

# **Introduction to Antiretroviral Therapy / Goals and Principles**

# Objectives



1. Describe the goals and basic principles of ARV
2. Describe the different types of ARV medications and what medications are available in Nigeria
3. Describe the essential components of an ARV Program necessary for excellent patient care

# The HIV viral load



## THE VIRAL LOAD is

1. A count of the number of HIV RNA molecules in 1 ml of plasma (copies/ml)
2. A direct measure of the level of HIV infection
3. A predictor of disease symptoms and of the rate of CD4+ T cell decline
4. What's a good viral load for a patient on treatment? *An undetectable viral load (<50 copies/ml)!*
  - \* If viral load is this low, patients are unlikely to have disease progression, resistance, or to pass HIV through MTCT

# Goals of Antiretroviral Therapy (ART)



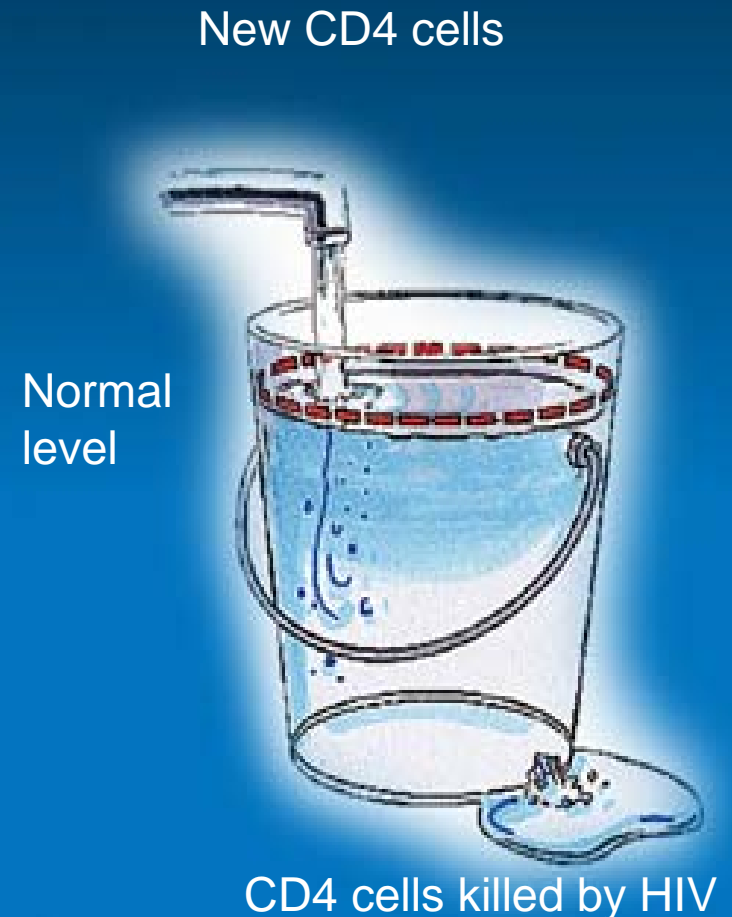
The goals of ARVs are as follows

1. Reduce HIV-related **morbidity** and **mortality**
2. Reduce the **viral load** (to undetectable levels) for as long as possible in order to halt disease progression and prevent/reduce resistant variants
3. Achieve **immune reconstitution** that is quantitative (CD4 count in normal range) and qualitative (fewer infections and illnesses)

