HIV and AIDS

Introduction

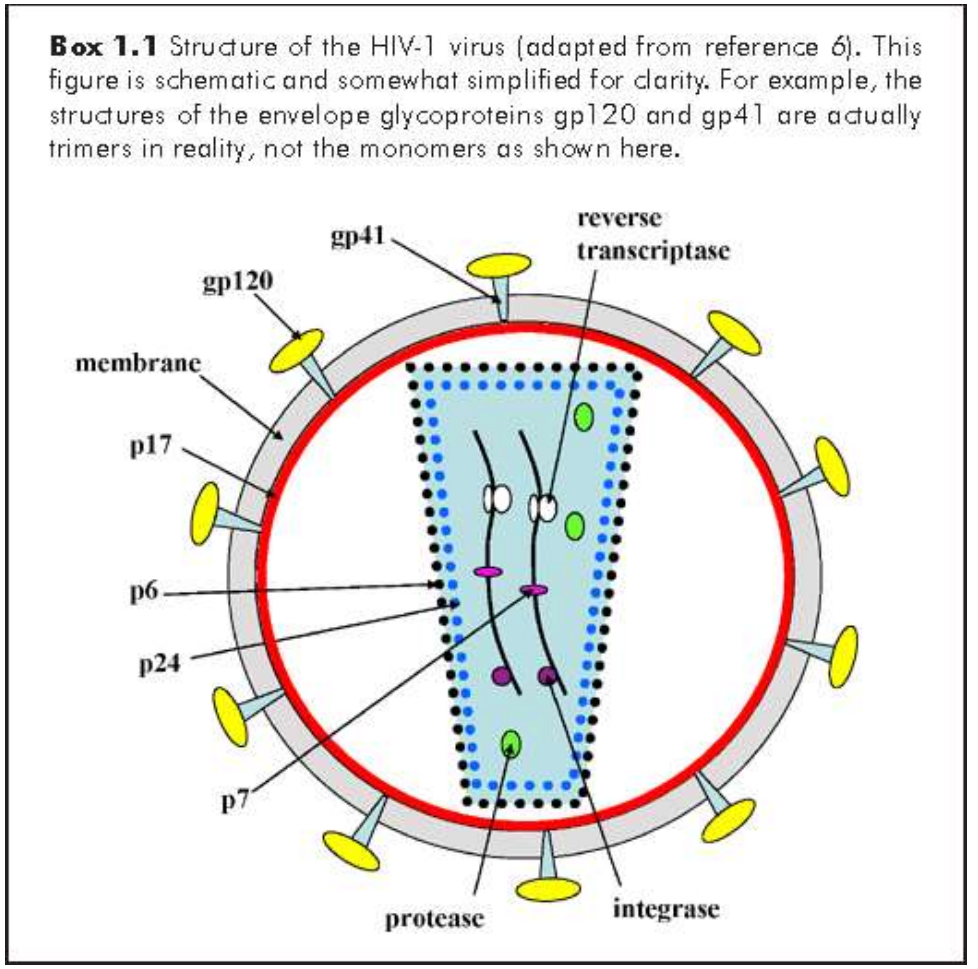
- HIV infection remains a significant global health concern despite being a treatable disease.
- Many persons living with HIV infection are not aware of their status because they have never been tested; others have been diagnosed but are not receiving care.
- Testing for HIV infection detects HIV-1 and HIV-2 antibodies
- Infection with HIV-2 primarily occurs in parts of Africa and remains rare in the United States; HIV-2 generally is a less progressive disease with less immunocompromise and lower risk of opportunistic infections.

