

The Primary Care Perspectives of HIV Management (adopted from the HIV Manual 3rd Edition, CHP, DH & CEID, CUHK)

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Introduction

HIV has become a chronic, manageable condition since the introduction of highly active antiretroviral therapy (HAART) which improved substantially the life expectancy of HIV-infected individuals. As a result, many HIV-infected individuals who are infected early in the course of their lives are confronted with the similar effects of aging as the general population. Non-AIDS diseases now account for the majority of deaths in HIV-infected individuals.^[1] The prevalence of developing these chronic non-communicable diseases however, may differ from that of the general population as a result of immune activation due to HIV infection, lifestyle factors and the effects of HAART.

It is therefore important for the primary care physicians to appreciate that they are important partners in the management of HIV-infected individuals in the community, and to recognize the similarities and differences in treatment strategies in areas such as, but not limited to non-communicable diseases, vaccination, prophylaxis and cancer screening. Diabetes mellitus, hyperlipidaemia and cardiovascular diseases are associated with HIV as well as HAART. Screening and management of these conditions also form part of the primary care aspects of HIV management.

Immunization

The risk of developing many infections is higher in the immunocompromised population compared to their immunocompetent counterpart. As a general rule, vaccinations are more efficacious in HIV-infected individuals when their immune function is relatively preserved, generally regarded as a CD4 count above at least 200 cells/uL. CD4 counts above 500/uL are optimal. Patients should therefore consider vaccination before their CD4 count falls below 200 cells/uL, or failing so, until immune reconstitution from HAART.

In general, live vaccines should be avoided in HIV-infected individuals, unless the benefits of prevention of an infection are outweighed by the risks of infection by the vaccine strain. Box 1 outlines vaccine recommendations in HIV-infected individuals.

Box 1 Vaccine recommendations in HIV-infected individuals

Vaccine Type	Recommendation
Hepatitis A vaccine	Recommended in all HIV-infected individuals without immunity, especially in chronic hepatitis B and C carriers and men who have sex with men (MSM).
Hepatitis B vaccine	Recommended in all HIV-infected individuals without immunity against hepatitis B and no evidence of chronic infection on serological tests due to the higher risk of sexual and needle-sharing transmission (in drug users).
Human papillomavirus vaccine	As the vaccine is most effective if given to those before sexual debut, the benefits conferred by vaccinating those who have been sexually active remain unclear.
Inactivated influenza vaccine	Annual influenza vaccine is recommended for all HIV-infected individuals to prevent complications due to underlying immunodeficiency. The live attenuated influenza vaccine is not recommended.
Varicella vaccine	Due to the high prevalence of seropositivity in adults, routine administration of the vaccine has not been proven to be effective in HIV-infected adults and is not currently recommended in the local setting.

Immunization for HIV-infected travellers should follow the same general guidance as above. Routine vaccines should be updated and destination-specific immunizations and prophylactic medications advised. Live vaccines may be substituted by inactivated vaccines should one be available e.g. diphtheria, polio and tetanus vaccine.

When travelling to yellow fever endemic areas, asymptomatic HIV-infected individuals with preserved immune function may consider receiving the live yellow fever vaccine. It is generally not advisable to administer the vaccine to severely immunocompromised individuals. All visitors should exercise stringent anti-mosquito measures. Up-to-date advice can be sought from the travel health clinic of the Department of Health.

Prophylaxis against opportunistic infections

Pneumocystis pneumonia (PCP) is the commonest AIDS-defining illness in Hong Kong. In some patients, PCP is the presenting illness prompting an HIV test. The risk of PCP is greatly increased in persons whose CD4 count has dropped below 200/ μ L. Primary prophylaxis is indicated in those with CD4 count below 200/ μ L or oropharyngeal candidiasis. Primary and secondary prophylaxis should be continued until immune reconstitution is achieved, defined as a CD4 count \geq 200/ μ L for more than 3 months.

Latent tuberculosis infection (LTBI) predicts the future risk of developing active TB. As TB is endemic in Hong Kong, patients should receive a tuberculin skin test (TST) annually to detect LTBI. The local cut-off is \geq 5 mm induration. In patients who had never been treated for active or latent TB and who tested positive on TST, isoniazid preventive therapy (IPT) for 9 months reduces the risk of developing active TB disease in the future. It is imperative to exclude active TB before initiation. IPT is also indicated in HIV-infected individuals who have been in close contact with another person harbouring active disease. Liver function tests should be monitored closely in those who have chronic hepatitis B or C infection.

