- Hepatitis Queensland: https://www.hepqld.asn.au/
- Queensland AIDS Council: https://quac.org.au/

South Australia:
- Positive Life SA: http://www.positivelifesa.org.au/
- SAMESH-SHINE SA: https://www.shinesa.org.au/health-services/samesh/
- AIDS Council of South Australia: http://www.aidscouncil.org.au/

Tasmania:
- Tasmanian Council on AIDS, Hepatitis and Related Diseases: https://www.redthread.org.au/

Victoria:
- Living Positive Victoria (LPV): https://livingpositivevictoria.org.au/
- Positive Women Victoria: https://positivewomen.org.au/
- Thorne Harbour Health (formerly the Victorian AIDS Council): https://thorneharbour.org/

Western Australia:
- Positive Organisation Western Australia (POWA): http://positivewa.org/
- WA AIDS Council: https://waaids.com/

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ISBN:978-1-921850-43-1
Published December 2009
Updated March 2020
ABN: 48 264 545 457

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Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
www.ashm.org.au