Virology Basics:

- Group: Lentivirus
- Subgroup: Retroviruses
- All viruses except retroviruses contain DNA
- HIV targets WBCs called T helper cells (CD4 cells)

Cont. Virology Basics:

- HIV enclosed with coat called **viral envelope**
- This envelope possess little spikes around **72 in number** which are made of proteins **gp120**, **gp41**
- Below the envelop a layer that is called **matrix** is made of **p17**
- Below matrix another layer of **protein p24** forming **viral core** (capsid), **bullet shaped**
- Inside the core, **three** types of enzymes are present which are required for **replication** (**Reverse transcriptase**, **Integrase** and **Protease**)
- Inside the core, genomes are present which consists of 2 identical copies of **ssRNA**



Cont. Virology Basics:

- HIV-1 :
  90% of all cases worldwide
- HIV-2:
  1% of cases worldwide
  slower progression
  more common in west Africa
  less easily transmitted
  less pathogenic
  duration of infection is shorter

Prevention:

- HIV transmission occurs through sexual contact or exposure to other body fluids.
- Reducing transmission can be accomplished by using barrier methods, such as condoms during sexual contact, and through clean syringe services programs (needle exchange programs) for persons who inject drugs.
- Universal blood donor testing has all but eliminated infection through blood transfusion in the United States, with current risk estimated to be one in 2 million.

Cont. Prevention:

- Antiretroviral therapy (ART) has extraordinary potential to reduce new infections in addition to benefiting the treated person.
- The CDC estimates that the undiagnosed and not-in care groups with HIV infection were responsible for 80% of HIV transmissions in the United States in 2016.
- Postexposure prophylaxis has been used successfully for many years to prevent infection after occupational and nonoccupational HIV exposure. Prophylaxis should be started as soon as possible after exposure.

Cont. Prevention:

Type of exposure[†]	Risk per 1000 exposures to an infected source
Needle-sharing injection-drug use	6.7
Receptive anal intercourse	5
Percutaneous needle exposure	3
Receptive vaginal intercourse	1
Mucous membrane exposure	0.9
Insertive anal intercourse	0.65
Insertive vaginal intercourse	0.5
Receptive oral intercourse	0.1
Insertive oral intercourse	0.05

[†]Estimated per-act risk for acquisition of HIV.
Data from [3,52,54,55].

Pathophysiology

- Most persons with acute HIV infection are symptomatic; however, because symptoms are nonspecific and self-limited, most acute infections are not diagnosed accurately

- During symptomatic acute infection, the fourth generation IgM and IgG antibody and p24 antigen may not yet be detectable, and diagnosis depends on an HIV viral load test demonstrating HIV RNA.

Cont. Pathophysiology

TABLE 62. Signs and Symptoms of Acute HIV Infection (Acute Retroviral Syndrome)

Sign/Symptom	Frequency (%)
Fever	75
Fatigue	68
Myalgia	49
Rash	48
Headache	45
Pharyngitis	40
Lymphadenopathy	39
Arthralgia	30
Night sweats	28
Diarrhea	27

Cont. Pathophysiology

- Patients with chronic HIV infection may present with opportunistic infections, especially when CD4 counts are less than 2OO/µL, meeting the definition for AIDS. Even before progression to AIDS, patients with HIV infection may present with recurrent or severe episodes of infections that do not qualify as opportunistic.

- Other symptoms can result from chronic HIV infection itself including lymphadenopathy, fever, night sweats, fatigue, weight loss, chronic diarrhoea, and various oral and skin conditions (seborrheic dermatitis, eosinophilic folliculitis, xerosis, atopic dermatitis, and psoriasis).

Screening and Diagnosis

- Testing only symptomatic persons neglects numerous persons who are infected.
- The fourth-generation HIV testing uses a combination assay for HIV antibody and HIV p24 antigen, which detects acute infection 15 to 20 days after the onset of infection.
- In chronic infection, the initial combination assay is nearly 100% sensitive and specific, but testing in low prevalence populations (such as general screening) can still result in false positives, so waiting for the results of the confirmatory antibody differentiation immunoassay or nucleic acid amplification testing is important for a definitive diagnosis.

Initiation of Care

Initial Evaluation and Laboratory Testing:

- All persons who test positive for HIV should immediately be referred to a health care provider with HIV infection management expertise.
- Initial evaluation should include complete history (including social and sexual) and examination for signs and symptoms of opportunistic infection or other complications.
- Patient education and counselling should include information on transmission and prevention.