Primary prophylaxis against disseminated *Mycobacterium avium* complex (MAC) disease is indicated in patients with a low CD4 count $<$ 50/ μ L and in whom active MAC disease has been excluded. Secondary prophylaxis after completion of treatment of MAC disease should also be instituted unless

immune reconstitution has occurred. Discontinuation of primary and secondary prophylaxis may be considered when there is sterilization of MAC and CD4 count rises to above 100/ μ L for more than 3 and 6 months respectively after HAART.

Toxoplasma gondii encephalitis may be prevented in the HIV-infected individual by the administration of cotrimoxazole. In patients who tested positive for *Toxoplasma* IgG, primary prophylaxis should be instituted when the CD4 count dropped below 100/ μ L. Cotrimoxazole has the advantage of prophylactic activity against PCP. Primary and secondary prophylaxis may be discontinued when CD4 count rise above 200/ μ L for more than 3 and 6 months respectively in patients on HAART. Box 2 provides the details of prophylaxis against common opportunistic infections.

Box 2 Prophylaxis against opportunistic infections

Infection and indication	Prophylaxis	Alternative regimen
PCP		
Primary prophylaxis	TMP-SMZ 1 DS or 1 SS daily po	Dapsone 100mg daily po or Aerolized pentamidine 200mg via Respigard II nebulizer monthly or Atovaquone 1500mg daily po
Secondary prophylaxis	Same as primary prophylaxis	Same as primary prophylaxis
Latent TB infection		
Isoniazid preventive therapy (IPT)	Isoniazid 200mg daily po for 9 months	NA
Disseminated MAC		
Primary prophylaxis	Azithromycin 1000mg weekly po or Clarithromycin 500mg bd po or Azithromycin 500mg twice per week po	Rifabutin 300mg daily po
Secondary prophylaxis	Same as treatment drug regimens	NA
<i>Toxoplasma gondii</i> encephalitis		
Primary prophylaxis	TMP-SMZ 1 DS daily po	Dapsone 50mg daily po + Pyrimethamine 75mg po + leucovorin 25mg po weekly
Secondary prophylaxis	Pyrimethamine 25-50 mg daily po + sulfadiazine 2000-4000 mg daily po (in 2-4 divided doses) + leucovorin 10-25 mg daily po	Clindamycin 600mg po every 8 hours + Pyrimethamine 25-50 mg daily po + leucovorin 10-25 mg daily po or Atovaquone 750mg po every 6-12 hours +/- [(Pyrimethamine 25mg po daily + leucovorin 10mg po daily) or sulfadiazine 2000-4000 mg daily po daily]
TMP-SMZ: trimethoprim-sulfamethoxazole DS: double strength SS: single strength		

Cancer screening

Cancer has been the major cause of death in Hong Kong for the last 2 decades. In the HAART era, non-AIDS defining cancers outnumbered AIDS-defining cancers in the HIV-infected individual. In one study, 71% of all observed cancers were non-AIDS defining cancers.^[12] HIV-infected individuals are at a higher risk of developing these non-AIDS defining cancer than the general population, contributed by incomplete immune recovery .

The risks of cervical and anal cancers are greatly increased compared to the general population. Female patients should undergo cervical screening half-yearly at the first year of diagnosis, and thereafter, annual screening. The recommendation calls for more frequent screening than the general female population due to the increased risk of cervical dysplasia.

Anal cancer is also becoming more common among HIV-infected individuals as they age. This is of particular importance in the MSM population due to the high prevalence of infection by oncogenic HPV types through anal sex. In HIV-infected MSM, the rate of anal cancer is a few times higher than the HIV-uninfected MSM. Most strikingly, HIV-infected MSM is almost 60 times as likely as the general population to develop anal cancer.^[13]

It is unclear whether detection of anal dysplasia by anal cytology is useful to reduce the burden of anal cancer among MSM who are infected with HIV. Currently, there is no consensus as to the screening strategies of this population. Abnormal anal cytology should be followed by high-resolution anoscopy and biopsy. There is a need to develop expertise skilled in interpreting anal cytology results and in managing anal dysplasia.

Screening of sexually transmitted infections (STI)

Sexually transmitted infections are frequently observed in HIV-infected individuals and represent a dual concern, as some STIs may increase the risk of HIV transmission; and HIV infection may alter the clinical manifestation of STIs.