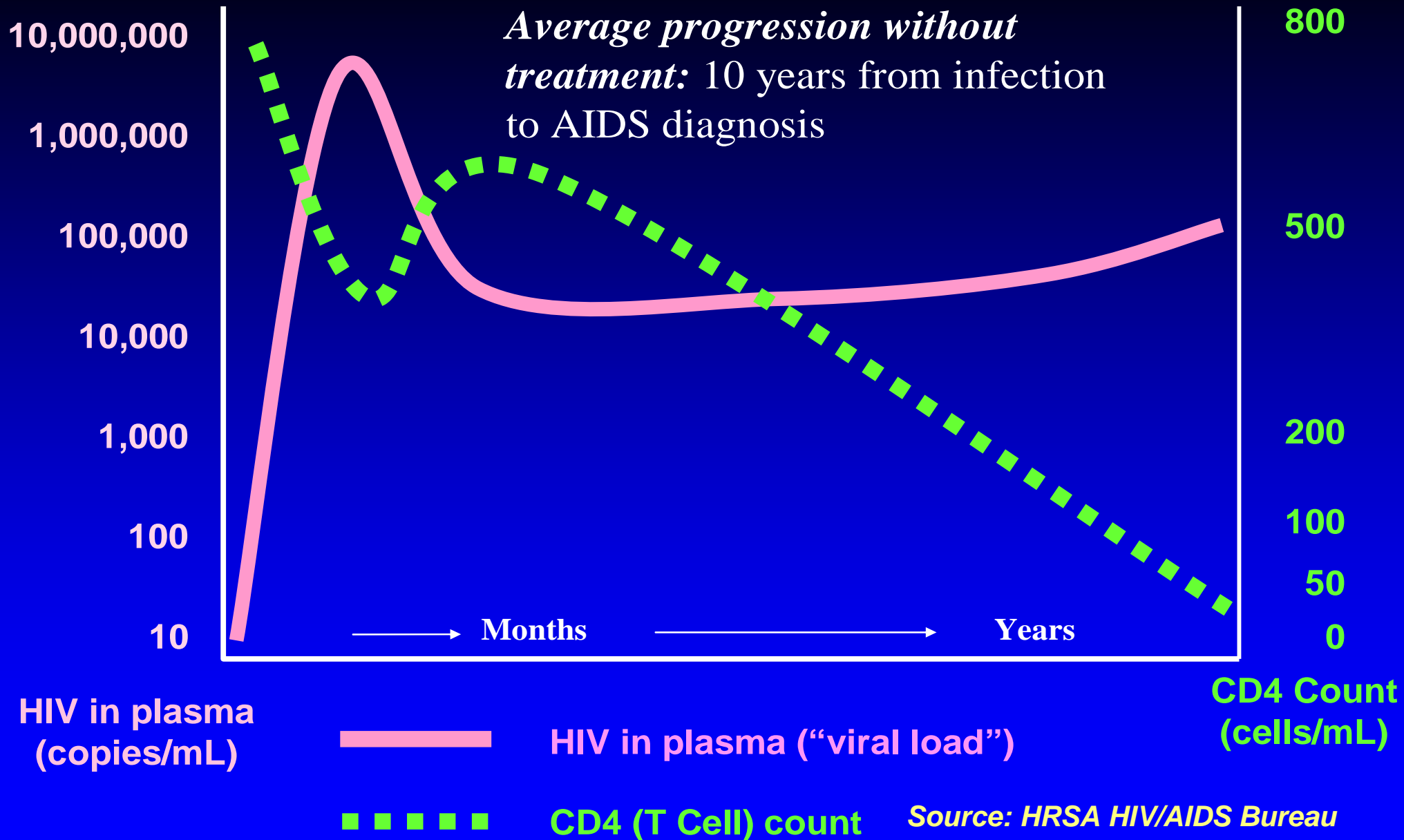
# Antiretrovirals keeps HIV from getting ahead