Cont. Laboratory Testing:

- Initial laboratory tests include baseline organ function and evaluation for other infections with higher prevalence in persons with HIV
- A baseline CD4 cell count guides opportunistic infection prophylaxis, and a baseline viral load supports monitoring ART effectiveness

Test	Comments
HIV-specific tests for all persons with HIV	
HIV antigen/antibody testing	If written evidence of diagnosis not available or if viral load low or undetectable
CD4 cell count and percentage	Assess need for opportunistic infection prophylaxis
Plasma HIV RNA polymerase chain reaction (HIV viral load)	Establish baseline and monitor viral suppression
HIV resistance testing	Baseline genotype for protease inhibitor, nonnucleoside RTI, nucleoside/nucleotide RTI mutations for persons who have never initiated therapy, are reengaging in care and not receiving therapy, or with inconsistent access to therapy. INSTI genotype is recommended only if suspicion for INSTI mutation transmission.
Other laboratory tests	
Complete blood count with differential	Assess for anemia, neutropenia, thrombocytopenia
Alanine aminotransferase, aspartate aminotransferase, total bilirubin, alkaline phosphatase	Assess for evidence of liver damage, hepatitis, or systemic infection (e.g., elevated alkaline phosphatase level with some opportunistic infections)
Total protein and albumin levels	High total protein level common with untreated HIV infection because of increased immunoglobulin fraction secondary to B-cell hyperplasia; low albumin level may indicate nutritional deficiency or nephrotic syndrome
Electrolytes, blood urea nitrogen, creatinine	Assess kidney function; creatinine level for calculation of estimated glomerular filtration rate
Lipid profile and blood glucose; hemoglobin A_{1c}	Fasting not needed for initial lipid and glucose assessment; if abnormal, repeat fasting Hemoglobin A_{1c} measured before ART initiation but not used for diagnosis of diabetes in those taking ART
Urinalysis	Assess for evidence of proteinuria, hematuria

Immunizations in HIV patients

- Numerous immunizations are recommended for all persons with HIV starting with the l3-valent pneumococcal conjugate and 23-valent pneumococcal polysaccharide vaccines, respectively, at least B weeks apart; a 23-valent polysaccharide vaccine booster is also recommended after 5 years.
- Patients who are not already immune or infected with HBV should receive the hepatitis B vaccine series.
- Influenza, COVID-19, tetanus diphtheria-pertussis, hepatitis A, and human papillomavirus vaccinations are indicated as for the general population.

Cont. immunization

- Measles-mumps-rubella, varicella, and recombinant zoster vaccines can be given as long as the CD4 cell count is greater than 200/µL.
- The recombinant zoster vaccine should be given to individuals 50 years and older with CD4 cell count greater than 200/µl.
- All persons with HIV infection should be vaccinated for meningococcal disease with the quadrivalent meningococcal vaccine, including boosters every 5 years.

Prophylaxis for Opportunistic Infections

Before beginning prophylaxis, active infection should be ruled out clinically and with any indicated testing to avoid undertreatment and selection for resistance, especially for tuberculosis and disseminated Mycobacterium avium complex.

TABLE 64. Prophylaxis against Opportunistic Infections in HIV/AIDS

Opportunistic Infection	Indication	Preferred Drug
Pneumocystis jirovecii	CD4 cell count <200/μL[a]	TMP-SMX, double-strength or single-strength tablet once daily[b]
Toxoplasmosis	CD4 cell count <100/μL and positive serologic results[a]	TMP-SMX, double-strength tablet once daily[c]
Mycobacterium avium complex	CD4 cell count <50/μL[d]	Azithromycin, 1200 mg once weekly or 600 mg twice weekly; clarithromycin, 500 mg twice daily
Latent tuberculosis	TST >5 mm or positive IGRA results	3 months of isoniazid plus rifapentine given once weekly
		3 months of isoniazid plus rifampin given daily[e]

