A detailed review on HIV AIDS and its treatment

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Abstract-

HIV/AIDS has always been one of the most thoroughly global of diseases. The human immunodeficiency virus (HIV) is a lent virus that causes HIV infection and AIDS. AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening infections and cancers to thrive. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. HIV infects vital cells in the human immune system such as helper CD4 T cells, macrophages. HIV infection leads to low levels of T cells through a number of mechanisms, including pyroptosis of infected T cells. The symptoms of AIDS are primarily the result of conditions that do not normally develop in individuals with healthy immune systems. Most of these conditions are opportunistic infections caused by bacteria, viruses, fungi and parasites that are normally controlled by the elements of the immune system that HIV damages. many drugs, treatment method and monitoring system helps to child and adults surfing from HIV AIDS.

CHAPTER-I

INTRODUCTION

INTRODUCTION

HIV stands for Human Immunodeficiency Virus. HIV is the virus that causes AIDS. Your immune system is your body's defense system. While the immune system can control many viruses, HIV targets and infects the same immune system cells that protect us from germs and illnesses. These cells are a type of white blood cell called CD4 cells (which are a type of T cells). Without medication to control the virus, HIV usually takes over CD4 cells and turns them into factories that produce millions of copies of the virus. As the virus makes copies, it damages or kills the CD4 cells, weakening the immune system. This is how HIV causes AIDS.

There are many different strains of HIV that are grouped into two main types:

HIV-1: most common type worldwide

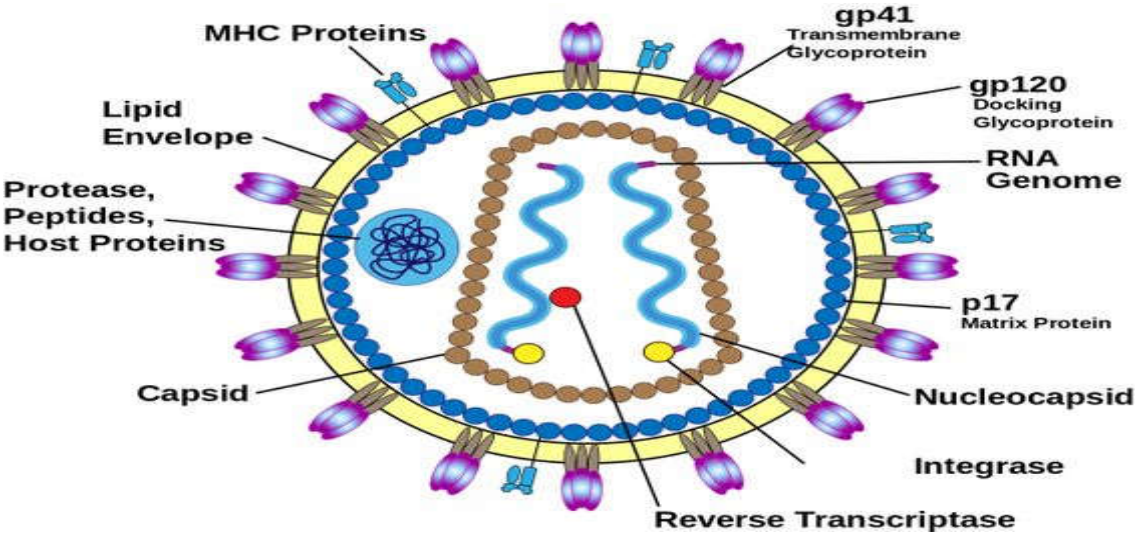
HIV-2: found mostly in West Africa, Asia, and Europe

It is possible for one person living with HIV to carry several different strains of HIV in their body at the same time

AIDS

AIDS stands for Acquired Immune Deficiency Syndrome. AIDS is the most advanced stage of HIV disease. HIV causes AIDS by attacking CD4 cells, which the immune system uses to protect the body from disease. When the immune system loses too many CD4 cells, the body is less able to fight off infections and can develop serious, often deadly, infections. These are called opportunistic infections (OIs). When someone dies of AIDS, death is usually due to OIs or other long-term effects of HIV. AIDS refers to the weakened state of the body’s immune system, which can no longer stop opportunistic infections.

STRUCTURE OF HIV VIRUS



Gp120

The 120 in its name comes from its molecular weight. It is essential for virus entry into the cells as it plays vital role in attachment to specific cell surface receptors.

GP41

It is a subunit of the envelope protein complex of retroviruses including human immuno deficiencies virus. It is family of enveloped viruses that replicate in host cell through process of reverse transcriptase. It targets a host cell.

Viral envelope

It is envelope through which virus binds.

P17

Viral core is made from protein. It is bullet shaped. Three enzymes required for HIV replication are reverse transcription, integrase and protease.

P24

P24 is component of HIV capsid.

Protease

It is a retroviral aspartyl protease that is essential for life cycle of HIV, the retrovirus that caused AIDS. This enzyme cleaves newly synthesized polyproteins at appropriate place to create nature protein components of infectious HIV virion.

Integrase

Enzyme produce by retrovirus that enables its genetic material to be integrated into the DNA of infected cell.

RNA

All organisms including most viruses store their genetic material on long strands of DNA. Retrovirus is exception because their genes are composed of RNA.

CHAPTER-2

STAGES OF HIV INFECTION

2. STAGES OF HIV INFECTION

1. Acute HIV Infection

Acute HIV infection is the earliest stage of HIV infection, and it generally develops within 2 to 4 weeks after infection with HIV. During this time, some people have flu-like symptoms, such as fever, headache, and rash. In the acute stage of infection, HIV multiplies rapidly and spreads throughout the body. The virus attacks and destroys the infection-fighting CD4 cells (CD4 T lymphocyte) of the immune system. During the acute HIV infection stage, the level of HIV in the blood is very high, which greatly increases the risk of HIV transmission. A person may experience significant health benefits if they start ART during this stage.

2. Chronic HIV Infection

The second stage of HIV infection is chronic HIV infection (also called asymptomatic HIV infection or clinical latency). During this stage, HIV continues to multiply in the body but at very low levels. People with chronic HIV infection may not have any HIV-related symptoms. Without ART, chronic HIV infection usually advances to AIDS in 10 years or longer, though in some people it may advance faster. People who are taking ART may be in this stage for several decades. While it is still possible to transmit HIV to others during this stage, people who take ART exactly as prescribed and maintain an undetectable viral load have effectively no risk of transmitting HIV to an HIV-negative partner through sex.

3. AIDS

AIDS is the final, most severe stage of HIV infection. Because HIV has severely damaged the immune system, the body cannot fight off opportunistic infections. (Opportunistic infections are infections and infection-related cancers that occur more frequently or are more severe in people with weakened immune systems than in people with healthy immune systems.) People with HIV are diagnosed with AIDS if they have a CD4 count of less than 200 cells/mm3 or if they have certain opportunistic infections. Once a person is diagnosed with AIDS, they can have a high

viral load and are able to transmit HIV to others very easily. Without treatment, people with AIDS typically survive about 3 years.

3.HIV TESTING

HIV testing determines if a person is infected with HIV. The human immunodeficiency virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS). AIDS is the most advanced stage of HIV infection.

HIV testing can detect HIV infection, but it cannot tell how long a person has had HIV or if the person has AIDS.

HIV TESTING IMPORTANT

Knowing your HIV status can help keep you—and others—safe.

If you are HIV negative

A negative HIV test result shows that you do not have HIV. Continue taking steps to avoid getting HIV, such as using condoms during sex and, if you are at high risk of getting HIV, taking medicines to prevent HIV (called pre-exposure prophylaxis or PrEP). For more information, read the HIVinfo fact sheet on The Basics of HIV Prevention.

If you are HIV positive

A positive HIV test result shows that you have HIV, but you can still take steps to protect your health. Begin by talking to your health care provider about antiretroviral therapy (ART). People on ART take a combination of HIV medicines every day to treat HIV infection. ART is recommended for everyone who has HIV, and people with HIV should start ART as soon as possible. ART cannot cure HIV, but HIV medicines help people with HIV live longer, healthier lives.

A main goal of ART is to reduce a person’s viral load to an undetectable level. An undetectable viral load means that the level of HIV in the blood is too low to be detected by a viral load test. People with HIV who maintain an undetectable viral load have effectively no risk of transmitting HIV to their HIV-negative partner through sex.

Who should get tested for HIV

The Centers for Disease Control and Prevention (CDC) recommends that everyone 13 to 64 years of age get tested for HIV at least once as part of routine health care. As a general rule, people at higher risk for HIV should get tested each year. Sexually active gay and bisexual men may benefit from getting tested more often, such as every 3 to 6 months. If you are over 64 years of age and at risk, your health care provider may recommend HIV testing.

Factors that increase the risk of HIV include:

- Having vaginal or anal sex with someone who is HIV positive or whose HIV status you do not know
- Injecting drugs and sharing needles, syringes, or other drug equipment with others
- Exchanging sex for money or drugs
- Having a sexually transmitted disease (STD), such as syphilis
- Having sex with anyone who has any of the HIV risk factors listed above
- Talk to your health care provider about your risk for HIV and how often you should get tested for HIV.

Pregnant women get tested for HIV

CDC recommends that all pregnant women get tested for HIV so that they can begin taking HIV medicines if they are HIV positive. Women with HIV take HIV medicines during pregnancy and childbirth to reduce the risk of perinatal transmission of HIV and to protect their own health. For more information, read the HIV info fact sheet on Preventing Perinatal Transmission of HIV.

TYPES OF HIV TESTS

There are three types of tests used to diagnose HIV infection: antibody tests, antigen/antibody tests, and nucleic acid tests (NATs). Your health care provider can determine the appropriate HIV test for you. How soon each test can detect HIV infection differs, because each test has a different window period. The window period is the time between when a person may have been exposed to HIV and when a test can accurately detect HIV infection.

1. **Antibody tests** check for HIV antibodies in blood or oral fluid. HIV antibodies are disease-fighting proteins that the body produces in response to HIV infection. Most rapid tests and home use tests are antibody tests.
2. **Antigen/antibody tests** can detect both HIV antibodies and HIV antigens (a part of the virus) in the blood.
3. **NATs** look for HIV in the blood.

A person's initial HIV test will usually be either an antibody test or an antigen/antibody test. NATs are very expensive and not routinely used for HIV screening unless the person had a high-risk exposure or a possible exposure with early symptoms of HIV infection.

When an HIV test is positive, a follow-up test will be conducted. Sometimes people will need to visit a health care provider to take a follow-up test. Other times, the follow-up test may be performed in a lab using the same blood sample that was provided for the first test. A positive follow-up test confirms that a person has HIV.

Talk to your health care provider about your HIV risk factors and the best type of HIV test for you.

HIV testing can be confidential or anonymous.

Confidential testing means that your HIV test results will include your name and other identifying information, and the results will be included in your medical record. HIV-positive test results will be reported to local or state health departments to be counted in statistical reports. Health departments remove all personal information (including names and addresses) from HIV test results before sharing the information with CDC. CDC uses this information for reporting purposes and does not share this information with any other organizations, including insurance companies.

Anonymous testing means you do not have to give your name when you take an HIV test. When you take the test, you receive a number. To get your HIV test results, you give the number instead of your name.

Where can someone get tested for HIV

Your health care provider can give you an HIV test. HIV testing is also available at many hospitals, medical clinics, substance use programs, and community health centers. Use CDC's Get Tested treatment locator to find an HIV testing location near you. Getting tested through a professional health care provider is recommended; however, there are HIV self-testing kits available. Rapid self-test and mail-in self-test are the two types of HIV self-tests, but state laws regarding self-testing may limit their availability in a location.

A rapid self-test is an oral fluid test done entirely at home or in private. There is currently one U.S. Food and Drug Administration (FDA)-approved rapid self-test called OraQuick In-Home HIV test. A mail-in self-test requires a person to provide a blood sample from a finger stick, which is then sent to a lab for testing.

