

UNIT NO. 6

DIAGNOSIS, SCREENING AND MANAGEMENT OF HIV INFECTION

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ABSTRACT

A large number of people with HIV Infection can remain well for many years. Physicians should take the opportunity to offer HIV screening if there is any clinical indication or risk factor for HIV transmission. The family physician is often the first doctor to disclose a positive HIV test to the patient. How we counsel the patient should be individualised as patients do react differently to the test results. Meanwhile, the medications used to treat HIV are extremely efficacious. Drug development has come a long way since zidovudine (AZT) was approved for use in 1987. New classes of drugs targeting the other stages of the HIV life cycle (e.g. CCR5 entry inhibitors, integrase inhibitors, maturation inhibitors) are currently in rapid development.

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INTRODUCTION

A large number of people with HIV Infection can remain well for many years. Physicians should take the opportunity to offer HIV screening if there is any clinical indication or risk factor for HIV transmission. In USA, there is an increasing trend to expand HIV testing to patients in medical facilities such that HIV testing may become an opt-out system¹. There are many benefits for diagnosing HIV infection early.

BENEFITS OF EARLY DIAGNOSIS

- Decrease the risk of further transmission. Studies have shown that people who are unaware of their HIV+ status transmit most of the HIV infections. Patients with HIV often take steps to reduce transmission to others^{2,3}.
- Prevent the progression of HIV infection to AIDS through monitoring of their CD4 counts and starting anti-retroviral therapy (ART) at the appropriate time.
- First AIDS-defining condition in patients who present late could be fatal (e.g. lymphoma, progressive multi-focal leucoencephalopathy) or the recovery may not be total (e.g. residual paralysis from cerebral infections).
- New incentive to test as treatment is available and more accessible at current time. Anti-HIV drugs are getting more affordable since 2002.

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CLINICAL INDICATIONS FOR OFFERING HIV TESTING

1. All patients with past history or presenting with sexually transmitted infections (STIs), e.g. syphilis, gonorrhea, acute hepatitis B, etc.
2. Patients whom physicians have assessed to be of high risk for HIV/AIDS. These include:
 - Intravenous drug abusers
 - Men who have sex with men (MSM) or bisexuals
 - Patients who reported exposure to sex workers or casual sex (with or without use of condoms)
 - Patients who reported exposure to HIV positive partner(s)
 - Patients who have been named as contacts of HIV index patients and who have been asked to have HIV test
3. Patients with clinical signs and symptoms suggestive of HIV/AIDS:
 - Unexplained prolonged fever
 - Unexplained weight loss and wasting syndrome
 - Unexplained or prolonged diarrhea
 - Unexplained oral candidiasis
 - Generalised lymphadenopathy
 - Acute HIV – Seroconversion illness, etc
4. Patients with AIDS-related diseases, e.g.:
 - Tuberculosis
 - Lymphoma, especially B-cell lymphoma, and primary cerebral lymphoma
 - Infections: PneumoCystis jirovecii Pneumonia (PCP), CMV retinitis, cerebral toxoplasmosis, extra-pulmonary cryptococcal infection, herpes zoster, recurrent Salmonella bacteraemias
 - Carcinoma : Kaposi's sarcoma, Cervical carcinoma
 - Unexplained dementia
 - Psoriasis, etc
5. Other patient groups:
 - Antenatal Screening
This is an opt-out testing in Singapore. Mother-to-Child HIV transmission can be reduced to < 1-2 % with effective anti-retroviral prophylaxis.
 - Occupational needle-stick injuries in health care workers
In these instances, the patient would have to consent to have his blood screened for HIV, hepatitis B and C.
6. Other indications for HIV testing:
When HIV test is compulsory or is a statutory requirement:
 - Organ or blood donation,
 - PR application,

- Work permit/ employment pass application or renewal,
- Domestic workers,
- Some insurance applications,
- Some pre- employment requirement,
- Sex workers who are on the medical scheme,
- Individuals who have been arrested for vice or under Police custody for various offences and for which the HIV testing is part of Police SOP.

IS CONSENT NEEDED FOR HIV TESTING?