Complications of HIV Infection in the Antiretroviral Therapy Era

1. Metabolic, Kidney, and Liver Disorders

- HIV infection itself and some antiretrovirals affect lipids and can worsen hyperlipidaemia.
- Fasting glucose or haemoglobin a1c and lipid levels should be checked at baseline and 3 months after initiating or changing antiretrovirals
- Chronic kidney disease is increasingly common in HIV infection, although, with effective ART, it is less often attributed to HIV nephropathy. It is recommended that kidney function be assessed at least every 6 months in patients with HIV.
- Bone mineral density is reduced in HIV and tenofovir is also associated with possible worsening of bone density.
- Liver disease is also increased in HIV infection, often because of coinfection with hepatitis B or C virus. All patients with HIV should be screened for hepatitis B and C viruses and immunized if they are HBV negative.

Cont. Complications of HIV Infection

2. Cardiovascular Disease

- Rates of cardiovascular disease, including myocardial infarction and stroke, are higher in persons with HIV infection; this association remains after correction for increased risk factors such as smoking.
- Guidelines from the American College of Cardiology/American Heart Association recommend patients with HIV infection and borderline risk for atherosclerotic cardiovascular disease should be engaged in risk discussion regarding initiating moderate intensity statin therapy.

Cont. Complications of HIV Infection

3. Neurocognitive Decline:

Manifestations of HIV associated neurocognitive disorders (HAND) range from asymptomatic neurocognitive impairment to severe HIV associated dementia; if not already being provided, ART should be instituted immediately as part of prevention and treatment of HAND.

4. Immune Reconstitution Inflammatory Syndrome:

Immune reconstitution inflammatory syndrome is caused by an inflammatory response to a pre-existing infectious process; it usually occurs within a few months of initiating effective antiretroviral therapy and presents with a wide variety of infections and non-infectious complications.

Cont. Complications of HIV Infection

5. Opportunistic Infections:

- Mucocutaneous Candida infections can occur in HIV infected patients at relatively preserved CD4 cell counts.
- Reactivation of latent tuberculosis is also significantly increased in HIV infection, even without a decreased CD4 cell count.

Cont. opportunistic infections:

- Pneumocystis jirovecii pneumonia:
  - ✓ subacute illness with fever, dyspnoea, and dry cough in a patient with a CD4 cell count less than 2OO/µL who is not receiving prophylaxis.
  - ✓ Normal lactate dehydrogenase levels and stable exercise oxygen saturation have a high negative predictive value
- Cryptococcus infection:
  - ✓ subacute meningitis with headache, mental status changes, and fever.
  - ✓ The diagnosis can be made most swiftly by antigen testing of cerebrospinal fluid and blood.

