

# Paediatric HAART 1: Indications for antiretroviral therapy

## Unit 8.1

Paediatric Antiretroviral Therapy Workshop  
Institute for Human Virology-Nigeria ACTION  
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# Goals



- Appreciate the rationale for initiating antiretroviral therapy in a child
- Know the current WHO guidelines for clinical indications for HAART
- Know the current WHO immune status guidelines for initiating HAART
- Be able to assess various clinical situations to determine if HAART is indicated according to guidelines

# Paediatric stage 1



- Asymptomatic
- Persistent generalized lymphadenopathy
  - Lymphadenopathy is a *good* prognostic sign- probability of death in HIV-infected children with adenopathy is half as much as those without

# Paediatric stage 2



- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema (red line along the gum line)
- Herpes zoster
- Recurrent upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis )
- Fungal nail infections

# Paediatric stage 3



- Moderate unexplained malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more )
- Unexplained persistent fever (above 37.5 °C, intermittent or constant, for longer than one month)
- Persistent oral *Candida* (after first 6 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis/periodontitis
- Lymph node TB
- Pulmonary TB
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis (LIP)
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia ( $<8.0$  g/dl ), neutropenia ( $<0.5 \times 10^9/L$ ) or chronic thrombocytopenia ( $<50 \times 10^9/L$ )

# Paediatric stage 4



- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site)
- Extrapulmonary TB (except lymph node TB)
- Kaposi sarcoma
- Oesophageal candidiasis (or *Candida* of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after the neonatal period)
- HIV encephalopathy

# Paediatric stage 4 (cont.)



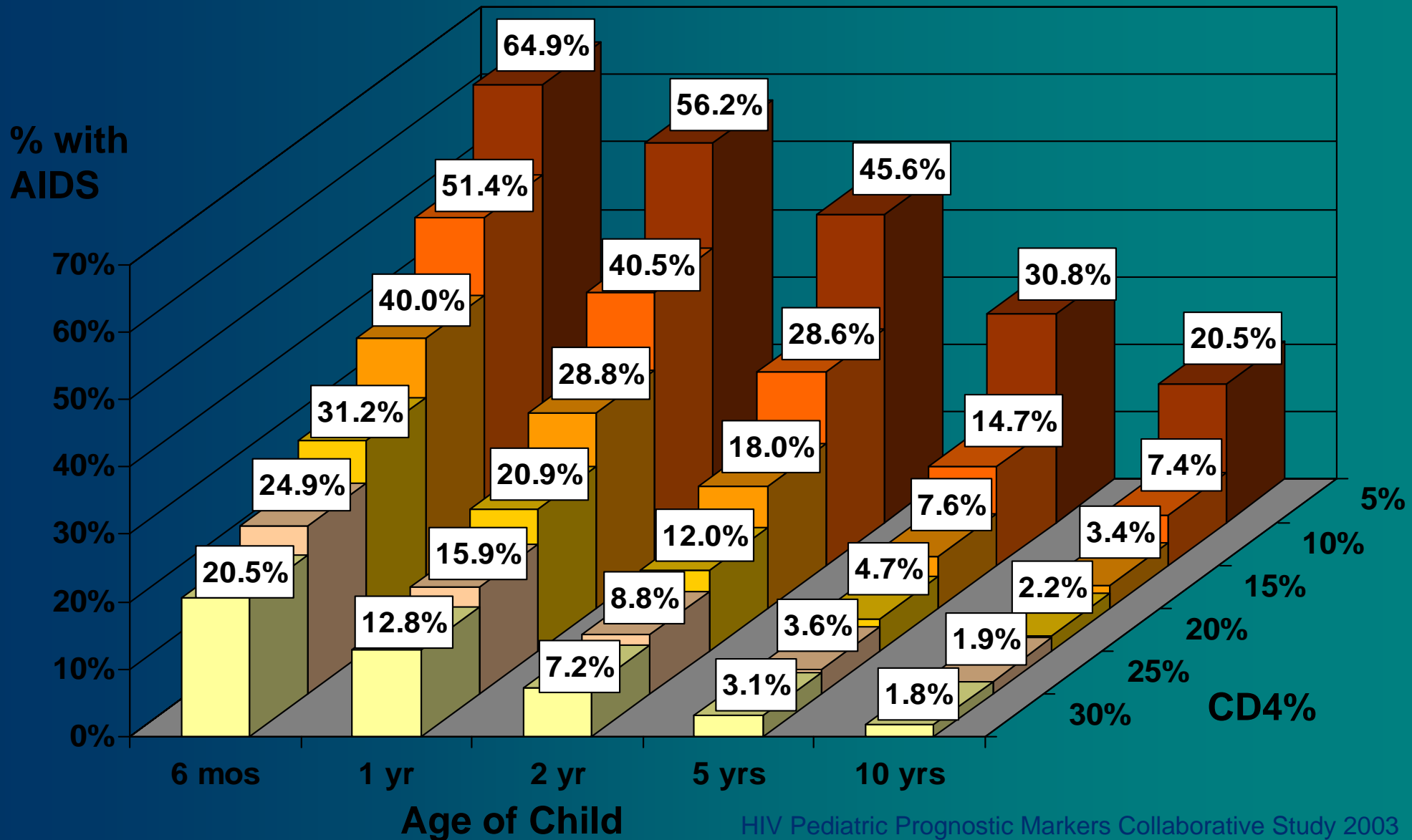
- Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over 1 month.
- Extrapulmonary cryptococcosis including meningitis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
- Chronic cryptosporidiosis (with diarrhoea )
- Chronic isosporiasis
- Disseminated non-tuberculous mycobacteria infection
- Acquired HIV-associated rectal fistula
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- HIV-associated cardiomyopathy or nephropathy