CHAPTER-3

TRANSMISSION

3.TRANSMISSION

HIV is transmitted principally in three ways: By sexual contact, by blood through transfusion, blood products or contaminated needles or by passage from mother to child. Although homosexual contact remains a major source of HIV within the United States, “hetero sexual transmission is the most important means of HIV spread worldwide today.” Treatment of blood products and donor screening has essentially eliminated the risk of HIV from contaminated blood products in developed countries, but its spread continues among intravenous drug users who share needles. In developing countries, contaminated blood and contaminated needles remain important means of infection. Thirteen to thirty-five percent of pregnant women infected with HIV will pass the infection on to their babies; transmission occurs before as well as during birth. Breast milk from infected mothers has been shown to contain high levels of the virus also. HIV is not spread by the fecal-oral route; aerosols; insects; or casual contact, such as sharing household items or hugging. The risk to health care workers is primarily from direct inoculation by needle sticks. Although saliva can

Contain small quantities of the virus, the virus cannot be spread by kissing. HIV can be transmitted from an infected person to another through:

• Blood (including menstrual blood),

• Semen,

• Vaginal secretions,

• Breast milk.

Activities That Allow HIV Transmission

• Unprotected sexual contact

• Direct blood contact, including injection drug needles, blood transfusions, accidents in health care settings or certain health care products.

• Mother to baby (before or during birth)

HIV is known to be transmitted only through

• Contact of infected blood, semen, or vaginal and cervical secretions with mucous membranes.

• Injection of infected blood or blood products.

• Vertical transmission (that is, from infected mother to fetus) and from mother to infant via breast milk. Contact of Sexual Fluids or Blood with Mucous

Membranes

The virus cannot pass through undamaged skin. HIV can enter the body through the mucous membranes that line the vagina, rectum, urethra, and possibly, on rare occasions, the mouth. Damage to a mucous membrane may increase the risk of transmission of HIV but is not necessary for transmission to occur.

Injection of Infected Blood:

HIV can be transmitted by infected blood getting directly into the bloodstream through intravenous, intramuscular, or subcutaneous injection.

Blood-to-blood transmission occurs in the following ways:-

• Transfusion of contaminated blood and blood products and other blood recipients.

• Sharing of unsterilized hypodermic needles and syringes.

The risk of HIV Transmission is dependent on:

• The concentration of HIV in the infected fluid.

• The QUANTITY of fluid introduced into the body.

• The ACCESS of the infected fluid to the t4 cells.

Fluid with high concentration of HIV:

• Semen,

• Blood and blood components,

• Menstrual flow,

• Vaginal secretions,

• Pre ejaculatory fluid,

• Breast milk

Fluids with LOW Concentration of HIV

• Pus,

• Saliva,

• Tears,

• Urine,

• Feces,

• Vomiting,

• Nasal mucosa.

HIV is not spread through contact with these body fluids:

- Sweat
- Tears

- Saliva (spit)
- Feces (poop)
- Urine (pee)

In other words, you CANNOT get HIV by touching or hugging someone who is living with HIV, kissing someone living with HIV, or by using a toilet also used by someone living with HIV.

LIFE CYCLE OF HIV AIDS

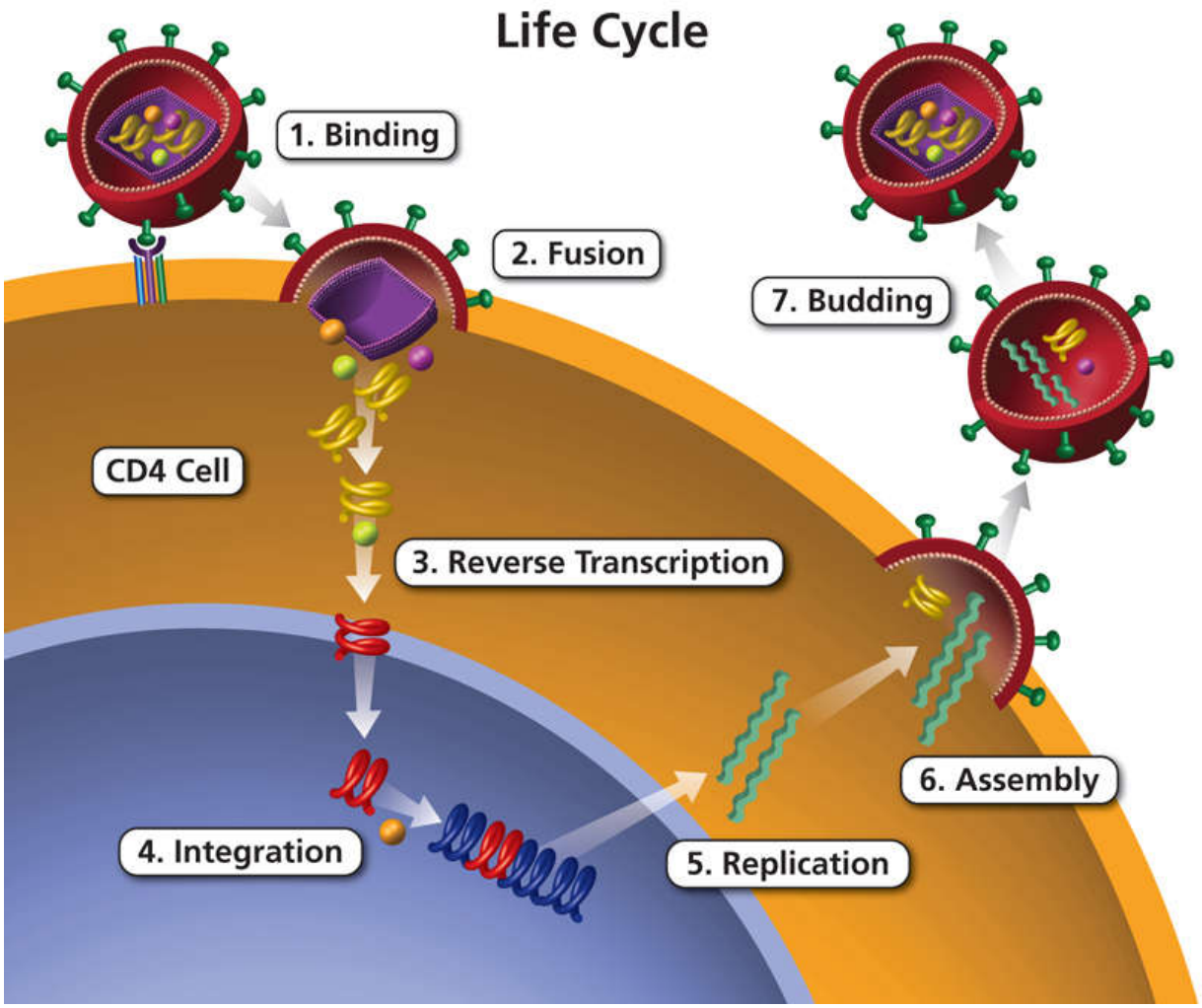


Fig-2 Life cycle

Entry to human cells

HIV is the only viruses which make new copies of itself inside the human cells. This process begins when this virus enters into cell that carries on its surface a protein that is cd4. The HIV virus stick to the cd4 receptor and allow them to fuse.HIV mainly infect immune cells i.e. T-helper cells that forms the body immune system. HIV infects more cells, therefore immune system becomes weak.

Reverse transcription

There is an enzyme reverse transcriptase which helps in reverse Transcription. The main function of reverse Transcriptase is conversion of viral RNA into DNA. After that DNA is transported to cell's nucleus where insertion of DNA is done by enzyme integrase.

Transcription and translation Now, transcription takes place. HIV virus converts HIV virus into messenger RNA.Assembly, budding and maturation Copies of HIV gather together with newly made HIV protein and enzymes to form new viral particle which are then bud off from the original CD4 cell. The enzyme protease breaks the long chains of HIV protein into smaller pieces. These newly virus has ability to target and infect other CD4 cells

CHAPTER-4

DIAGNOSIS OF HIV INFECTION IN ADULTS AND CHILDREN.

4.DIAGNOSIS OF HIV INFECTION IN ADULTS AND CHILDREN.

4.1 Diagnosis of HIV

HIV is now considered a chronic manageable disease and majority of the PLHIV remain healthy if correct and timely treatment is started. Late diagnosis is an important factor associated with HIV-related morbidity and mortality. Voluntary HIV testing with informed consent should be offered and encouraged in a wide variety of settings. HIV infection in any individual beyond 18 months of age can be detected by laboratory test/s that demonstrate(s) either the virus or viral products or antibodies to the virus in the blood/serum/plasma. In children below 18 months of age, due to the persistence of maternal antibodies, diagnosis of HIV is made by Polymerase Chain Reaction (PCR) tests that detect HIV nucleic acid. The national programme recommends that HIV testing should be done using highly sensitive and specific rapid tests in HIV

Counselling and Testing Services (HCTS) facilities, which provide reliable, timely and accurate test results, as per the prescribed quality standards.

Under the NACP, the most commonly used rapid tests are based on the principle of enzyme immunoassay, immune-chromatography (lateral flow), immune-concentration /dot-blot assays (vertical flow) and particle agglutination. All these different rapid tests should have a sensitivity of ≥ 99.5% and specificity of ≥ 98%. Window period represents the period between infection with HIV and the time when HIV antibodies can be detected in the blood (6–12 weeks). A blood test performed during the window period may yield a negative test result for HIV antibodies. These cases may require further testing after 12 weeks.

4.2 Diagnosis of HIV infection in adults and children above the age of 18 months

Confirmatory diagnosis of HIV infection is essential for ensuring access to care and treatment services. National HIV testing strategies enable the programme to screen for HIV or confirm the diagnosis of HIV at the nearest Integrated Counseling and Testing Centre (ICTC). In view of the low prevalence of HIV in India, it is necessary to use three different principles or antigen-based rapid tests to confirm the diagnosis. All samples reactive in the first test should further undergo confirmatory second/third tests based on different principles/antigens using the same serum/ plasma sample as that of the first test. The same blood sample is utilized for performing all the tests for identifying HIV antibodies. For indeterminate results, testing should be repeated on a second sample taken after 14–28 days.

A testing strategy for diagnosis describes a testing sequence for the specific testing objective of diagnosis (as opposed to screening only), taking into consideration the presumed HIV prevalence in the population. The national programme follows strategy I for screening and strategy II for surveillance purposes, whereas it uses strategy II (B) and strategy III for diagnosis in symptomatic and asymptomatic persons, respectively. The following strategies are to be used for HIV testing and diagnosis in adults and children above the age of 18 months:

- For clinically symptomatic individuals: the sample should be reactive with two different kits (Strategy II (B);
- For clinically asymptomatic individuals: the sample should be reactive with three different kits (Strategy III).

For clinically symptomatic individuals: A patient who is clinically symptomatic and suspected to have HIV infection/disease is referred to the ICTC for confirmation of the diagnosis. In this case, the same blood sample is tested twice using kits with either different antigens or principles. The patient is declared HIV negative if the first test is non-reactive and HIV positive when both tests show reactive results. When there is discordance between the first two tests (first reactive and the second non-reactive), a third test is done. If the third test is also negative, it is reported as negative. If the third test is reactive, it is reported as indeterminate and the individual is retested after 14–28 days, as shown in Strategy II (B).