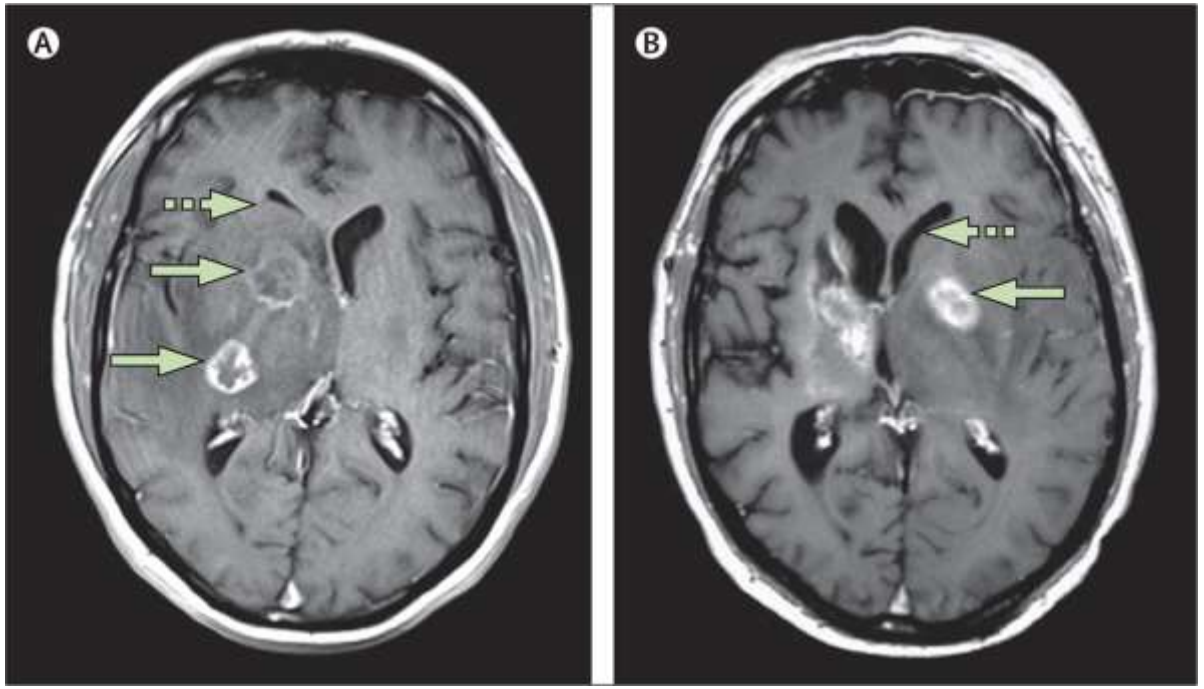
Cont. opportunistic infections:

- Toxoplasma gondii infection:

✓ patients with CD4 cell counts less than 100/µL.

✓ Clinical presentation includes headache, fever, and focal neurologic deficits.

✓ Imaging by CT or MRI (which is more sensitive) reveals multiple ring-enhancing lesions



Cont. opportunistic infections:

- Mycobacterium avium complex infection:
  - ✓ presents as disseminated disease in patients with CD4 cell counts less than 50/µL
  - ✓ symptoms and signs include fever, sweats, weight loss, hepatosplenomegaly, lymphadenopathy, and cytopenia.
  - ✓ Blood cultures for acid-fast bacilli will usually grow M. avium complex, but it may also be found on lymph node or liver biopsy when necessary.
- Cytomegalovirus:
  - ✓ commonly presents with CD4 cell counts less than 50/µL.
  - ✓ Cytomegalovirus retinitis, presenting with vision changes or floaters, is much more likely in AIDS
  - ✓ Gastrointestinal cytomegalovirus disease is also common, most often as esophagitis or colitis.

Cont. opportunistic infections:

- Patients with AIDS are also more likely to develop certain malignancies, especially those related to viruses.
- Non-Hodgkin lymphoma, especially primary CNS lymphoma related to EBV, is significantly increased compared with age-matched controls.
- Kaposi sarcoma is caused by human herpes virus type 8 and presents as dark red, brown, or violaceous lesions of the skin or mucous membranes
- HPV -related malignancies are significantly increased in HIV including cervical and anal cancers.

Management:

When to Initiate Treatment:

- All persons with HIV infection should begin ART as soon as they are ready, regardless of CD4 cell count.
- Rapid initiation of ARI (on the day or within 2 weeks of initial diagnosis) has been shown to improve viral suppression and should be considered if no medical (symptoms suggesting opportunistic infections in which immediate ART is contraindicated) or structural (staffing and linkage to care service availability) barriers prevent doing so.