In July 2005, DMS issued a Professional Circular (13A/2005) that stated:

“With immediate effect, HIV testing, when indicated, in a health care setting should be administered with the same preliminaries as for any other test that is carried out on a patient – the principle being the patient should be appropriately kept informed and tests should be undertaken only when medically indicated, i.e. when it would assist you in your management of the patient.”

A signed documented consent is not needed for HIV testing. Pre-test counselling is also not required. However, just like any test or investigation, it is prudent to tell the patients that you are doing the test and offer to answer any queries. You may also want to document that patient is agreeable for HIV testing. Reasons for refusal should also be documented.

It should be noted that while HIV test is compulsory for some of the above-mentioned indications, we should still inform them that we are doing the test, as the person may refuse testing and opt out of the PR, insurance or job application.

HIV SCREENING AND CONFIRMATORY TESTS

Antibodies appear in > 99% of cases 2 – 12 weeks after exposure. Long interval (6 months) may sometimes occur, but this is rare (e.g. taking post-exposure prophylaxis/co-infections with Hepatitis C).

These serological tests are > 98% sensitive and > 98% specific. The window period (time delay from infection/exposure to positive screening test) is about 22 days. This has been shortened to an average of 10-14 days with newer generation assays. Negative anti-HIV screening tests must be repeated at 6 weeks, 3 and 6 months from the time of exposure. Regular screening is recommended if there is continuing risk factors.

Screening tests include the EIA (Elisa), PA (particle agglutination), and the various rapid test kits. These screening tests detect ‘whole’ anti-HIV antibodies, while the Western Blot (WB) confirmatory HIV test detect antibody response to individual HIV proteins, e.g. gp 41, gp 120, etc. Any positive screening test will be confirmed by the WB test. Presence of gp41 + gp 120/160 or p24 + gp120/160 will be deemed positive, and presence of any other band patterns will be deemed as indeterminate. Patients with negative/indeterminate WB either have no HIV infection (false positive screening test) or are patients undergoing seroconversion.

OTHER NON-ANTIBODY-BASED HIV TESTING

HIV-1 DNA PCR is used for neonatal HIV infection as HIV antibodies transferred from infected mothers can remain for 18 months in the neonate. It can also be used to clarify indeterminate WB or diagnose suspected **acute symptomatic** HIV infection when the screening test could be negative. All positive tests would need to be followed up with a positive antibody test (WB) to confirm the diagnosis. Singapore blood banks use the Nucleic acid amplification test (NAT) to detect HIV RNA for our blood screening.

Management

The family physician is often the first doctor to disclose a positive HIV test to the patient. How we counsel the patient should be individualised as patients do react differently to the test results. They can range from shock, panic, denial, anger, no affect, to being nonchalant. In patients who are in shock and anxious, the counselling should be geared towards positive aspects of the disease. These should include the following:

- That treatment is now available and the infection can be treated and controlled without progression to AIDS.
- That with proper treatment, they can expect many years of quality life.
- That treatment can be affordable, and that help and support are available at the Communicable Disease Centre, Tan Tock Seng Hospital.
- Provide a referral for HIV care. The CDC provides comprehensive HIV care with specialists and nurses trained in HIV medicine, psychiatrist, dermatologist, medical social workers, patient care center and patient support groups.
- Foreigners should also be referred to our center for initial assessment and referral to HIV centers in their countries of origin.
- Counselling on prevention of HIV transmission.
- Offer to answer queries (we provide them with written materials).

It may be difficult to address all issues at a single meeting, especially if the patient is very anxious. However, the above points will be reiterated at the Communicable Disease Centre. In addition, more details about HIV transmission risk and sexual practices will be enquired in order to give appropriate counselling on safer sex (positive prevention).

Patients will be advised to inform their spouse and sex partners so that they can be screened for HIV infection. Their contacts can also be notified of the risk exposure without the patient being named (contact tracing; Infectious Disease Act, section 8). Patients will also be informed of Infectious Disease Act section 25A and section 23 at our center.

All patients are assigned to a trained medical social worker who, together with the doctor and psychiatrist will deal with the psychological, emotional, and financial difficulties faced by many of our patients. We have a large pool of trained volunteers who can provide invaluable support to our needy patients.