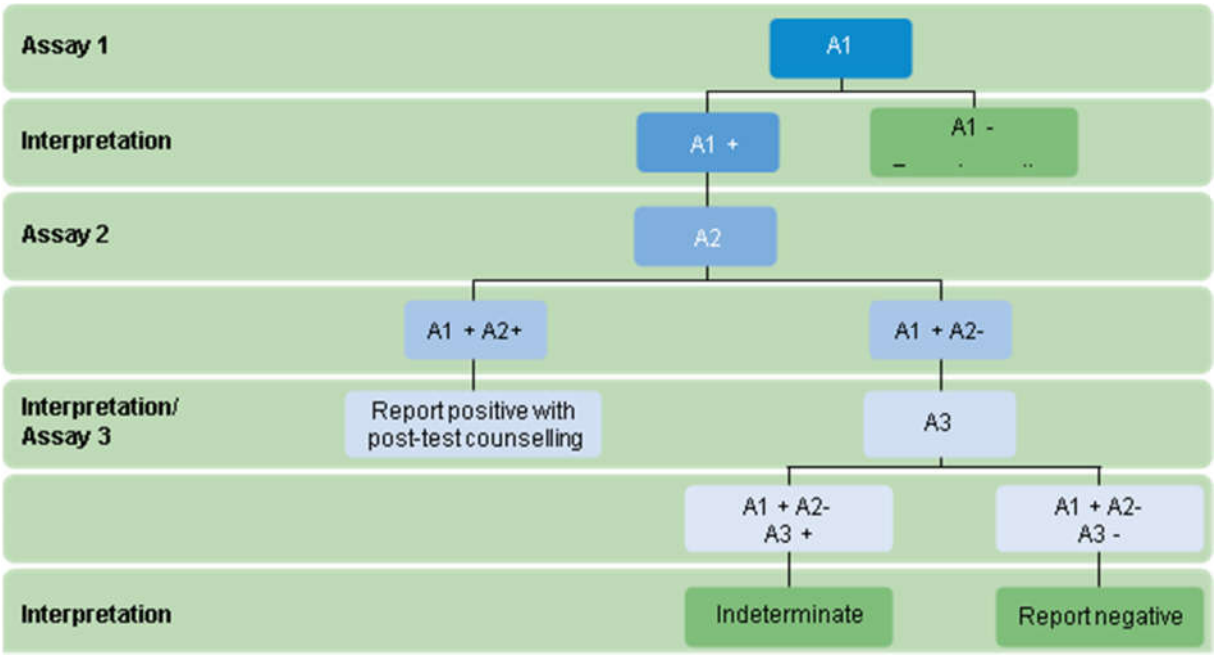


Figure 4.1: Strategy II (B): For diagnosis of clinically symptomatic individuals

For clinically asymptomatic individuals: Confirmation of HIV diagnosis in asymptomatic individuals is done at an ICTC using three rapid tests of three different antigens or principles. The individual is considered HIV negative if the first test is non-reactive and HIV positive when all three tests show reactive results. For indeterminate results, testing should be repeated on a second sample taken after 14–28 days, as shown in Strategy III.

All HIV testing should be provided following five essential Cs: Consent, Confidentiality, Counseling, Correct test results and immediate Connection/linkages to services for HIV prevention, treatment and care. All persons should undergo pre-test and post-test counselling and confidentiality should be maintained while disclosing the results. Post-test counselling is important both for those with reactive results and those with negative results.

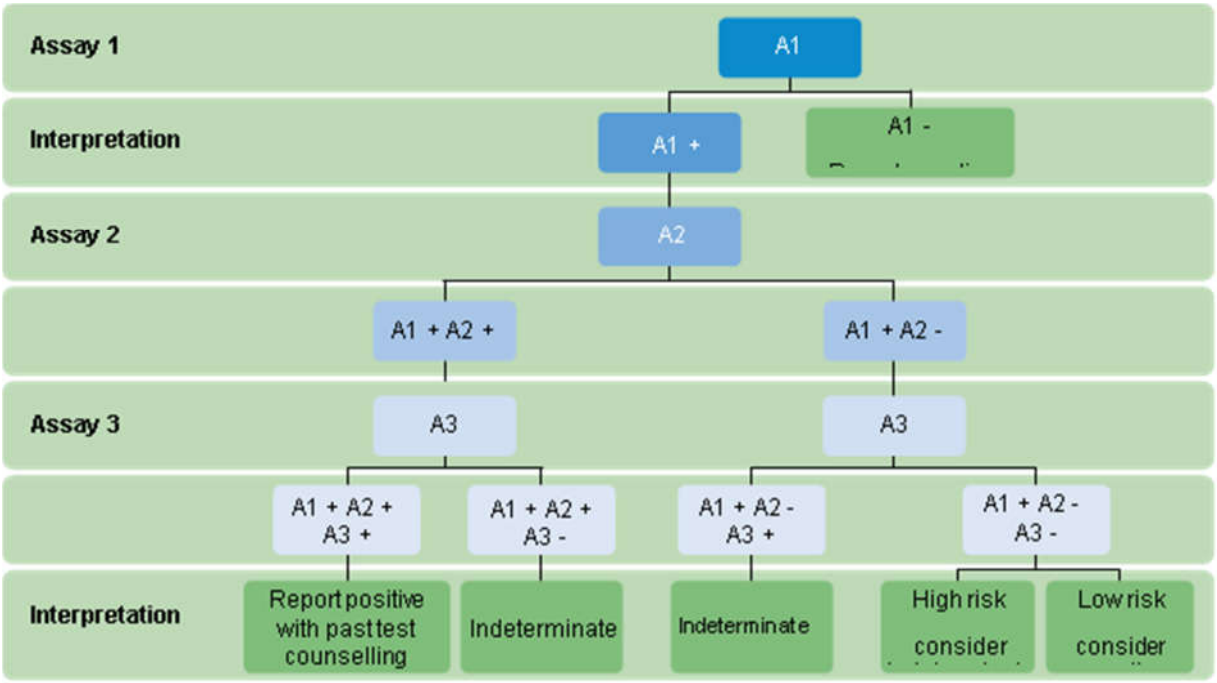


Figure 4.2: Strategy III: For diagnosis of clinically asymptomatic individuals

In addition to the walk-in clients and community-based HIV testing, Provider-Initiated Testing and Counseling (PITC) is recommended in all healthcare settings for adults, adolescents or children, who present in clinical settings with signs and symptoms or medical conditions that could indicate possible HIV infection.

The spouses/partners of those with HIV-positive results and children of HIV-infected mothers should also be counselled and offered HIV testing. All persons found positive for HIV should be immediately linked to appropriate HIV care, support and treatment services.

For more details, please refer to the national HIV Counselling and Testing Services (HCTS) Guidelines, NACO, December 2016.

4.3 Diagnosis of HIV infection in infants and children less than 18 months of age

Maternal antibodies to HIV, transferred passively to the infant during pregnancy, usually persist for nearly 9–12 months in the infant. In some children, they may persist for as long as 18 months. Thus, during this period, children born to HIV-infected mothers will test positive for HIV antibodies regardless of their own infection status. A positive ELISA/Rapid test that detects antibodies to HIV, therefore, does not necessarily indicate the presence of HIV infection in the infant/child. Rather, a positive ELISA/Rapid test indicates exposure to HIV. More reliable indicators of the HIV infection status of the infant are tests that detect HIV viral RNA or antigens.

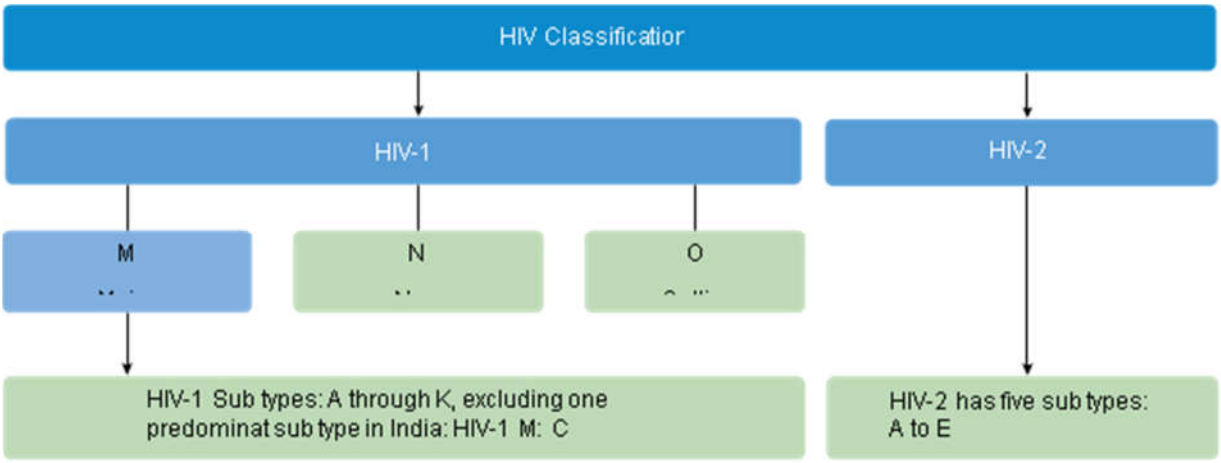
NACO recommends the use of Total Nucleic Acid (TNA) PCR test on a Dried Blood Spot (DBS) sample of the infant to detect viral nucleic acids for diagnosis of HIV-1 infection during infancy. This test is performed at 6 weeks of age or at the earliest opportunity when the infant and the mother come in contact with healthcare system/workers. At and after 6 months of age, TNA PCR must be performed after screening for HIV antibodies. It is also important to take breastfeeding into consideration in the HIV testing algorithm. Since breastfed children have an ongoing risk of HIV acquisition, they are tested (TNA PCR) 3 months after complete cessation of breastfeeding or 18 months of age, whichever is later, to reliably exclude HIV-1 infection. For more detailed information, refer to Chapter 2.1 on (Assessment of Adults and Adolescents with HIV Infection) and Annexure 1 and 1x.

4.4 Diagnosis of HIV-2

There are two types of HIV: HIV type I (HIV-1) and HIV type 2 (HIV-2). The most common cause of HIV infection throughout the world is HIV-1 that comprises of several subtypes with different geographic distributions.

Information on the epidemiology of HIV-2 and dual infection in India is limited. However, cases of HIV-2 infection have been reported.

Figure 4.3: Classification of HIV-1 and HIV-2



Natural history studies indicate that HIV-2 is less pathogenic than HIV-1. Those infected with HIV-2 have slower disease progression, a much longer asymptomatic stage, slower decline in CD4 count, lower rates of vertical transmission, lower viral loads while asymptomatic and smaller gains in CD4 count in response to ART.

It is observed and well documented that infection with HIV-2 does not protect against HIV-1 or dual infection. Patients with dual infection (HIV-1 and HIV-2) tend to present at a more

advanced stage of the disease than those infected with HIV-2 only. Infection with both HIV-1 and HIV-2 generally carries the same prognosis as that of HIV-1 single infection.

Although HIV-1 and HIV-2 are related, there are important structural differences between them. Accurate diagnosis and differentiation of HIV-1 and HIV-2 is crucial for treatment initiation and in the assessment of treatment failure. Since Dolutegravir (DTG) is now recommended as the preferred drug for all lines of treatment of HIV infection, it is expected that patients with HIV- 2 infection will benefit. However, in patients with HIV-2 infection, either alone or with HIV-1, treatment failure assessment entirely depends on the falling CD4 counts and not on virological failure, as HIV-2 viral load assessment in them is not possible in programme conditions. Hence, the knowledge/information of those PLHIV with HIV-2 infection is crucial for the treatment of

infected individuals as well as for understanding the extent of HIV-2 infections in India. Rapid kits that differentiate between HIV-1 and HIV-2 are being used at ICTCs. Test results that show HIV-2 reactivity by two different testing kits/principles are reported as reactive for HIV-2 and no further testing is required.