Cont. Management:

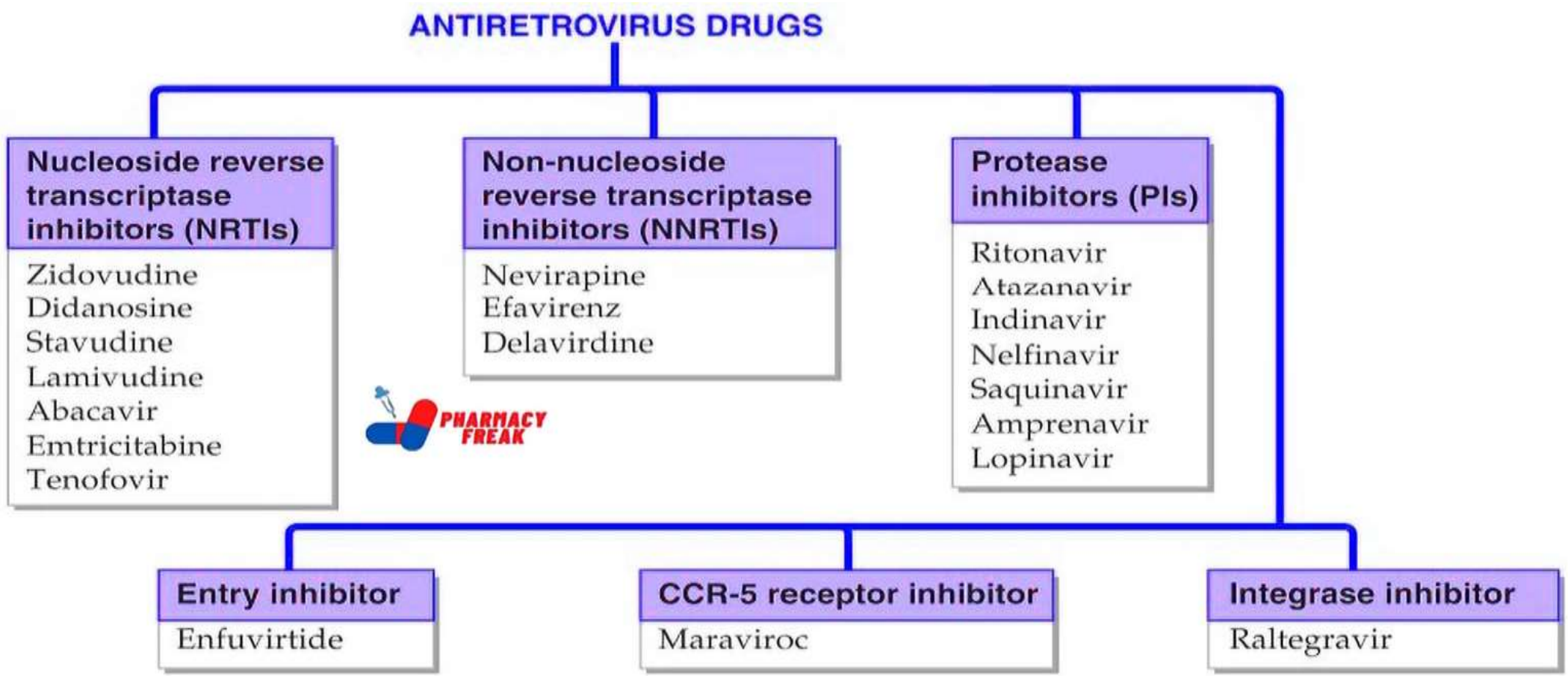
Antiretroviral regimen:

- Standards for effective antiretroviral regimens include use of three drugs from two different classes, preferably combining two nucleoside reverse transcriptase inhibitors (NRTIs) with an integrase strand transfer inhibitor (INSTI).
- Preferred regimens also feature a high barrier to resistance, good tolerability and safety, and combination pills with once-daily dosing to facilitate adherence
- Viral load levels and CD4 cell counts are monitored to ensure effectiveness and to determine immune recovery. With optimal therapy, HIV RNA in blood should become and stay undetectable.

Cont. Management:

- Goal: undetectable viral load → untransmitable (“U=U”)
- CD4 cell counts will increase, although cell counts may take time to improve and may not show full recovery especially in those who are older or who have other factors affecting lymphocytes.
- Patients taking ART who are stable with a CD4 cell count of 500/µL or more for more than 2 years can stop T-cell monitoring as long as viral load remains undetectable.

Cont. Management:



Thank you!