Screening of HIV patients for STIs is advised. One useful approach is to screen for syphilis infection by serology every 3-4 months in MSM due to the high risk of co-infection, and annually in other patients. Urine screening tests for *Neisseria gonorrhoea* or *Chlamydia trachomatis* by nuclei acid amplification test is convenient and improves the yield as some infections may be asymptomatic. In women, swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoea* are routinely performed for females undergoing annual cervical smear.

Mental health

Mental health symptoms are commoner in HIV-infected individuals than the general population. Depression, anxiety, substance misuse and suicidality are but a few of the commoner conditions encountered. These symptoms should be differentiated from non-psychiatric conditions associated with the infection or adverse events associated with treatment. These include HIV-associated dementia, neurosyphilis, Vitamin B12 deficiency, thyroid disease, adrenal insufficiency or hypogonadism. Primary care practitioners are first point of contact of HIV-infected individuals; and if equipped with the necessary tools to pick up early symptoms, may prevent the occurrence of debilitating disease. At the first and subsequent visits, symptoms of depression or anxiety, sleeping pattern, suicidal ideation and current or past use of alcohol or other psychotropic substances should be evaluated. Understanding the broader context of family circumstances and social support network would aid subsequent management. Prompt referral to specialist is warranted in some circumstances.

Smoking cessation

The proportion of daily cigarette smokers in Hong Kong stands at 11.1% in 2010, and a greater number is seen amongst males (19.9%) than females (3%). Smoking appears to be more prevalent in the HIV-infected population compared to the general public.

The effects of tobacco smoking on HIV-infected patients are manifold. Apart from demonstrating a poorer virologic and immunologic response to HAART, HIV-infected smokers bear a higher toll of tobacco-related maladies than the HIV-uninfected, notably cancers affecting the lungs, head and neck region, cervix, anus; as well as oral candidiasis and oral hairy leukoplakia.^[4]

The clinician should include assessment of smoking status as part of the day-to-day clinic management. It is the responsibility of the attending health care team to assess the patient's readiness to quit smoking using for example the transtheoretical model of health behaviour change. This model encompasses the hallmark five stages of behaviour change: pre-contemplation, contemplation, preparation, action and maintenance. Brief interventions by clinicians improve abstinence rates of smokers. Motivational interviewing is another strategy which may be combined with the above for those who are not thinking of quitting.

Pharmacological interventions e.g. nicotine replacement therapy, are also used in the HIV-infected individuals. Both bupropion and varenicline may affect sleep and exacerbate psychiatric symptoms. They should be used with caution in patients taking efavirenz. Clinicians should familiarize themselves with potential drug interactions when considering these options.

References

1. Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clin Infect Dis* 2010;50(10):1387-96.
2. Crum-Cianflone N, Hullsiek KH, Marconi V, Weintrob A, Ganesan A, Barthel RV, Fraser S, Agan BK, Wegner S. Trends in the incidence of cancers among HIV-infected persons and the impact of antiretroviral therapy: a 20-year cohort study. *AIDS* 2009;23(1):41-50.
3. Frisch M, Biggar RJ, Goedert JJ. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. *J Natl Cancer Inst* 2000;92(18):1500-10.
4. Crothers K, Goulet JL, Rodriguez-Barradas MC, Gibert CL, Oursler KA, Goetz MB, Crystal S, Leaf DA, Butt AA, Braithwaite RS, Peck R, Justice AC. Impact of cigarette smoking on mortality in HIV-positive and HIV-negative veterans. *AIDS Educ Prev* 2009;21(Suppl 3):40-53.

Further reading

- A. Kaplan JE, Benson C, Holmes KH, Brooks JT, Pau A, Masur H; Centers for Disease Control and Prevention (CDC); National Institutes of Health; HIV Medicine Association of the Infectious Diseases Society of America. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR Recomm Rep* 2009;58(RR-4):1-207.
- B. Screening Tools for Completing Mental Health Assessments in HIV Primary Care Settings. New York State Department of Health AIDS Institute, 2007. Available from <http://www.hivguidelines.org/resource-materials/screening-tools/mental-health-screening-tools/>

Test paper - The Primary Care Perspectives of HIV Management

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- Please indicate one answer to each question.