Samples that test reactive for HIV-1 and HIV-2 or test reactive for HIV-2 with only one kit need confirmation; NACO has established a network of laboratories for this designated as HIV-2 referral laboratories. The designated laboratories are responsible for confirming the presence of HIV-2 infection. Patients requiring confirmation of the HIV-2 reactive report will be referred, by the ICTC, to the nearest ART centre with the ICTC report and a referral slip. The guidance for HIV-2 diagnosis confirmation is as follows:

Figure 4.4: Guidance for HIV-2 diagnosis confirmation

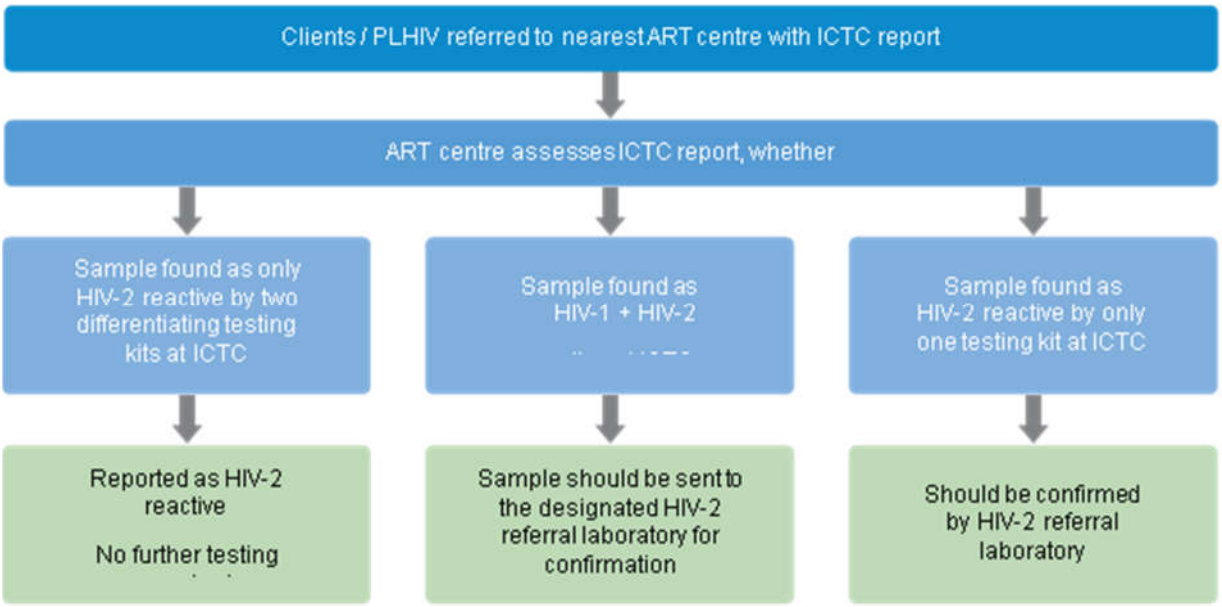
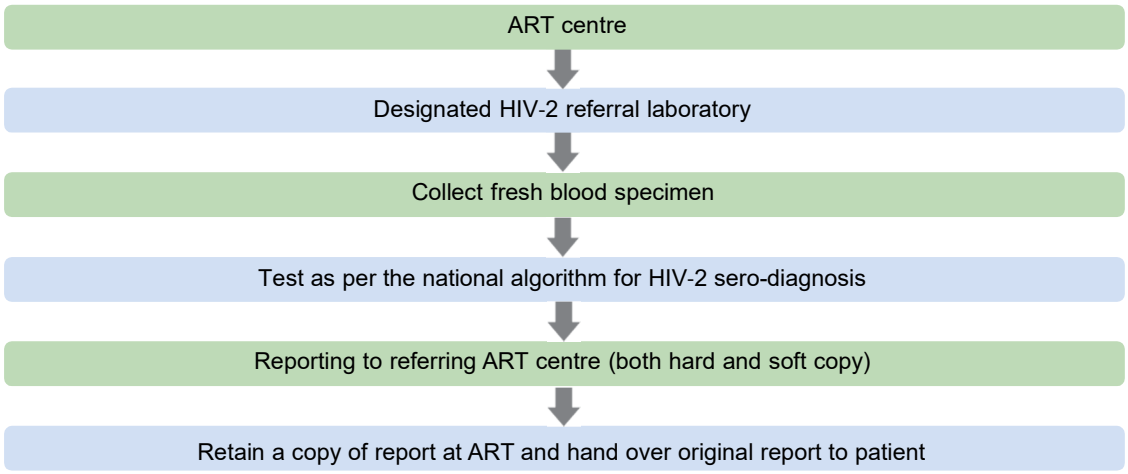


Figure 4.5: Flow chart for referring patient for HIV-2 testing from ART center to reference laboratory

[with ICTC Report

"Specimen is positive for



HIV antibodies" (HIV-1 and HIV-2 or HIV-2 in one test only) and referral slip]

CHAPTER-5

ASSESSMENTS OF ADULTS AND ADOLESCENTS WITH HIV INFECTION

5 ASSESSMENTS OF ADULTS AND ADOLESCENTS WITH HIV INFECTION

All persons diagnosed with HIV at the ICTC should be enrolled in the ART centres for HIV care and treatment services. 'Adolescents' are defined as persons aged between 10 and 19 years. Thorough clinical assessment, clinical history, physical examination and access to basic laboratory diagnostics are essential for rapid ART initiation.

This section deals with the assessment of adults and adolescents with HIV infection. The steps to be followed during initial evaluation of PLHIV are as below:

Step 1: Clinical assessment and medical history

Step 2: Physical examination

Step 3: Baseline laboratory evaluation

5.1 Clinical Assessment

Once the PLHIV are enrolled in an ART centre, a comprehensive clinical assessment should be done to obtain baseline clinical status and to rule out OIs. This helps to

- Determine the clinical stage of the HIV infection;
- Identify the current HIV-related illnesses that may require treatment;
- Identify any prior exposure to ARVs in the past;
- Determine the need for OI prophylaxis;
- Identify coexisting medical conditions such as Diabetes, Hypertension, Hepatitis or any other treatment that may influence the choice of ARV drugs;
- Determine nutritional status and needs;
- Elicit the history of past illnesses (especially TB, Sexually Transmitted Infections [STIs]);
- Elicit HIV status of family members/partners; offer index testing services for spouse, sexual and injecting partners and biological children;
- Assess the need for psychosocial support.

5.2 Medical History

Assessment and history taking should include the following:

- HIV testing
- 4 symptom screening for TB (Adults: fever, cough, weight loss, night sweats; Children: fever, cough, poor weight gain/reported weight loss, h/o contact with a TB case);
- Any persistent symptoms – headache, poor concentration, seizures;
- General medical history for comorbid conditions like Diabetes, Hypertension and others;
- History of tuberculosis in past/family;
- Prior exposure to ARVs in the past;
- History of STI;
- HIV risk behavior – multiple partners, key populations, injecting drug use;

- Substance abuse – alcohol, tobacco, oral or injecting drugs;
- Pregnancy and contraception;
- Allergies/medication/vaccines;
- Nutritional status;
- Psychosocial assessment.

Medical officers of the ART centers must obtain detailed medical history as per the checklistprovided in Table 4.5

Table 5.1: medical history checklist

HIV Testing	HIV Risks (can be multiple)
• Ever tested for HIV in the past • Date and place of the first HIV test • Reason for HIV testing • Documentation of the test result • Date of the last negative HIV test result • Previous CD4 cell counts (if applicable) • Previous viral load (if applicable)	• Unprotected sexual contact • Injecting drug use • Commercial sex work • Men having sex with men • Occupational exposure (Healthcare Worker [HCW]) • Perinatal transmission • Recipient of blood products • Sero-discordant couple • Unknown
Review of Clinical symptoms	**Past History of HIV-related Illness**
• Unexplained weight loss • Swollen lymph nodes • Night sweats and fever • Unusual headaches, poor concentrationor confusion • Fever with chills/rigor • Change in appetite	• Oral oesophageal candidiasis • Persistent diarrhoea • Tuberculosis • Varicella zoster (Shingles) • Oral hairy leucoplakia (OHL) • Pneumocystis jiroveci pneumonia (PCP) • Recurrent bacterial pneumonia

• Skin rash • Sores/Ulcers or white spots in mouth • Painful swallowing • Chest pain, cough, or shortness of breath	• Cryptococcal meningitis • Toxoplasmosis • Kaposi's sarcoma
• Abdominal pain, vomiting or diarrhoea • Numbness or tingling in hand or feet • Muscular weakness / abnormal movements • Partial loss of vision or visual field defects	• Disseminated Mycobacterium avium complex • Cytomegalovirus (CMV) infection • Invasive cervical cancer
Tuberculosis History	ART History
• History of past TB infection and type of TB • Old chest X-ray (if available) • Treatment given (drugs and duration) • History of TB in family/close contacts • Ask the four TB screening questions '4S screening' (current cough, fever, weight loss and night sweats)	• Current and past exposure to ARVs • ARV use during pregnancy for prevention of mother to child transmission (PMTCT) • Use of Post Exposure Prophylaxis (PEP) in the past • Current/past use of Pre-Exposure Prophylaxis (PrEP) • Drugs taken and for how long • An understanding of the treatment and readiness to commence ART • Partner's ART history (if HIV positive)
Sexually Transmitted Infections	Substance Use
• Genital ulcer or other lesions • Genital discharge (abnormal vaginal discharge in women)	• Alcohol, stimulant, opiate and use of other drugs • Smoking history

• Scrotal swelling, urethral discharge, anal ulcers • Lower abdominal pain	
General Medical History	Allergies
• Any other past medical condition such as diabetes, hypertension, coronary artery disease, Hepatitis B, Hepatitis C, hyperlipidemia, mental health issues, e.g., depression	• Known allergies to drugs or other substances or materials
Medication	Vaccination History
• Past use of drugs and reasons for taking those drugs • Current use of drugs and reasons • Current use of traditional/herbal remedies • Opioid Substitution Therapy (OST)	• BCG • Hepatitis A vaccine • Hepatitis B vaccine • Vaccination against Covid
Gynecological History	Pregnancy and Contraception History
• Last PAP smear • Menstrual irregularities ▪ Pelvic pain or discharge	• Previous pregnancies and medical termination of pregnancy (MTP) (years) • Children and HIV status of the children (living and dead) • Exposure to ARVs during pregnancy • Drugs and duration of ART • Contraception used

	• Last menstrual period
Psychosocial History	Functional Status
• Family history, e.g., other immediate family members with known HIV infection • Social history e.g., marital status, education, occupation, source of income • Financial and family support status • Disclosure status, readiness to disclose • Availability of care and treatment supporter	• Able to work, go to school, do housework • Ambulatory but not able to work • Bedridden • Amount of day-to-day care needed

5.3 Physical Examination

It is essential to conduct a thorough physical examination to determine the clinical stage and screen for OIs. Table 5.2 details the specific physical signs related to HIV/AIDS that should be screened.

Checklist for physical examination

All PLHIV must be assessed for WHO clinical staging on the first and all the subsequent visits by the medical officer. (Please refer Table 5.3)

Signs of serious illness

On examination, if the PLHIV present with any of the following signs of serious illness, then immediate referral for expert evaluation is a must:

- Temperature ≥ 39°C with headache
- Respiratory rate ≥ 30/min
- Heart rate ≥ 120/min
- SpO2 (pulse oximeter) < 90%
- Altered mental status (e.g., confusion, strange behavior, reduced consciousness)
- Other neurological problem (persistent severe headache, seizure, paralysis, difficulty in
- talking, rapid deterioration of vision)
- Unable to walk unaided
- Any other condition that requires emergency management.

Advanced HIV Disease

PLHIV with advanced HIV disease are defined as presenting with CD4 count <200 cells/mm3 or WHO clinical stage 3 or 4 or children aged less than 5 years. PLHIV presenting with advanced HIV disease must be managed by the components of advanced disease package of services. Details of ADM package of services are provided in chapters 5.2 (Advanced Disease Management in PLHIV) and 3.3 (Advanced Disease Management in CLHIV less than 5 years of age).

