

# Pediatric HAART 1: What is highly active antiretroviral therapy (HAART)?

Unit 1

Paediatric Antiretroviral Therapy Workshop  
Abuja 24-28 June 2006

# Goals

- Understand how **potency** and **durability** define HAART
- Understand why **adherence** is necessary for HAART success

# The defining characteristics of HAART

- **Potency:** The ability to stop HIV from growing
- **Durability:** The ability to maintain potency indefinitely by presenting a high ***genetic barrier*** to the evolution of ***resistance***

*Potency and durability depend on **adherence** to therapy*

# The definition of HAART

Highly active antiretroviral therapy (HAART) is any treatment that, when adhered to, is potent enough to suppress HIV replication to an undetectable level and has a genetic barrier to the evolution of resistance high enough to indefinitely maintain viral suppression, thereby preventing disease progression and maximizing the opportunity for recovery.

# 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.
- **Non-toxic**
- **Tolerable:** Side-effects are transient or tolerable; reasonable palatability
- **Sustainable:** Cost supportable, supply assured

# Why does the viral load need to be undetectable?

- If the viral load is undetectable, HIV will not cause any harm
- Most importantly, if the viral load is undetectable, resistance to the drugs will not develop
- Once resistance develops, the viral load increases AND more resistance develops

# What is resistance?

- Resistance is when *mutations* 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

# How does resistance evolve?

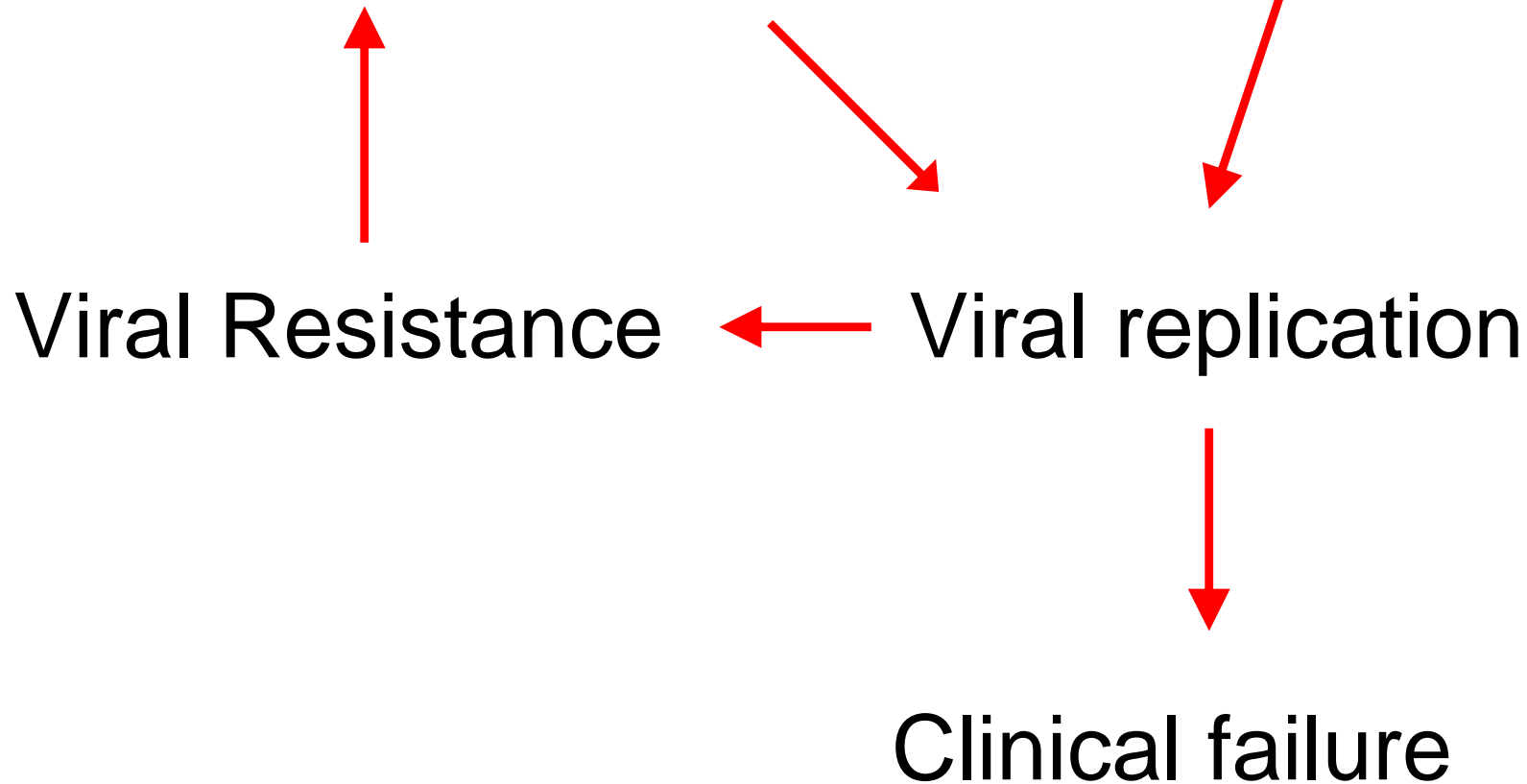
- HIV reverse transcription is error-prone: random changes in HIV reverse transcriptase and protease genes are commonly made
- Most of these changes do not help the virus
- BUT, rarely one of these changes will cause a change in the reverse transcriptase or protease that lets the virus grow even if drug continues to be used.