# Immunologic classification of paediatric HIV

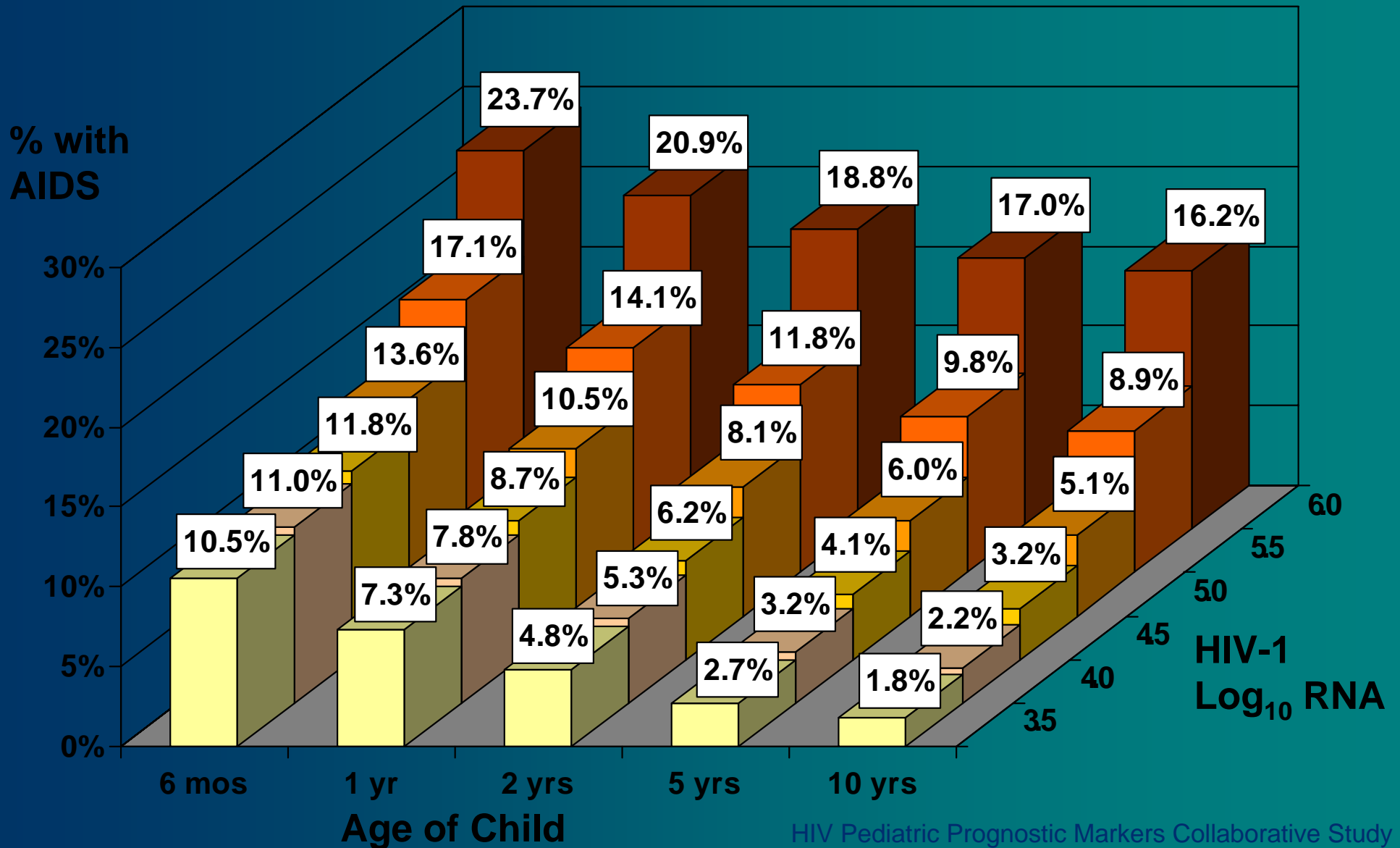


HIV immunodeficiency class	Age-related CD4 values			
	≤11 months (%)	12–35 months (%)	36–59 months (%)	≥5 years (cells/μl)
Not significant	>35	>30	>25	>500
Mild	30–35	25–30	20–25	350–499
Advanced	25–30	20–25	15–20	200–349
Severe	<25	<20	<15	<200 <i>or</i> <15%