Table 5.3: WHO Clinical Staging in Adults, Adolescents and Children

Adults and adolescents	Children
Clinical stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy (PGL)	• Asymptomatic • Persistent generalized lymphadenopathy (PGL)
Clinical stage 2	

• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (Sinusitis, Tonsillitis, Otitis Media, Pharyngitis) • Herpes Zoster • Angular Cheilitis • Recurrent oral ulceration • Popular Pruritic Eruption • Fungal nail infections • Seborrheic Dermatitis	• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (Otitis Media, Otorrhea, Sinusitis, Tonsillitis) • Herpes Zoster • Lineal gingival erythema • Recurrent oral ulceration • Popular Pruritic Eruption • Fungal nail infections • Extensive wart virus infection • Extensive Molluscum Contagiosum • Unexplained persistent parotid enlargement

Clinical stage 3	
• Unexplained severe weight loss (>10% of the presumed or measured body weight) • Unexplained chronic diarrhea for more than1 month • Unexplained persistent fever (intermittent or constant for longer than 1 month) • Persistent Oral Candidiasis • Oral Hairy Leucoplakia • Pulmonary Tuberculosis • Severe bacterial infections (such as Pneumonia, Empyema, Pyomyositis, bone orjoint infection, Meningitis, bacteremia) • Acute necrotizing ulcerative stomatitis, Gingivitis or Periodontitis • Unexplained anemia (<8 g/dl), neutropenia (<0.5 x 10^9/L) and/or chronic thrombocytopenia (<50 x 10^9/L)	• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhea (14 days ormore) • Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than 1 month) • Persistent Oral Candidiasis (after the first 6 weeks of life) • Oral Hairy Leucoplakia • Lymph node Tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial Pneumonia • Acute necrotizing ulcerative gingivitis or Periodontitis • Unexplained anemia (<8 g/dl), neutropenia(<0.5 x 10^9/L) or chronic thrombocytopenia (<50 x 10^9/L) • Symptomatic Lymphoid Interstitial Pneumonitis • Chronic HIV-associated lung disease, including Bronchiectasis
Clinical stage 4	

• HIV wasting syndrome • Pneumocystis (jiroveci) Pneumonia • Recurrent severe bacterial Pneumonia • Chronic Herpes Simplex infection (orolabial, genital or anorectal of more than 1 month duration or visceral at any site) • Oesophageal Candidiasis (or Candidiasis of trachea, bronchi or lungs) • Extra pulmonary Tuberculosis • Kaposi's sarcoma • Cytomegalovirus infection (retinitis or infectionof other organs) • Central nervous system Toxoplasmosis • HIV encephalopathy • Extra pulmonary Cryptococcosis, including Meningitis • Disseminated non-tuberculous mycobacterial infection (NTM) • Progressive Multifocal Leukoencephalopathy (PML) • Chronic Cryptosporidiosis • Chronic Isosporiasis • Disseminated mycosis (extra pulmonary Histoplasmosis, Coccidioidomycosis) • Lymphoma (cerebral or B-cell non-Hodgkin's) • Symptomatic HIV-associated nephropathy or cardiomyopathy	• Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy • Pneumocystis (jiroveci) Pneumonia • Recurrent severe bacterial infections (such as Empyema, Pyomyositis, bone orjoint infection, Meningitis, but excluding Pneumonia) • Chronic Herpes Simplex infection (orolabial or cutaneous of more than 1 month duration or visceral at any site) • Oesophageal Candidiasis (or Candidiasis of trachea, bronchi, or lungs) • Extra pulmonary Tuberculosis • Kaposi's sarcoma • Cytomegalovirus infection (retinitis or infectionof other organs with onset at age more than 1month) • Central nervous system Toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extra pulmonary Cryptococcosis, including Meningitis • Disseminated nontuberculous mycobacterial infection (NTM) • Progressive Multifocal Leukoencephalopathy (PML)

5.4 Nutritional Assessment

Good nutrition is a key factor for maintenance of good health and quality of life for all people whereas poor nutrition reduces a person's ability to work and be active. In PLHIV, poor nutrition worsens the effects of HIV by further weakening the immune system. This leads to frequent illnesses and an inability to replace and repair body cells and tissues, resulting in severe weight loss. It may lead to a more rapid progression of the disease.

Food and nutritional intake can influence the adherence to ARVs as well as the effectiveness of ARVs. HIV and associated infections increase the need for energy, proteins and micronutrients like iron, zinc, vitamin C, etc. OIs like TB, Pneumonia and Diarrhoea further increase the nutritional demands of the body, accelerating the decline in nutritional status. Thus, a vicious cycle exists between HIV infection and malnutrition.

Appropriate nutritional support from the early stages of HIV infection can prevent the onset of malnutrition and other nutritional deficiencies. It will also help maintain the performance of the immune system. Nutritional care and support, which includes counselling, education, information sharing and linkage to social welfare schemes, is an important component of the comprehensive package of care and support services for all PLHIV, including adults, adolescents and CLHIV

Nutritional assessment

A BMI less than 18.5 kg/m2 is a recognized independent risk factor for morbidity and mortality in HIV-positive adolescents and adults.

An initial nutritional status assessment and targeted further care are therefore essential components of comprehensive care of the HIV-positive patient. This attention to the nutritional care of patients can also improve adherence to ART and retention in care as well as supporting their continuation or return to a productive life

There are many factors responsible for change in nutritional status of PLHIV. The details can be

found in the chapter 3.6 (Nutritional Care of HIV-infected Children).

Nutritional assessment should include the following:

Anthropometric measurements: There are no specific measurements; however, BMI may be considered for clinical evaluations (Table 5.3).

Table 5.4: Nutritional classification and BMI value for adults (kg/m²)

Nutritional Classification	BMI (kg/m²)
Obese	30 and more
Overweight	25 to <30
Normal	18.5 to <25
Risk of acute malnutrition	17 to <18.5
Moderate acute malnutrition	16 to <17
Severe acute malnutrition	<16

- Assessment of oedema: Bilateral oedema is a sign of severe malnutrition. However, oedema in adults can be caused by other pathologies (renal, cardiac, hepatic, etc.); so these must be checked for before deciding that the oedema is being caused by malnutrition.
- Dietary/food history: This is important to modify the dietary requirements if PLHIV are deficient as per the recommended needs

5.5 Comprehensive Laboratory Evaluation in HIV/AIDS

The purpose of the baseline laboratory evaluation is as follows:

- To rule out other concomitant infections, OIs;
- To determine baseline safety parameters.

The following investigations (Table 2.1.5) are recommended for monitoring of PLHIV at the ART centers

Baseline Investigations: Essential tests for all patients registering in HIV care at ART center
• Hemogram /CBC • Urine for routine and microscopic examination • Fasting blood sugar • Blood urea, Serum creatinine • Serum bilirubin, ALT (SGPT) • VDRL • CD4 count • X-ray chest PA view

:

Additional tests at baseline as per the physician's decision

- Symptoms and signs directed investigations for ruling out OIs, including MTB by sputum/ appropriate specimen using Nucleic Acid Amplification Test (CBNAAT/Truenat) and/or other required investigations
- Complete Liver function test (LFT) for those being initiated on Anti-tubercular treatment (ATT) and for patients with Hepatitis B or C co-infection
- Lipid profile (if available)
- Ultrasonography (USG) whole abdomen
- rK-39 strip test to confirm or rule out leishmaniasis (especially in patients with HIV infection who live in or travel to endemic areas i.e., Bihar, Eastern Uttar Pradesh, Jharkhand and West Bengal)
- Pregnancy test (if applicable)
- For women, cervical PAP smear or other method of cervical cancer screening (if available)
- For men having sex with men (MSM), anal PAP smear (if available)

NON-AVAILABILITY/NON-FEASIBILITY OF ANY OF THESE TESTS SHOULD NOT DELAY THE INITIATION OF ART

Note: All the above investigations other than CD4 estimation shall be done from the health facility where the centreis located, with support from the State Health Department.

5.6 Assessment and Management of the Patient at First and at Follow-up Visits

Table 5.6: Assessment and management of the patient during the first and follow-up visits at the ART center

Visit	Activities
Visit 1 (Day 1)	• Registration in HIV care • Medical history • Follow symptom screening checklist • 4-symptom TB screening • Physical examination • Behavioral/psychosocial assessment • Educational level, employment history, financial resources • Social support, family/household structure • Disclosure status, readiness to disclose • Understanding of HIV/AIDS, transmission, risk reduction, treatment options • Nutritional assessment • Family/household assessment to determine if there are other HIV-infected family members who may need care • Recommend condom use during every visit • Readiness assessment/Preparedness counselling

Visit	Activities
	• Baseline investigation: Essential tests including CD4 count and additionaltests as per requirement • Initiate Cotrimoxazole Preventive Therapy (CPT), if eligible • Commence ART if the patient is adequately prepared: ART to be dispensedfor one month and concurrently send samples for CD4 count and other baseline investigations as per NACO guidelines (Refer to Rapid ART initiation in chapter 2.2 [ART in Adults and Adolescents])
Before follow-up visits (within 3–15 days after initiating ART)	• Review test results: If test reports are not normal, PLHIV to be called back to ART centre (as soon as possible, within 2 weeks of ART initiation) • ART counsellor to call all patients to learn about general well-being of patients within 2 weeks of ART initiation
Subsequent follow-up visits (after initiating ART)	• History (new problems) • Symptom checklist • Clinical examination • 4-symptom TB screening • Note any side effects (Insomnia, anaemia, rash, fever, signs of hepatotoxicity/nephrotoxicity) • Investigations as per monitoring and follow-up related to ARV • Counselling • Adherence assessment/support

CHAPTER-6

ART IN ADULTS AND ADOLESCENTS

6 ART IN ADULTS AND ADOLESCENTS

There has been a rapid decline in HIV-related mortality and morbidity due to the wider availability of affordable, more efficacious and less toxic ARVs over the last two decades. ART consists of the use of a combination of at least three ARV drugs from different classes to inhibit the replication of HIV and reduce viraemia to undetectable levels. Continued suppression of viral replication leads to the restoration of immune response, reflected by an increase in the CD4 count. Increase in CD4 count leads to slowing of the disease progression, reduced frequency of OIs, improvement in the quality of life and increased longevity. Successes achieved by ART have now transformed the perception about HIV infection from being a 'virtual death sentence' to a 'chronic manageable illnesses. ART was earlier known as Highly Active ART (HAART) and as combination ART (cART).

6.1 Goals of Antiretroviral Therapy

ART cannot cure HIV infection, as the currently available ARV drugs cannot eradicate the virus from the human body. This is because a pool of latently infected CD4 cells is established during the earliest stages of acute HIV infection. HIV persists within the organs/cells and fluids (e.g., brain, liver and lymphoid tissue) despite prolonged suppression of plasma viraemia to undetectable level by ART. The primary goals of ART are maximal and sustained reduction of plasma viral load and restoration of immunological functions. The reduction in the viral load also

leads to reduced transmissibility and reduction in new HIV infections. The defined goals of ART are depicted in Table 6.1.

Goals of ART	
Clinical goals	Increased survival and improvement in quality of life
Virological goals	Greatest possible sustained reduction in viral load
Immunological goals	Immune reconstitution, that is, both quantitative and qualitative
Therapeutic goals	Rational sequencing of drugs in a manner that achieves clinical, virological and immunological goals while maintaining future treatmentoptions, limiting drug toxicity and facilitating adherence
Preventive goals	Reduction of HIV transmission by suppression of viral load

Due to continued viral suppression, the destruction of CD4 lymphocyte cells is reduced and, over time, there is an increase in the CD4 count, which is accompanied by partial restoration of pathogen-specific immune function. This leads to a reduction in incidence of OIs, reduced morbidity and mortality

6.2 Principles of Antiretroviral Therapy

A continuous high level of HIV replication takes place in the body right from the early stages of the infection. At least one billion viral particles are produced during the active stage of replication. The ARVs act on various stages of the HIV viral replication and interrupt the process of viral replication in the body. Figure 2.2.1 depicts the various enzymes involved in viral replication and the points where ARVs target the virus. The ARV drugs act on the viral replication in the following steps and their classes are labelled according to the site of their action:

- Block binding of HIV to the target cell (Fusion Inhibitors and CCR-5 co-receptor blockers)
- Block the viral RNA cleavage and one that inhibits reverse transcriptase (Reverse Transcriptase Inhibitors)
- Block the enzyme integrase, which helps in the pro-viral DNA being incorporated into the
- host cell chromosome (Integrase Inhibitors)

- Block the RNA to prevent viral protein production
- Block enzyme protease (Protease Inhibitors)
- Inhibit the budding of virus from host cells

Table 6.2 Classes of ARV Drugs

Nucleoside reverse transcriptase inhibitors (NsRTI)	Non-nucleoside reverse transcriptase inhibitors (NNRTI)	Protease inhibitors (PI)
Zidovudine (AZT)*	**Nevirapine (NVP)***	**Saquinavir (SQV)**
Stavudine (d4T)	**Efavirenz (EFV)***	**Ritonavir (RTV)***
Lamivudine (3TC)*	Delavirdine (DLV)	**Nelfinavir (NFV)**
Abacavir (ABC)*	Rilpivirine (RPV)	**Amprenavir (APV)**
Didanosine (ddl)	Etravirine (ETV)	**Indinavir (INV)**
Zalcitabine (ddC)	Doravirine (DOR)	**Lopinavir (LPV)***
Emtricitabine (FTC)	**Integrase Inhibitors**	**Fosamprenavir (FPV)**
Nucleotide reverse transcriptase inhibitors (NtRTI)	**Dolutegravir (DTG)***	**Atazanavir (ATV)***
	Raltegravir (RGV)*	**Tipranavir (TPV)**
	Elvitegravir (EVG)	**Darunavir (DRV)***
Tenofovir Disoproxil Fumarate (TDF)*	Bictegravir (BIC)	
Tenofovir Alafenamide (TAF)	Cabotegravir (CAB)	
Fusion inhibitors (FI)	**CCR5 entry inhibitor**	**Post attachment maturation inhibitor**
Enfuvirtide (T-20)	Maraviroc (MVC)	**Ibalizumab (IBA)**
***Available in the national programme**		