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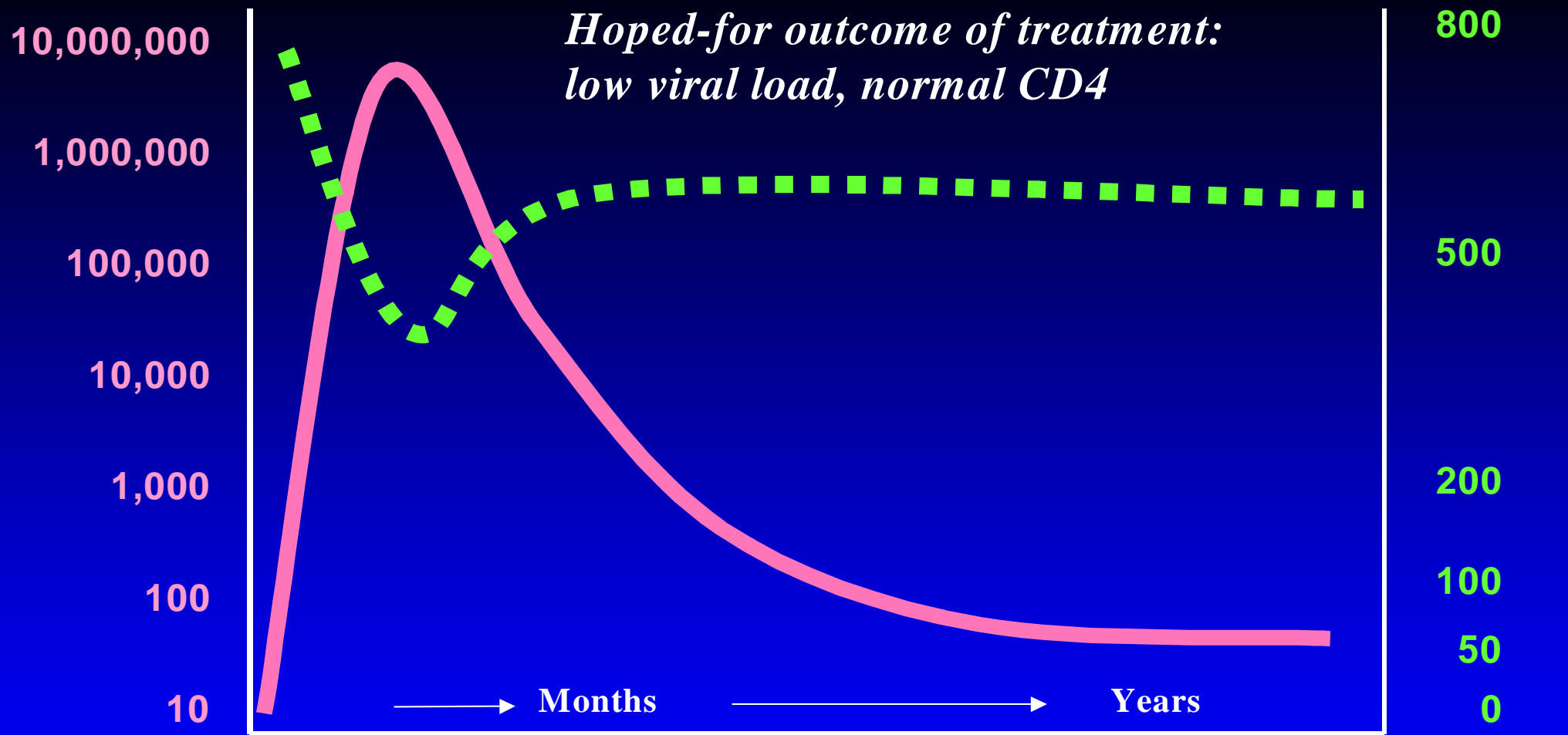
- Sometimes viral load can be reduced so much that the virus cannot be detected. That does not mean the virus is gone from the body.
- When this happens, HIV is still reproducing but not enough to weaken the immune system
- When there isn't a constant attack from HIV, CD4 cell levels rise and they can do their job



# HIV Progression without treatment



# HIV Progression with treatment



HIV in plasma  
(copies/mL)



HIV in plasma ("viral load")



CD4 (T Cell) count

CD4 Count  
(cells/mL)

Source: HRSA HIV/AIDS Bureau

# Benefits of ARV



## The benefits of ARVs include:

- I.     ↑ voluntary testing/counseling
- II.    ↑ awareness of HIV
- III.   ↑ motivation of health care workers
- IV.    ↓ expenses for palliative and OI care
- V.     ↓ number of orphans
- VI.    Keeps households and businesses intact
- VII.   Potential to enhance prevention
  - a.     Behavioral: access to prevention education during care encounters
  - b.     Biological: decreased transmission due to lowered viral load

# Risks Of ARV



## The risks of ARVs include:

- I. If the virus is not suppressed fully, drug resistance can develop which will make the current ARV regimen less effective and limit future ARV treatment options
- II. Possible short and long term side effects for patients
- III. Possible interactions with other medications or natural remedies