# Likelihood of Developing AIDS Within 12 Months By Age and CD4+ Percentage in HIV-Infected Children Receiving No Therapy or Zidovudine Monotherapy



# Likelihood of Developing AIDS Within 12 Months By Age and HIV-1 RNA Log<sub>10</sub> Copy Number in HIV-Infected Children Receiving No Therapy or Zidovudine Monotherapy



# The use of guidelines for initiating HAART



- Guidelines are a guide to a standard for best practice in a particular setting
- Each case has its own complexities. There are likely to be competing arguments for *when* (not *if*) to initiate HAART-these must be assessed on an individual basis
- Guidelines will change as knowledge and available resources change

# When to start HAART?



## Earlier

- Prevent CD4 decline
- Prevent infection
- Protect brain & other organs
- Preserve immune response to HIV (HIV immune response does not improve on therapy)

## Later

- Avoid toxicity, side-effects, and cost
- Avoid resistance
- Children generally respond very well to ART

# Weighing benefits and risks of HAART



## Benefits

- Reduce viral load
- Increase CD4 cells
- Prevent infections & other symptoms
- Prolong life
- Provide hope

## Risks

- Drug resistance
- Toxicity
- Side-effects
- Cost: Drugs, labs, staff, family

# DRAFT revised WHO guidelines for initiating ART in infants and children: clinical criteria **with** or **without** CD4



WHO Stage	<18 months	>18 months
I	<b>CD4-guided</b> (No CD4: do not treat)	
II	<b>CD4-guided</b> (No CD4: do not treat)	
III	<b>Treat all</b> (No CD4: treat all)	<b>Treat all (except TB, LIP, OHL, ITP: take account of CD4)</b> No CD4: Treat all except TB- consider other factors
IV	<b>Treat all</b>	

# DRAFT revised WHO guidelines for initiating ART in infants and children: immunologic criteria



## Age-specific CD4 criteria at or below which initiation of ART is recommended

Immunologic marker	Age-specific CD4 criteria at or below which initiation of ART is recommended			
	<12 months	12-35 months	36-59 months	>5 years
CD4 % (% of total lymphocytes)	25%	20%	15%	15%
CD4 count (cells/ $\mu$ l)	1500	750	350	200

# Considerations for starting HAART in children



1. **How certain is the diagnosis?**
  - Do you have *documentation* of test results?
  - In absence of PCR, may need to make presumptive diagnosis in infant: this must later be confirmed.
2. **Does the child have *either***
  - CD4 count *or* percentage that meet guidelines? *OR*
  - Recent or ongoing symptoms that meet guidelines?
    - \* Any Stage 4 symptoms
    - \* Any Stage 3 symptoms (Except if mild LIP, mild thrombocytopenia, or TB, treatment is optional)
3. **How urgent is initiation of HAART?**
4. **Does the child have other complications that need or can be resolved prior to starting HAART?**
  - Is the complication a likely cause of symptoms that would otherwise indicate treatment needed: e.g. If TB is likely cause of weight loss *and* CD4 count does not meet guidelines, then treat TB and monitor for weight gain.

# Considerations for starting HAART in children-2



5. Is family ready to adhere?
6. Are all the medications available with a reasonably assured supply?
7. Is the breastfeeding mother starting on HAART?
  - If infant is infected *and* mom is ready to start HAART, then infant should start before or at same time as mother (to prevent infant from receiving low-dose ARVs from milk)

# Unit 8.1 Case 1



- 4 year old boy with fever and cough X 1 month
- Wt = 11 kg, Ht = 95 cm
- Thin, mildly pale.
- CXR- opacity in L lower lobe
- Hgb = 7 gm/dl
- Rapid test for antibodies to HIV is positive, confirmed on second test
- CD4 = 400 (18%)
- What is his paediatric HIV class? Based on what?
- How would you proceed?

# Unit 8.1 Case 2



- 8 year old girl started on anti-TB therapy 8 weeks ago after multiple courses of antibiotics for “cough for 3 years”. She has not improved, according to father, who is a school teacher.
- Pleasant. Frequent cough.
- Wt = 16 kg, Ht = 115 cm
- Large parotid glands. Crackles throughout the chest, mild adenopathy, digital clubbing.
- CXR- small patchy infiltrates and small densities throughout the lung fields.
- CD4 = 300 (16%)
- What diagnoses do you give?
- What is her paediatric HIV class? Based on what?
- How would you proceed?