6.3 Clinical Pharmacology of Commonly Used ARV Drugs

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

The first effective class of ARV drugs discovered was the Nucleoside analogues, which act by incorporating themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and cannot create new viruses. Nucleotide analogues work in the same way as nucleosides, but they have a non-peptidic chemical structure. The details of individual ARV drugs of this class are listed in Table 6.2

Table 6.3.1: Commonly used NRTIs

Generic Name	Dose	Adverse effects
Tenofovir Disoproxil Fumarate (TDF)	300 mg once daily	Renal toxicity, bone demineralization
Zidovudine (AZT)	300 mg twice daily	Anaemia, neutropenia, bone marrow suppression, GI intolerance, headache, insomnia, myopathy, lactic acidosis, skin and nail hyperpigmentation
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily	Minimal toxicity, rash (though very rare)
Abacavir (ABC)	300 mg twice daily or 600 mg once daily	Hypersensitivity reaction in 3% to 5% (can be fatal), fever, rash, fatigue, nausea, vomiting, anorexia, respiratory symptoms (sore throat, cough, shortness of breath); rechallenging after reaction can be fatal

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) stop HIV production by binding onto the reverse transcriptase and preventing the conversion of RNA to DNA. These drugs are called 'non-nucleoside' inhibitors because, even though they work at the same stage as nucleoside analogues, as chain terminators, they inhibit the HIV reverse transcriptase enzyme by directly binding to it. The details of individual ARV of this class are shown in Table 6.3.1.

Table 6.3.2: Commonly used NNRTIs

Generic Name	Dose	Food-related advice	Adverse Effects
Efavirenz (EFV)	600 mg once daily (bedtime administration is suggested to decrease central nervous system side effects	Avoid taking after high-fat meals	Central nervous system symptoms (dizziness, somnolence, insomnia, confusion, hallucinations, agitation) and personality change. Rash occurs, but lesscommon than with NVP
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily	None	Hepatitis (usually within 12 weeks); sometimes, life-threatening hepatic toxicity. Skin rash occasionally progressing to severe conditions, including Stevens Johnson's syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Patients who develop severe hepatic toxicity or grade 4 skin rashes should not be rechallenged.

Integrase Inhibitors (Integrase Strand-Transfer Inhibitor [INSTI])

Integrase inhibitors are a class of ART drugs designed to block the action of integrase, a viral enzyme that inserts the viral genome into the DNA of the host cell.

Since integration is a vital step in retroviral replication, blocking it can halt further replication of the virus.

Raltegravir (RAL):

Raltegravir was the Integrase inhibitor approved for use in 2007. It is metabolized primarily through uridine diphosphate glucuronosyltransferase 1A1 and has a single inactive glucuronide metabolite.

It is not a substrate, inhibitor or inducer of cytochrome P450 enzymes and it exhibits low potential for drug–drug interactions. It is well tolerated; most reported adverse effects include nausea,

headache, diarrhea, fever, CPK elevation, muscle weakness and insomnia. The major toxicities are given in Table 2.2.5. Raltegravir was approved for use in both treatment-naive and treatment-experienced patients, and it had been primarily used for second- or third-line ART in the national ART programme.

Dolutegravir (DTG)

It was first approved for its usage by US FDA in 2013. Later, it was recommended by WHO in 2019 and NACO Technical Resource Group approved its usage since July 2020. NACO recommends Dolutegravir as the preferred drug for treatment of HIV-positive adults, adolescents and children (aged more than 6 years with bodyweight more than 20 kg) under the NACP. DTG is an orally bioavailable INSTI with activity against HIV type 1 and 2 (HIV-1/2 and both) infections. Upon oral administration, dolutegravir binds to the active site of integrase, an HIV enzyme that catalysis the transfer of viral genetic material into human chromosomes. This prevents integrase from binding to retroviral DNA, and blocks the strand transfer step, which is essential for the HIV replication cycle. This prevents HIV replication. Dolutegravir is currently the preferred drug in the first-line and also in second-line treatment regimens.

Table 6.3.3 Integrase Inhibitors used in National Programme

Generic Name	Dose	Adverse Effects
Dolutegravir (DTG)(Preferred INSTI in programme)	50 mg once daily	• Insomnia: Patients with complaints of sleep disturbancesneed to be reviewed and to be managed accordingly. Sedatives should be added with appropriate consultationif that is affecting the daily routine of the patient. • Headache: If headache is persistent and affecting daily routine of activities, the PLHIV should be referred for expert opinion. • Dizziness • Tiredness • Allergic reactions • Weight gain: Weight gain is a known side effect and strict monitoring is required and information should begiven to the PLHIV about the same.
Raltegravir (RAL)	400 mg twice daily	• Rhabdomyolysis, Myopathy, Myalgia, diarrhoea, fever, rash, Stevens-Johnson's syndrome, Toxic Epidermal Necrolysis, Hepatitis and Hepatic failure • Insomnia

Dolutegravir has drug interactions with the drugs listed in Table 6.3.3.

Key Drug Interaction	Suggested Management
Amodiaquine	Use an alternative antimalarial agent
Carbamazepine	Use DTG twice daily or substitute with an alternativeanticonvulsant agent
Phenytoin and phenobarbital	Use an alternative anticonvulsant agent
Dofetilide	Use an alternative antiarrhythmic agent
Metformin	Limit daily dose of metformin to 1000 mg when usedwith DTG and monitor glycaemic control
Polyvalent cation products containing Al, Ca, Fe, Mg and Zn (e.g., antacids, multivitamins and supplements)	Use 2 hours before or 6 hours after DTG
Rifampicin	Use DTG 50 mg twice daily or substitute with rifabutin

Protease Inhibitors

Protease inhibitors (PIs) work at the last stage of the viral reproduction cycle. They prevent HIV from being successfully assembled and released from the infected CD4 cell. All PIs can produce GI intolerance, altered taste, abnormal liver function test and bone disorder and all have been associated with metabolic abnormalities, such as hyperglycaemia, insulin resistance and increase in triglycerides, cholesterol and body fat distribution (lipodystrophy). The details of individual ARVs of this class are shown in Table 6.3.4.

Table 6.3.4: Commonly used PIs

Generic Name	Dose	Adverse Effects
Atazanavir/ ritonavir (ATV/r)	300 mg Atazanavir + 100 mg Ritonavir once daily	Unconjugated hyperbilirubinemia, lipid abnormality, hyperglycaemia, fat maldistribution, nephrolithiasis, cholelithiasis, PR prolongation
Lopinavir/ ritonavir (LPV/r) Heat-stable tablets	200 mg Lopinavir/ 50 mg Ritonavir Fixed dose tablet 2 tablets twice daily	Diarrhoea, nausea, vomiting, abnormal lipid profiles, glucose intolerance
Darunavir (DRV)	600 mg twice a day (when used with Ritonavir 100 mg twice daily)	Hepatotoxicity, skin rash (10%), diarrhoea, nausea, headache, hyperlipidaemia, serum transaminase elevation, hyperglycaemia
Ritonavir (RTV)	100 mg once or twice daily according to the PI to be boosted	Common: GI (diarrhoea, nausea, vomiting, abdominal pain (upper and lower); Rarely, neurological disturbances (including paranesthesia)

6.4 Considerations before Initiation of ART

All people with confirmed HIV infection should be referred to the ART centre for registration into HIV care, comprehensive clinical and laboratory evaluation to assess baseline status, treatment of pre-existing opportunistic infections, treatment preparedness, counselling and rapid ART initiation, preferably the same day unless contraindicated otherwise.

The following principles need to be kept in mind:

- The patient should be adequately prepared, and informed consent should be obtained from the patient or from the caregiver in case the patient is a minor, before initiating HIV care and ART. (For modified consent form, refer to National Operational Guidelines for ART Services, 2021.)
- Treatment should be started based on the person's informed decision and preparedness to initiate ART with information and understanding of the benefits of

treatment, lifelong course of medication, issues related to adherence and positive prevention.

- A caregiver should be identified for each person to provide adequate support. Caregivers must be counselled and trained to support treatment adherence, follow-up visits and shared decision-making.
- All patients with clinical stages 3 and 4 and those with CD4 less than 350 cells/mm3 need to be put on CPT. All patients to be screened for TB using the 4-symptom tool (current cough, fever, night sweats and weight loss) and those who do not have TB need to be started on Tuberculosis Preventive Therapy (TPT) / (Isoniazid Preventive Therapy) in addition to ART.
- ART should not be started in the presence of an active OI. In general, OIs should be treated or stabilized before commencing ART. Mycobacterium Avium Complex (MAC) and Progressive Multifocal Leukoencephalopathy (PML) are exceptions in which commencing ART may be the preferred treatment, especially when specific MAC therapy is not available. For details on starting ART in patients with HIV–TB co-infection, please refer to the management of HIV–TB in Chapter 2.8 (HIV-TB co-infection: Case Finding, Management and Prevention of Tuberculosis). Some clinical conditions, which may regress following the commencement of ART, include candidiasis and cryptosporidiosis. The following OIs and HIV-related illnesses (Table 6.5.1) need treatment or stabilization before commencing ART

Table 6.4.1: Opportunistic infections and HIV-related conditions and ART initiation

Clinical Picture	Action
Any undiagnosed active infection with fever	Diagnose and treat first; start ART when stable
Tuberculosis	• ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count (except whensigns and symptoms of meningitis are present). • Among PLHIV with TB meningitis, ART should be delayed at least 4 weeks (and initiated within 8 weeks) after treatment for TB meningitis is initiated. Corticosteroids should be considered for adjuvant treatment of TB

	meningitis.
PCP	Treat PCP first; start ART when PCP treatment is completed.

Once the evaluation is completed, the following are the key questions pertaining to ART:

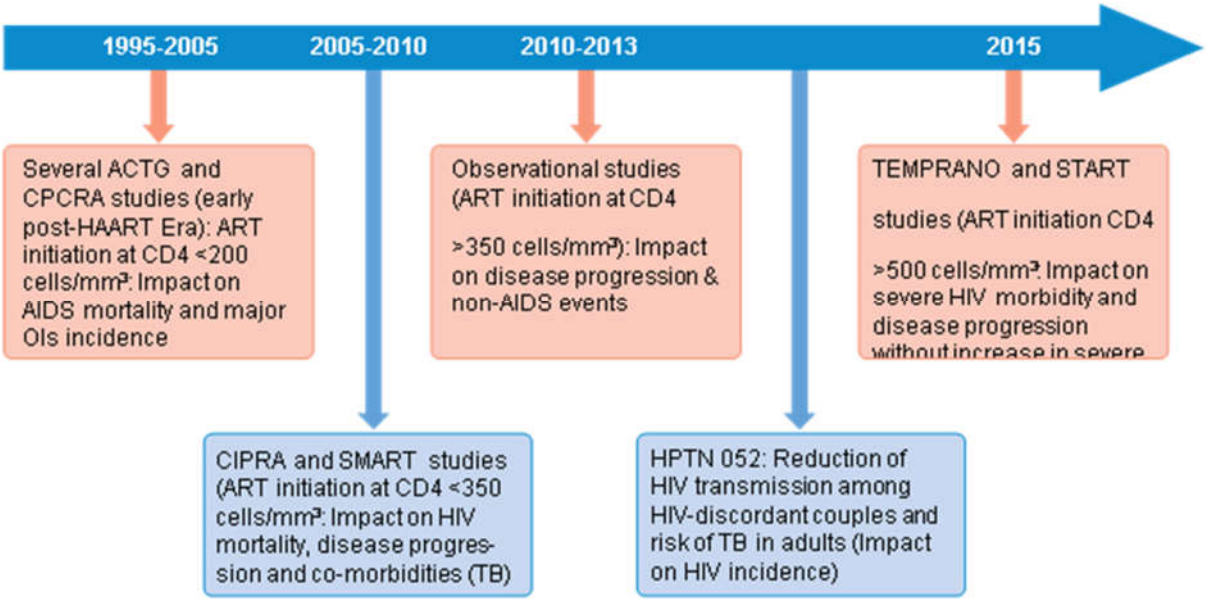
- When to start treatment?
- Which and how many agents to use? Choice of optimal regimen.
- How to monitor the therapy?
- How long to give therapy?
- When to change therapy and to what?
- Drug interactions involving ART

6.5 When to Start ART in Adults and Adolescents

In general, the clinical management of an HIV-infected patient revolves around optimizing the treatment regimen, reducing drug toxicity, reducing the pill burden and increasing adherence to the treatment.