MEDICAL TREATMENT

The medications used to treat HIV are extremely efficacious. My longest-living patient who is well and healthy was diagnosed in 1987. He has been taking anti-retrovirals since 1990 with minimal side effects. Drug development has come a long way since zidovudine (AZT) was approved for use in 1987.

New formulations with 3 drugs in one pill are now available. Patients need only to take 1 – 2 pills a day. These combination pills contain the HIV reverse transcriptase enzyme inhibitors (nucleosides and the non-nucleosides reverse transcriptase inhibitors). They are potent and simple to take. However, resistance to these drugs develops quickly if patients do not adhere strictly to their drug regimen. Non-adherence to medication is the main cause of treatment failure ('drugs don't fail, patients fail').

The other class of anti-retrovirals, the protease inhibitors are more expensive and are mainly used for salvage therapy in Singapore. The 4th class of drugs, fusion inhibitors are not used in Singapore as they are too expensive and are only available in injectable formulation.

New classes of drugs targeting the other stages of the HIV life cycle (e.g. CCR5 entry inhibitors, integrase inhibitors, maturation inhibitors) are currently in rapid development. They are needed as many patients have failed on the previous 3 classes of drugs due to non-adherence, toxicity or sub-optimal therapy.

WHEN TO START ANTI-RETROVIRAL THERAPY (ART) TREATMENT AND MONITORING

The CD4 count test is the most important investigation as HIV infection causes disease by depleting the CD4 cell pool. A normal CD4 count should comprise at least 25% (280 – 1430 cells) of the total lymphocyte pool.

ART should be started in any patient who is symptomatic (e.g. oral thrush) or with an AIDS-defining illness. Patients with multiple AIDS-defining illnesses can still do very well if they start on ART. In patients who are asymptomatic, ART must be offered if the CD4 count < 200 cells/mm³ and recommended if CD4 count is 200 – 350 cells/mm³. Most importantly, the patient must be ready to initiate therapy. Counselling on drug adherence is highly recommended.

After 6 months of ART, the plasma HIV viral load should be undetectable, corresponding with an increase in CD4 count. In a recent study at our center, we were happy to find that 71%

of our patients who were on ART for the past 2 years had an undetectable viral load⁴.

Some serious side-effects from the long-term use of these medications include the disturbing disfiguring lipoatrophy of face and limbs, peripheral neuropathy, hyperlipidaemia, and insulin resistance resulting in diabetes mellitus for some of our patients.

A typical follow-up visit of our patient can include the following: General well-being and drug adherence, addressing medical complaints if any, physical examination, review of laboratory data viz. CD4 count, viral load, liver and renal panels, glucose and lipid levels, update on vaccinations (e.g. annual flu vaccinations) and treatment of co-infections (e.g. hepatitis B), etc.

CONCLUSIONS

The main important and challenging role of the family physician in HIV/AIDS will be to diagnose a patient with HIV infection at the earliest opportunity. A family physician would also need to be adept at counselling an anxious patient who has just been diagnosed with HIV infection, and provide the patient with correct information about the illness. Some family physicians have expressed interest in seeing our patients at their clinics. This endeavour is certainly most welcomed, but details on its feasibility needs to be looked into first. Further reading, e.g. drug interactions with ART, would also be useful especially when physicians have to treat HIV patients at their clinics for other illnesses.

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LEARNING POINTS

- o Negative anti-HIV screening tests must be repeated at 6 weeks, 3 and 6 months from the time of exposure. Regular screening is recommended if there is continuing risk factors.
- o HIV-1 DNA PCR is used for neonatal HIV infection as HIV antibodies transferred from infected mothers can remain for 18 months in the neonate.
- o ART should be started in any patient who is symptomatic (e.g. oral thrush) or with an AIDS-defining illness. Patients with multiple AIDS-defining illnesses can still do very well if they start on ART.
- o In patients who are asymptomatic, ART must be offered if the CD4 count < 200 cells/mm³ and recommended if CD4 count is 200 – 350 cells/mm³.