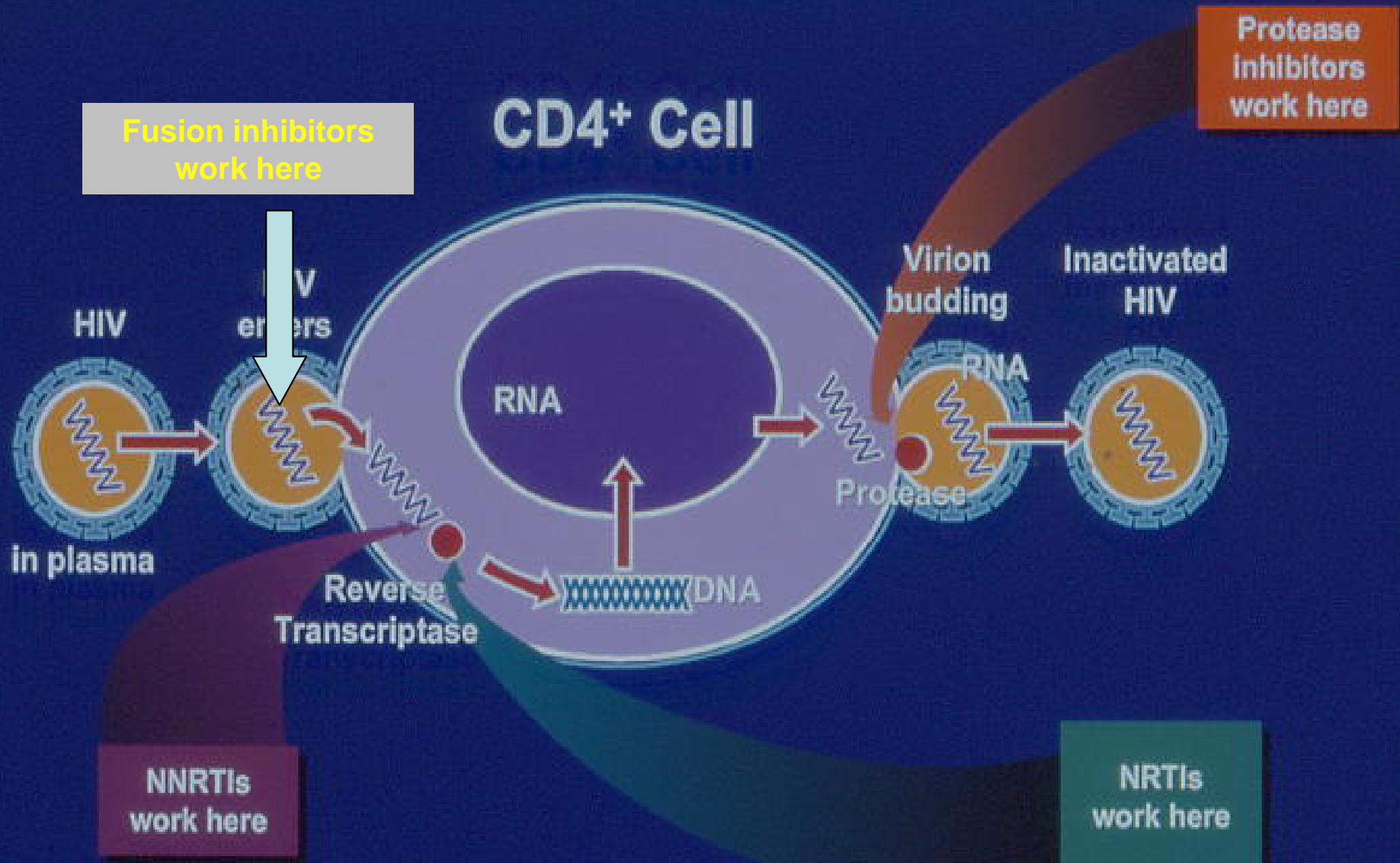
# Strategies to reduce ARV risks



## Strategies to Reduce Risks:

- A comprehensive ARV program
- Excellent patient education and preparation before starting ARVs
- Perfect or near perfect patient adherence to ARVs
- Provider knowledge of ARVs and proper use
- Excellent patient follow-up and monitoring

# HIV Lifecycle and Antiretroviral Therapy



# Highly active antiretroviral therapy (HAART)



HAART is defined as:

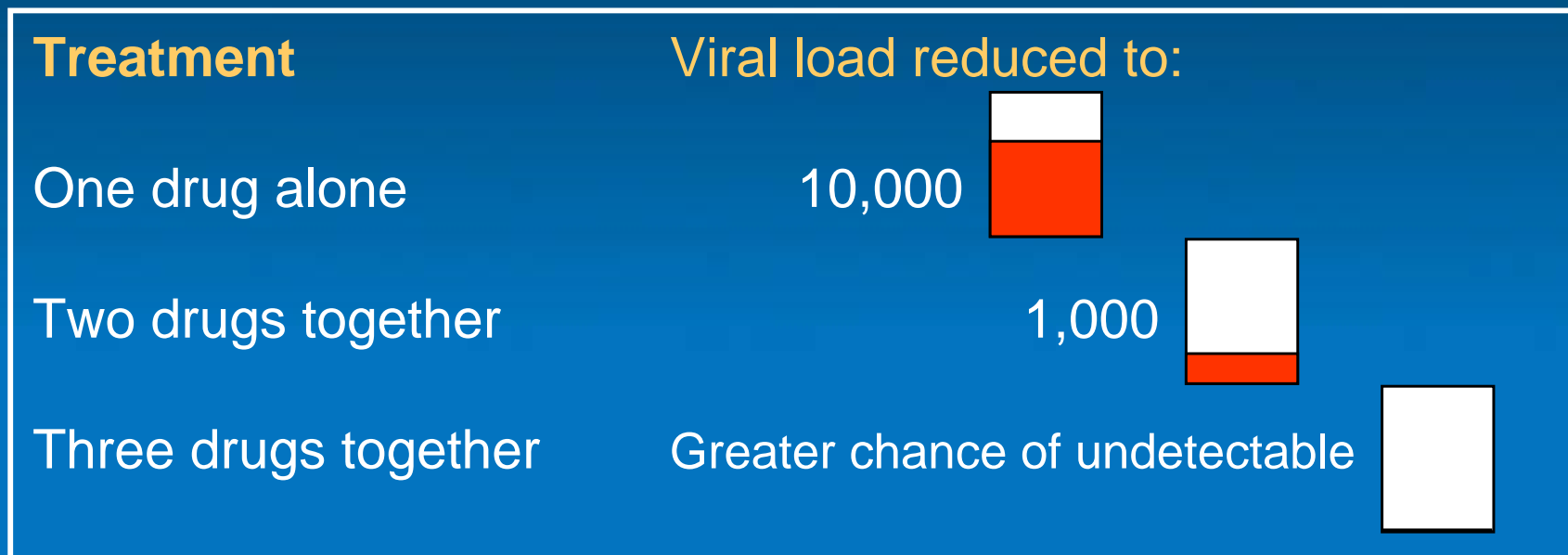
- Any antiretroviral regimen that will:
  - \* Prevent disease progression
  - \* Optimize opportunity for recovery
  - \* Prevent selection for drug resistance
- In practice, must maintain viral load  $<50$  copies/ml *to prevent resistance*
- Usually requires 3 or more drugs in at least 2 different classes

# Different drugs work together to reduce viral load

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## *Example:*

Viral load before treatment might be 100,000 copies/ml



# ARV Agents Included in Nigeria's ARV Guidelines



| Nucleoside reverse transcriptase inhibitors<br><br><b>(NsRTIs)</b>  | Nucleotide reverse transcriptase inhibitor<br><br><b>(NtRTI)</b>                               | Non-nucleoside reverse transcriptase inhibitors<br><br><b>(NNRTIs)</b>  | Protease inhibitors<br><br><b>(PIs)</b>   |
|---|--|---|---|
| <ul style="list-style-type: none"> <li>• Zidovudine (ZDV, AZT)</li> <li>• Didanosine (<b>ddl</b>)</li> <li>• Stavudine (<b>d4T</b>)</li> <li>• Lamiduvine (3TC)</li> <li>• Emtricitabine (<b>FTC</b>)</li> <li>• Abacavir (<b>ABC</b>)</li> </ul> | <ul style="list-style-type: none"> <li>• Tenofovir disoproxil fumarate (<b>TDF</b>)</li> </ul> | <ul style="list-style-type: none"> <li>• Nevirapine (<b>NVP</b>)</li> <li>• Efavirenz (<b>EFZ</b>)</li> </ul> | <ul style="list-style-type: none"> <li>• Saquinavir (<b>SQV</b>)</li> <li>• Ritonavir (<b>RTV</b>) (pharmacoenhancer)</li> <li>• Indinavir (<b>IDV</b>)</li> <li>• Nelfinavir (<b>NFV</b>)</li> <li>• Lopinavir/ritonavir (<b>LPV/r</b>)</li> <li>• Atazanavir (<b>ATV</b>)</li> <li>• Amprenavir (<b>APV</b>)</li> </ul> |