The guidelines on when to start ART have evolved over the years towards early and rapid initiation of ART; CD4 count cut-off point for ART initiation moving from less than 200 cells/mm3 in 2004 to less than 350 cells/mm3 in 2011 and then to less than 500 cells/mm3 in 2016. The current recommendation to TREAT ALL, regardless of the clinical stage or CD4 count is in the National Programme since 2017. These changes have been based on the evidence from various randomized clinical trials (RCT) and large observational cohorts, which have revealed that with early ART initiation, there is a significant delay in progression to AIDS and reduction in the incidence of TB. These studies are summarized in Figure 2.2.2.

Figure 6.5.1: Evolution of CD4 cut-offs for ART initiation over time



Current NACO guidelines on when to start ART

Ensuring good adherence to treatment is imperative for the success of the treatment as well as for the prevention of drug resistance. To achieve this, counselling must start from the first contact of the patient with the clinical team. Counselling should include preparing the patient for treatment and providing psychosocial support through an identified caregiver/guardian/treatment support and support networks. All patients should undergo two to three counselling sessions (preparedness counselling) before the initiation of ART. The period of waiting for investigations and their results should be utilized for counselling, Cotrimoxazole prophylaxis, TPT in eligible patients, and treatment preparation. All efforts should be made to trace the patients who have missed their visits or are lost to follow-up to initiate ART in all PLHIV registered at the ART centers. NGOs and positive network linkages should be established by each ART Centre for its respective locality.

6.6 What to Start: Antiretroviral Therapy Regimens

Fixed-dose combinations (FDCs) of ARVs are preferred because they are easy to prescribe and easy for patients to take, thereby facilitating improved and desirable treatment adherence. This is essential for PLHIV as the treatment is life-long and we need to minimize the chance of developing drug-resistant mutants in their body and the resultant treatment failure. Further, FDCs have distinct advantages in drug procurement and distribution, essentially the drug stock

management itself. National experience has shown that regimens with FDCs are more acceptable, well tolerated and adequately complied with.

In consideration of the WHO guidelines and based on recommendations of NACO Technical Resource Group, it has been decided to include DTG-containing regimens as the preferred first-line treatment for HIV-positive adults, adolescents and children (weighing more than 20 kg/age more than 6 years) under the NACP since July 2020.

Dolutegravir is known to have the following features:

- High genetic barrier: It is highly potent and has high genetic barrier. That is why it is an ideal drug.
- Rapid viral suppression: It helps in achieving rapid viral suppression. It has been found to reduce the viral copies to <50 copies/ml within 4 weeks and this helps reduce the chances of transmission.
- Fewer toxicities and side effects: DTG-based regimens are expected to have fewer side effects as compared to NNRTI-based regimens. These have lesser allergic reactions and chances of neuropsychiatric events compared to NNRTI-based regimens.
- Minimal drug interactions: DTG has minimal drug interactions with concomitant medications PLHIV might be on. Common drug interactions are listed in Table 2.2.6.
- Effective against HIV-2: DTG-based regimens can be prescribed for PLHIV infected with HIV-2 or combined HIV-1 and HIV-2. Prior to the availability of DTG in the programme, those infected with HIV-2 were being initiated with two NRTIs plus boosted PI regimen. With DTG in the programme, this will further bring harmonization across patient populations.
- No need for substitution of DTG-based ART regimen in PLHIV if co-infected with TB or HBV or HCV.

6.7 Monitoring of Patients on ART

Follow-up and monitoring are essential in patients initiated on ART to track clinical progress, monitor well-being and to identify adverse drug reactions and toxicities.

ART monitoring includes clinical monitoring and laboratory monitoring. Clinical monitoring includes monitoring of adherence to ART as well. The client should be monitored every month

for clinical progress, side effects of the ARVs and treatment adherence. Clinical and laboratory evaluations are carried out at specified intervals for patients on ART.

A combination of clinical and laboratory monitoring is to be carried out in all PLHIV after initiation of ART as depicted in Table 6.5.1.

Monitoring Tool	When to Monitor
Body weight Height / length in children	Every visit
Treatment adherence	Every visit
Clinical monitoring and T-staging	Every visit
4-symptom TB screening	Every visit
Screening for common NCD; Hypertension,Diabetes mellitus	Every 6 months or symptom directed
Laboratory evaluation based on ART regimen	Every 6 months or symptom directed
CD4 Count	CD4 must be done every 6 months*
Viral load	At 6 months, 12 months and then every 12 months**

***CD4 Count:**

1. As routine virological monitoring is available, CD4 testing should be done every 6 months and can be discontinued in PLHIV (except those with HIV-2 infection) when CD4 count reaches greater than 350 cells/mm^3 and viral load is less than 1000 copies/ml (when both tests are conducted at the same time).
2. CD4 monitoring should be restarted for any patient if
   a. the patient has been switched due to treatment failure, that is, virologic failure (Plasma Viral Load ≥1000 copies/ml

   or

b. when deemed necessary for clinical management by the clinician at any point in time

**For patients on second/third-line ART, Plasma Viral Load testing to be done every 6 months

CHAPTER-7

CLINICAL MONITORING

7. CLINICAL MONITORING

Monthly clinical evaluation

- Body weight, overall well-being, any new symptoms/signs, 4-symptom screening for TB at **every visit**
- Monthly treatment adherence evaluation, pill count, self-reported adherence
- Adherence to ART must be assessed at each visit and adherence must be reinforced through counselling at each visit.
- Adverse reactions of ART/OI drugs
- Drug–drug interactions, look for all concomitant drug use (prescribed and over the counter)
- Look for IRIS

Immunological monitoring

- CD4 testing should be done every 6 months.
- As routine virological monitoring is available, CD4 testing should be done every 6 months and can be discontinued in PLHIV (except those with HIV-2 infection) when CD4 count reaches greater than 350 cells/mm3 and plasma viral load is less than 1000 copies/ml (when both tests are conducted at the same time).

Virological monitoring: At 6 months and 12 months after ART initiation and then every 12 months

Interpretation of Plasma Viral Load testing results

PLHIV with plasma viral load report <1000 copies/ml should continue the same ART regimen. Next viral load testing should be done as per guidelines.

- PLHIV with plasma viral load report ≥1000 copies/ml should undergo step-up enhanced adherence counselling for three months. ART centre counsellor should provide intensive support to improve adherence.
- Repeat viral load testing should be done once treatment adherence is > 95% for three
- consecutive months.
    - If repeat plasma viral load report is <1000 copies/ml, patient should be continued on sameART regimen.
    - If repeat plasma viral load report is ≥1000 copies/ml, patient should be referred electronically to SACEP (e-SACEP) for further management.
- In case of PLHIV with high viral load, declining CD4 counts and poor clinical conditions, ART Medical Officer may refer the patient to SACEP, even based on a single viral load report, for further management. For more details, including viral load algorithm,

CHAPTER-8

LABORATORY MONITORING

8.LABORATORY MONITORING

The laboratory monitoring of PLHIV on ART is also very important. Regular monitoring of the patient's laboratory parameters is crucial to identify ARV-related toxicities, inter-current illnesses, drug–drug interactions and other metabolic abnormalities. The frequency of monitoring and the parameters to be monitored depend on the components of the regimen. The summary of the laboratory monitoring recommended under the programme is presented in Table 2.2.11. Additional laboratory tests outside this schedule may be performed as clinically indicated by the ART medical officer

Table 8.1 Laboratory monitoring of individual ARV drugs

For all patients on ART, we need to do CD4, Hb, TLC, DLC, ALT (SGPT) and serum creatinineonce every six months								
Tests for monitoring patients on ART (Follow-up tests): Drug-specific tests frequency as below								
Monitoring ARV drug in regimen	**Monitoring test**	**Baseline**	**15th Day**	**First month**	**Third month**	**Sixth month**	**Then every6 months**	**At 12 months**
On Tenofovir-based ART	Serum creatinine	Yes	&	&	&	Yes	Yes	&
	Urine for protein	Yes	&	&	&	Yes	Yes	&
On Zidovudine-based ART	CBC	Yes	Yes	Yes	Yes	Yes	Yes	&
Efavirenz-containing ART	Lipid profile	Yes	&	&	&	&	&	Yes
Atazanavir-containing ART	LFT Lipid profile	Yes	&	&	&	Yes	Yes	&
Lopinavir-containing ART	Lipid profile & Blood sugar	Yes	&	&	&	Yes	Yes	&
Dolutegravir- containing ART	ALT (SGPT) & blood sugar	Yes				Yes	Yes	&

8.2 Immune Reconstitution Inflammatory Syndrome

"The worsening of signs and symptoms due to known infections" or "the development of disease due to occult infections that result from an inflammatory response by a reinvigorated immune system following the initiation of ART.".

People with CD4 counts below 100 cells/mm3 before starting therapy (lower CD4 counts at ART initiation) or lower CD4:CD8 ratio at ART initiation;

- People with rapid initial fall in HIV viral load due to therapy;

- People with diagnosis of another infection before starting therapy; the closer the appearance or diagnosis is to starting therapy, the higher the risk (shorter interval between OI therapy initiation and ART initiation);
- Severity of TB disease, especially high pathogen burden, and short interval between initiation of ATT and ART;
- sex;
- Younger age;
- Higher HIV RNA at ART initiation;
- Genetic susceptibility.

Working definition of IRIS in Programme Conditions

"The worsening of signs and symptoms due to known infections, or the development of disease due to occult infections within 6 weeks to 6 months after initiating ART, with an increase in CD4 count."

The various categories of IRIS along with the possible antigen are mentioned in Table **2.2.12.**

Table 8.2 Categories of IRIS

Categories	Antigen Target
Infection – unmasking	Viable replicating infective antigen
Infection – paradoxical	Dead or dying organisms
Auto immune	Host
Malignancies	Possible tumour or associated pathogen

- Unmasking IRIS refers to, for e.g., the initial clinical expression of active TB occurring soon after ART is started. Paradoxical IRIS refers to, for e.g., the worsening of TB, clinical manifestations after the initiation of ART in patients, who are receiving anti-TB treatment. IRIS should be considered only when the presentation cannot be explained by

a new infection, expected course of a known infection or drug toxicity. IRIS should be diagnosed by excluding the following:

- Active OI
- Treatment failure
- Side effect from ARV
- Failure to Antimicrobial Therapy
- The clinical spectrum of IRIS is diverse in terms of early or delayed onset, atypical symptoms, generalized or localized infection, variation in severity and it may be infectious or non-infectious.
- The following can help in the diagnosis of IRIS:
- Temporal association between the initiation of ART and the development of new clinical
- event (mostly within 3 months);
- Typically, IRIS occurs within 2–12 weeks of the initiation of ART, although it may present later (usually between 6 weeks to 6 months).
- The incidence of IRIS is estimated to be 10% among all patients in whom ART has been initiated and up to 25% among those initiated on ART having CD4 cell count of below 50cells/mm^3.

Unusual clinical manifestations in patients responding to ART include the following:

- Unexpected, localized disease, e.g., lymph nodes (appearance or enlargement and/or suppuration), or involving liver or spleen or development of pleural effusion;
- Exaggerated inflammatory reaction, e.g., severe fever, with exclusion of other causes;
- Painful lesions;
- Atypical inflammatory response in affected tissues, e.g., granulomas, suppuration, necrosis;
- Perivascular lymphocytic inflammatory cell infiltrate;
- Progression of organ dysfunction or enlargement of pre-existing lesions;
- Development or enlargement of cerebral space-occupying lesions after treatment, for e.g., cerebral cryptococcosis or toxoplasmosis;

  Progressive pneumonitis or the development of organizing pneumonia after treatment
- for pulmonary TB or PCP;

- Onset or worsening of uveitis/virtutis after the resolution of CMV retinitis;
- Fever and cytopenia after treatment for disseminated MAC.