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1. Which of the following is not true regarding the outlook of HIV disease with the advent of highly active antiretroviral therapy (HAART)?
 - (a). The life expectancy of HIV infected patients has greatly improved
 - (b). Non-AIDS complications has become more common
 - (c). HAART itself plays a role in shaping long-term conditions in people living with HIV nowadays
 - (d). Immune activation from HIV is an important underlying mechanism of non-communicable conditions in people living with HIV
 - (e). None of the above
 2. Which of the following is not true about smoking in HIV patients?
 - (a). The prevalence of smoking is higher than general population
 - (b). Smoking cessation modalities is generally different from those in non-HIV infected people
 - (c). Smoking accounts for an important modifiable cardiovascular risk
 - (d). A multidisciplinary team approach is desirable for effective smoking cessation service
 - (e). Drug interaction with anti-HIV drugs has to be cautioned in using pharmacological interventions for smoking cessation
 3. Which of the following is not true about cervical cancer and its screening in HIV infected patients?
 - (a). Frequency of cervical screening can be higher than non-HIV infected population
 - (b). Cervical dysplasia is more common in HIV infected patients
 - (c). Cervical cancer is not increased in HIV infected patients
 - (d). The role of human papillomavirus vaccination to prevent cervical cancer is unclear
 - (e). All of the above
 4. Which of the following chronic medical condition is a not concern in HIV infected patients?
 - (a). Diabetes mellitus
 - (b). Dyslipidaemia
 - (c). Coronary heart disease
 - (d). Hypertension
 - (e). None of the above
 5. Which of the following is not true regarding immunization in HIV infected patients?
 - (a). Immune response to vaccination is usually better with a higher CD4 level, say >350-500/uL
 - (b). Inactivated influenza vaccination is recommended once
 - (c). Hepatitis B vaccination is recommended for those with neither immunity nor chronic infection
 - (d). Hepatitis A vaccine is recommended, especially for those at higher risk of liver complications
 - (e). None of the above
 6. Which of the following is not true for a HIV infected patient who needs to travel to areas with concern of tropical diseases?
 - (a). Both routine vaccines and destination-specific preventive measures have to be updated or implemented
 - (b). Live vaccine should be avoided and replaced by inactivated vaccine if available

- (c). Patients with preserved immunity can consider yellow fever vaccine
 - (d). Anti-mosquito measures are integral component in the prevention of vector-borne diseases including malaria
 - (e). None of the above
7. Which of the following is not true about prophylaxis against opportunistic infections in HIV patients?
- (a). Primary prophylaxis for *Pneumocystis* pneumonia is indicated for patients with CD4 below 200/uL or presence of oral thrush
 - (b). Single strength tablet daily of cotrimoxazole is the drug of choice in preventing toxoplasmosis in patients with positive anti-toxoplasma IgG, and has the added benefit of preventing *Pneumocystis* pneumonia
 - (c). Discontinuation of secondary prophylaxis for *Pneumocystis* pneumonia can be considered when CD4 improved to $\geq 200/\mu\text{L}$ for more than 3 months after HAART
 - (d). Dapsone and aerosolised pentamidine are both alternative to cotrimoxazole in *Pneumocystis* pneumonia prophylaxis
 - (e). All of the above
8. Which of the following is not true regarding the prophylaxis of tuberculosis or atypical *Mycobacterium* infection in HIV/AIDS patients?
- (a). Tuberculin skin test (TST) is useful to determine latent TB infection
 - (b). When considering primary prophylaxis for *Mycobacterium avium* complex (MAC), active MAC disease has to be excluded
 - (c). A cut-off of 5mm skin redness from TST is used for diagnosing latent TB infection
 - (d). Isoniazid for 9 months is the standard to treat latent TB and reduce the risk of developing active TB in the future
 - (e). Discontinuation of primary and secondary MAC prophylaxis is possible with immune reconstitution after HAART
9. Which of the following is not true of anal cancer in HIV infected patients?
- (a). Anal cancer is more common in HIV patients than the general population
 - (b). Oncogenic human papillomavirus infections contribute to anal cancer development
 - (c). HIV positive men who have sex with men (MSM) are at higher risk of developing anal cancer than HIV negative MSM
 - (d). Ageing also plays a role in HIV patients developing anal cancer, like other cancers
 - (e). None of the above
10. Which of the following is not true screening of sexually transmitted infections (STI) in HIV patients?
- (a). Syphilis screening is done more frequently at 3-4 months interval for HIV infected men who have sex with men because of the higher risk of co-infection than patients with other HIV transmission modes
 - (b). Urine screening for *Neisseria gonorrhoea* or *Chlamydia trachomatis* by nucleic acid amplification test is recommended
 - (c). Screening is necessary as asymptomatic STIs are not uncommon
 - (d). Screening followed by prompt treatment of STIs help in reducing the risk of HIV transmission
 - (e). None of the above