## So, HAART means:

- A combination of drugs that is ***POTENT*** enough to stop HIV from growing **AND...**
- Requires many different mutations to fail- i.e. has ***HIGH GENETIC BARRIER TO RESISTANCE*** AND...
- That the patient takes every day, **ALL DOSES.**

Decreased or low  
potency of prescribed  
antiretroviral therapy

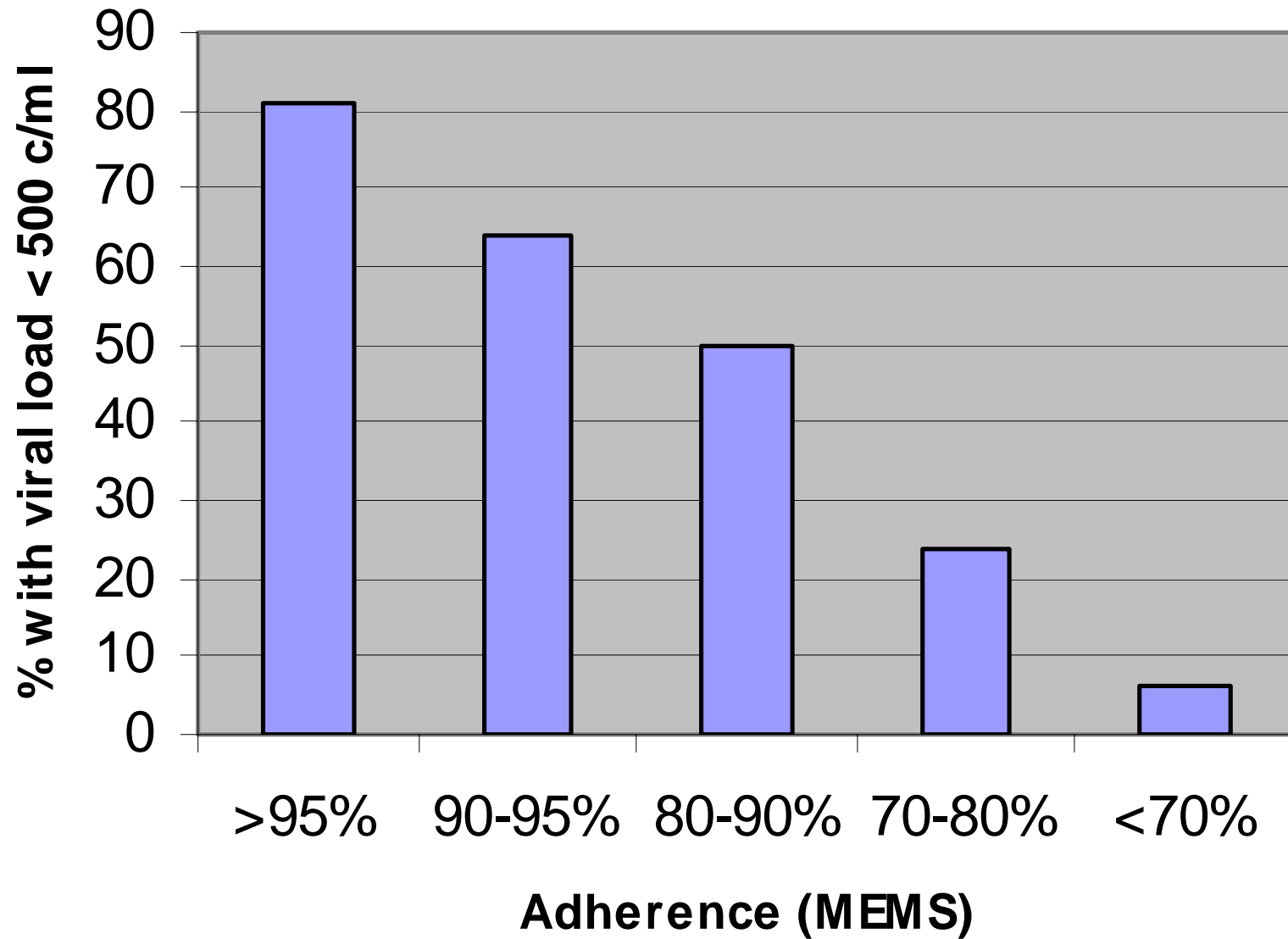
Nonadherence



# 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

## Adherence and virologic response at 6 months (Paterson, et al. Chicago 1999)



# 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

# Pediatric antiretroviral therapy: Choosing a regimen

- Optimizing potency
  - Activity of drugs and combinations
  - Ease of developing resistance
  - Assess resistance status
    - History
    - Resistance testing
- Optimizing adherence
  - Palatability
  - Side effects
  - Schedule

# Response to HAART in children

- Viral load drops very rapidly- About 100-fold in 2-3 weeks
- CD4 response
  - Return to normal in about a year
  - Can stop TMP/SMX (Co-trimoxazole) when CD4 above prophylaxis guidelines
- Rapid clinical response
  - May feel better in 1-2 weeks
  - Risk of opportunistic infection rapidly decreases
  - Rapid weight gain