IRIS Management

IRIS is generally self-limiting and interruption of ART is rarely indicated, but people may need to be reassured in the face of protracted symptoms to prevent discontinuation of ART or poor adherence to ART.

- Mild form (with ongoing ART)
- Observation
- Localized IRIS (with ongoing ART)
- Local therapy such as minor surgical procedures for lymph node abscesses (drainage)
- As per system involvement e.g., neurological, respiratory
- Most of the situations (with ongoing ART)
- Recognition and management of ongoing infections
- Antimicrobial therapy is required to reduce and to eliminate the triggering pathogen (antigenic load)
- Reconstituting immune reaction to non-replicating antigens
- No antimicrobial therapy is required

Short-term therapy with corticosteroids or non-steroidal anti-inflammatory drugs can be given to reduce the inflammation – Prednisolone at 1.5 mg/kg orally for two weeks followed by 0.75 mg/ kg orally for two weeks and then tapered off.

Temporary cessation of ART must be considered, only if potentially life-threatening forms of IRIS develops.

CHAPTER-9

LIST OF MEDICINES USED IN HIV AIDS

9.LIST OF MEDICINES USED IN HIV AIDS

Drug Class	Generic Name (Other names and acronyms)	Brand Name	FDA Approval Date
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
NRTIs block reverse transcriptase, an enzyme HIV needs to make copies of itself.	abacavir (abacavir sulfate, ABC)	Ziagen	December 17, 1998
	emtricitabine (FTC)	Emtriva	July 2, 2003
	lamivudine (3TC)	Epivir	November 17, 1995
	tenofovir disoproxil fumarate (tenofovir DF, TDF)	Viread	October 26, 2001
	zidovudine (azidothymidine, AZT, ZDV)	Retrovir	March 19, 1987
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
NNRTIs bind to and	doravirine	Pifeltro	August 30, 2018

later alter reverse transcriptase, an enzyme HIV needs to make copies of itself.	(DOR)		
	efavirenz (EFV)	Sustiva	September 17, 1998
	etravirine (ETR)	Intelence	January 18, 2008
	nevirapine (extended-release nevirapine, NVP)	Viramune	June 21, 1996
		Viramune XR (extended release)	March 25, 2011
	rilpivirine (rilpivirine hydrochloride, RPV)	Edurant	May 20, 2011
Protease Inhibitors (PIs)			
PIs block HIV protease, an enzyme HIV needs to make copies of itself.	atazanavir (atazanavir sulfate, ATV)	Reyataz	June 20, 2003
	darunavir (darunavir ethanolate, DRV)	Prezista	June 23, 2006
	fosamprenavir (fosamprenavir calcium, FOS-APV, FPV)	Lexiva	October 20, 2003
	ritonavir (RTV) *Although ritonavir is a PI, it is generally used as a pharmacokinetic enhancer as recommended in the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV and the Guidelines for the Use of Antiretroviral Agents in	Norvir	March 1, 1996

	Pediatric HIV Infection.		
	tipranavir (TPV)	Aptivus	June 22, 2005
Fusion Inhibitors			
Fusion inhibitors block HIV from entering the CD4 T lymphocyte (CD4 cells) of the immune system.	enfuvirtide (T-20)	Fuzeon	March 13, 2003
CCR5 Antagonists			
CCR5 antagonists block CCR5 coreceptors on the surface of certain immune cells that HIV needs to enter the cells.	maraviroc (MVC)	Selzentry	August 6, 2007
Integrase Strand Transfer Inhibitor (INSTIs)			
Integrase inhibitors block HIV integrase, an enzyme HIV needs to make copies of itself.	cabotegravir (cabotegravir sodium, CAB)	Vocabria	January 22, 2021
	dolutegravir (dolutegravir sodium, DTG)	Tivicay Tivicay PD	August 12, 2013 June 12, 2020
	raltegravir (raltegravir potassium, RAL)	Isentress	October 12, 2007
		Isentress HD	May 26, 2017
Attachment Inhibitors			
Attachment inhibitors bind to the gp120 protein on the outer surface of HIV, preventing HIV from entering CD4 cells.	fostemsavir (fostemsavir tromethamine, FTR)	Rukobia	July 2, 2020

Post-Attachment Inhibitors			
Post-attachment inhibitors block CD4 receptors on the surface of certain immune cells that HIV needs to enter the cells.	ibalizumab-uiyk (Hu5A8, IBA, Ibalizumab, TMB-355, TNX-355)	Trogarzo	March 6, 2018
Capsid Inhibitors			
Capsid inhibitors interfere with the HIV capsid, a protein shell that protects HIV's genetic material and enzymes needed for replication.	lenacapavir (GS-6207, GS-HIV, GS-CA2, GS-CA1)	Sunlenca	December 22, 2022
Pharmacokinetic Enhancers			
Pharmacokinetic enhancers are used in HIV treatment to increase the effectiveness of an HIV medicine included in an HIV treatment regimen.	cobicistat (COBI, c)	Tybost	September 24, 2014
Combination HIV Medicines			
Combination HIV medicines contain two or more HIV medicines from one or more drug classes.	abacavir and lamivudine (abacavir sulfate / lamivudine, ABC / 3TC)	Epzicom	August 2, 2004
	abacavir, dolutegravir, and lamivudine(abacavir sulfate / dolutegravir sodium / lamivudine, ABC / DTG /	Triumeq	August 22, 2014
		Triumeq PD	March 30, 2022

	3TC)		
	abacavir, lamivudine, and zidovudine (abacavir sulfate / lamivudine / zidovudine, ABC / 3TC / ZDV)	Trizivir	November 14, 2000
	atazanavir and cobicistat (atazanavir sulfate / cobicistat, ATV / COBI)	Evotaz	January 29, 2015
	bictegravir, emtricitabine, and tenofovir alafenamide (bictegravir sodium / emtricitabine / tenofovir alafenamide fumarate, BIC / FTC / TAF)	Biktarvy	February 7, 2018
	cabotegravir and rilpivirine (CAB and RPV, CAB plus RPV, Cabenuva kit, cabotegravir extended-release injectable suspension and rilpivirine extended-release injectable suspension)	Cabenuva	January 22, 2021
	darunavir and cobicistat (darunavir ethanolate / cobicistat, DRV / COBI)	Prezcobix	January 29, 2015
	darunavir, cobicistat, emtricitabine, and tenofovir alafenamide (darunavir ethanolate / cobicistat / emtricitabine /	Symtuza	July 17, 2018

	tenofovir AF, darunavir ethanolate / cobicistat / emtricitabine / tenofovir alafenamide, darunavir / cobicistat / emtricitabine / tenofovir AF, darunavir / cobicistat / emtricitabine / tenofovir alafenamide fumarate, DRV / COBI / FTC / TAF)		
	dolutegravir and lamivudine (dolutegravir sodium / lamivudine, DTG / 3TC)	Dovato	April 8, 2019
	dolutegravir and rilpivirine (dolutegravir sodium / rilpivirine hydrochloride, DTG / RPV)	Juluca	November 21, 2017
	doravirine, lamivudine, and tenofovir disoproxil fumarate (doravirine / lamivudine / TDF, doravirine / lamivudine / tenofovir DF, DOR / 3TC / TDF)	Delstrigo	August 30, 2018
	efavirenz, emtricitabine, and tenofovir disoproxil fumarate (efavirenz / emtricitabine / tenofovir DF, EFV / FTC / TDF)	Atripla	July 12, 2006
	efavirenz, lamivudine, and	Symfi	March 22, 2018

	tenofovir disoproxil fumarate (EFV / 3TC / TDF)		
	efavirenz, lamivudine, and tenofovir disoproxil fumarate (EFV / 3TC / TDF)	Symfi Lo	February 5, 2018
	elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide fumarate, EVG / COBI / FTC / TAF)	Genvoya	November 5, 2015
	elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate (QUAD, EVG / COBI / FTC / TDF)	Stribild	August 27, 2012
	emtricitabine, rilpivirine, and tenofovir alafenamide (emtricitabine / rilpivirine / tenofovir AF, emtricitabine / rilpivirine / tenofovir alafenamide fumarate, emtricitabine / rilpivirine hydrochloride / tenofovir AF, emtricitabine / rilpivirine hydrochloride / tenofovir alafenamide, emtricitabine / rilpivirine	Odefsey	March 1, 2016

	hydrochloride / tenofovir alafenamide fumarate, FTC / RPV / TAF)		
	emtricitabine, rilpivirine, and tenofovir disoproxil fumarate (emtricitabine / rilpivirine hydrochloride / tenofovir disoproxil fumarate, emtricitabine / rilpivirine / tenofovir, FTC / RPV / TDF)	Complera	August 10, 2011
	emtricitabine and tenofovir alafenamide (emtricitabine / tenofovir AF, emtricitabine / tenofovir alafenamide fumarate, FTC / TAF)	Descovy	April 4, 2016
	emtricitabine and tenofovir disoproxil fumarate (emtricitabine / tenofovir DF, FTC / TDF)	Truvada	August 2, 2004
	lamivudine and tenofovir disoproxil fumarate (3TC / TDF)	Cimduo	February 28, 2018
	lamivudine and zidovudine (3TC / ZDV)	Combivir	September 27, 1997
	lopinavir and ritonavir (ritonavir-boosted lopinavir, LPV/r, LPV / RTV)	Kaletra	September 15, 2000

HIV DRUG RESISTANCE

Once a person gets HIV, the virus begins to multiply in the body. As HIV multiplies, it sometimes changes form (mutates). Some HIV mutations that develop while a person is taking HIV medicines can lead to drug-resistant HIV.

Once drug resistance develops, HIV medicines that previously controlled the person's HIV are no longer effective. In other words, the HIV medicines cannot prevent the drug-resistant HIV from multiplying. Drug resistance can cause HIV treatment to fail.

Drug-resistant HIV can spread from person to person (called transmitted resistance). People with transmitted resistance have HIV that is resistant to one or more HIV medicines even before they start taking HIV medicines.

Drug-resistance testing

Drug-resistance testing identifies which, if any, HIV medicines that will not be effective against a person's HIV. Drug-resistance testing is done using a sample of blood.

People with HIV should start taking HIV medicines as soon as possible after their HIV is diagnosed. But before a person starts taking HIV medicines, drug-resistance testing is done.

Drug-resistance test results help determine which HIV medicines to include in a person's first HIV treatment regimen.

Once HIV treatment is started, a viral load test is used to monitor whether the HIV medicines are controlling a person's HIV. If viral load testing indicates that a person's HIV treatment regimen is not effective, drug-resistance testing is repeated. The test results can identify whether drug resistance is the problem and, if so, can be used to select a new HIV treatment regimen.

How can a person taking HIV medicines reduce the risk of drug resistance?

Taking HIV medicines every day and exactly as prescribed (called medication adherence) reduces the risk of drug resistance. Skipping HIV medicines allows HIV to multiply, which increases the risk that the virus will mutate and produce drug-resistant HIV.

Before starting HIV treatment, tell your health care provider about any issues that can make medication adherence difficult. For example, a busy schedule or lack of health insurance can make it hard to take HIV medicines consistently. Once you start treatment, use a 7-day pill box or other medication aid to stay on

CHAPTER-10

CONCLUSION

CONCLUSION-

Historically, HIV prevention programs have focused primarily on developing risk reduction interventions for those at high risk for becoming infected with HIV. In 1999, a review of 55 state and city applications to the CDC for funds for HIV prevention programs demonstrated that only 18 (32.7%) listed HIV-infected individuals as a priority population for HIV prevention programs. Although there are millions of people in the United States at "behavioral risk" for HIV infection, transmission can occur only from people who are infected with the virus. As the number of individuals with HIV continues to increase because of ART, so does the urgency for lifelong prevention strategies customized for them.

CHAPTER-11

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