# Choosing a regimen



## Considerations for Regimen Choice

Provide an antiretroviral regimen which

- Has a high likelihood of success
- preserves future therapeutic options
- has relatively few side effects
- is tailored to individual needs for adherence

# The ideal HAART regimen



- *Potent* enough to stop viral replication
- *Durable*: high genetic barrier to resistance (multiple mutations required for resistance)
- *Convenient*: Family can adhere, low pill count, does not need refrigeration
- *Non-toxic*
- *Tolerable*: Side-effects are transient or tolerable; reasonable palatability
- *Sustainable*: Cost supportable, supply assured

There is no perfect ARV regimen!

# Importance of adherence



ARVs, when taken correctly, can tremendously enhance a patient's life and dramatically halt progression of disease

However, in order to derive the most benefit from the medications, adherence must be EXCELLENT

## Adherence Points

- Should *work with the patient/family* to develop adherence strategy
- If ARVS are taken improperly, problems may occur on a personal and public health level
  - \* Implications on resistance, cross resistance, spreading resistant virus and cost

# What is resistance?



- Resistance is when *mutations (changes)* in HIV genes allow it to grow in the presence of a drug
- Resistance may be partial or high-level
- For some drugs, only one mutation will cause high-level resistance (e.g. NVP, EFV)
- For other drugs, many mutations are needed (e.g. ZDV, LPV)
- Resistance may be to one drug, or to several related drugs

# Patterns that lead to resistance



Decreased or low  
potency of prescribed  
antiretroviral therapy

Nonadherence

Viral Resistance

Viral replication

Clinical failure



# How good must adherence be?



- Generally > 95% of doses
- Some treatment regimens are more “forgiving” than others: AZT/3TC/NVP is a less “forgiving” regimen- *but can work excellently for years if adherence is maintained.*
- Missing 1 dose per week is 93% adherence
- Adherence < 80% almost always fails
- “Good” adherence taking “most” doses will lead to failure
- *Rare* missed dose is tolerated

# But what happens when patient *can't* take all ARVs?



- If circumstances make >95% adherence impossible, patient can safely (and should) STOP ALL ARVs
- Stop NVP 7-14 days before D4T/AZT and 3TC if possible
- Stay off all ARVs until adherence problem resolved
- Restart all ARVs simultaneously when ready

# Challenges for ART Programs in Resource-Constrained Countries



## CHALLENGES

- Limited resources
- Procurement of affordable ARVs
- Ensuring ARV supply
- Security of ARV storage
- Limited physical infrastructure
- Providing necessary laboratory monitoring
- Need for trained doctors and nurses
- Staff turnover

# Prerequisites for a Successful ARV Program



## A SUCCESSFUL ARV PROGRAM SHOULD HAVE:

- Adequate infrastructure
- Lab facilities for patient diagnosis and monitoring
- Access to OI/symptomatic treatment
- Continuous supply of ARVs
- Informed communities
- Counseled patients
- Physicians/nurses/ other team members trained
- ARV treatment guidelines in place
- Political will & view for sustainable program

# The 3 most important things to know about HIV treatment



## MUST NOT FORGET

- Resistance will evolve if virus grows in the presence of drug
- Treatment must be potent enough to stop virus from growing and must present a high genetic barrier to resistance
- All drugs must be taken every day *or all drugs must be stopped* (but can later be restarted).

*Accomplishing successful treatment requires that the patient and HIV care team work together.*

# Summary



- Antiretroviral therapy should reduce morbidity and mortality from HIV/AIDS
- While there are risks of drug resistance and anticipated side effects from medications, antiretroviral therapy's benefits outweigh the risks
- Monitoring patients on therapy is critical
- Adherence to therapy is the key to success
- ART programs should address programmatic challenges to ensure success in scaling up ART

THANK YOU