



South to South



# Diagnosis of HIV in Infants and Children



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FROM THE AMERICAN PEOPLE



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# Learning Objectives

- Review key concepts about diagnosing HIV infection in infants and young children
- Review the available tests
- Introduce the algorithms for diagnosing HIV in infants and young children
- Describe the role of the parent and multidisciplinary team in the monitoring HIV-exposed infants

# The importance of early HIV Diagnosis

- HIV-infected infants are at risk of rapid progression and death often before a diagnosis is made
- Early diagnosis facilitates intervention and close monitoring
  - Prevention and treatment of opportunistic infections
  - Access to HAART
- Infant diagnosis is the logical continuation of the pMTCT program
  - It is important to monitor and evaluate the success of pMTCT programs

# Different entry pathways into HIV care and Treatment services

- Look for infants in:
  - PMTCT follow up clinics
  - MCH clinics
  - Vaccine clinics
  - Hospital wards
- Test for HIV in:
  - Children presenting with signs and symptoms suggestive of HIV/AIDS
  - all children with an HIV-infected sibling/family member
  - all orphans and vulnerable children
  - all victims of sexual abuse
  - all unwell children

# Diagnosis of infection is more complicated in infancy

- Antibody tests can not be used to confirm infection in children < 18 months of age
- Specialized virologic tests should be used according to clinical algorithm if at all available if children are < 18 months of age
- Making a presumptive diagnosis of HIV in children < 18 months of age may be the only way for many children to initiate Rx (clinical diagnosis)
- Exposure to HIV and risk for acquiring infection continues throughout the breastfeeding period

# Available Laboratory Tests (assays)

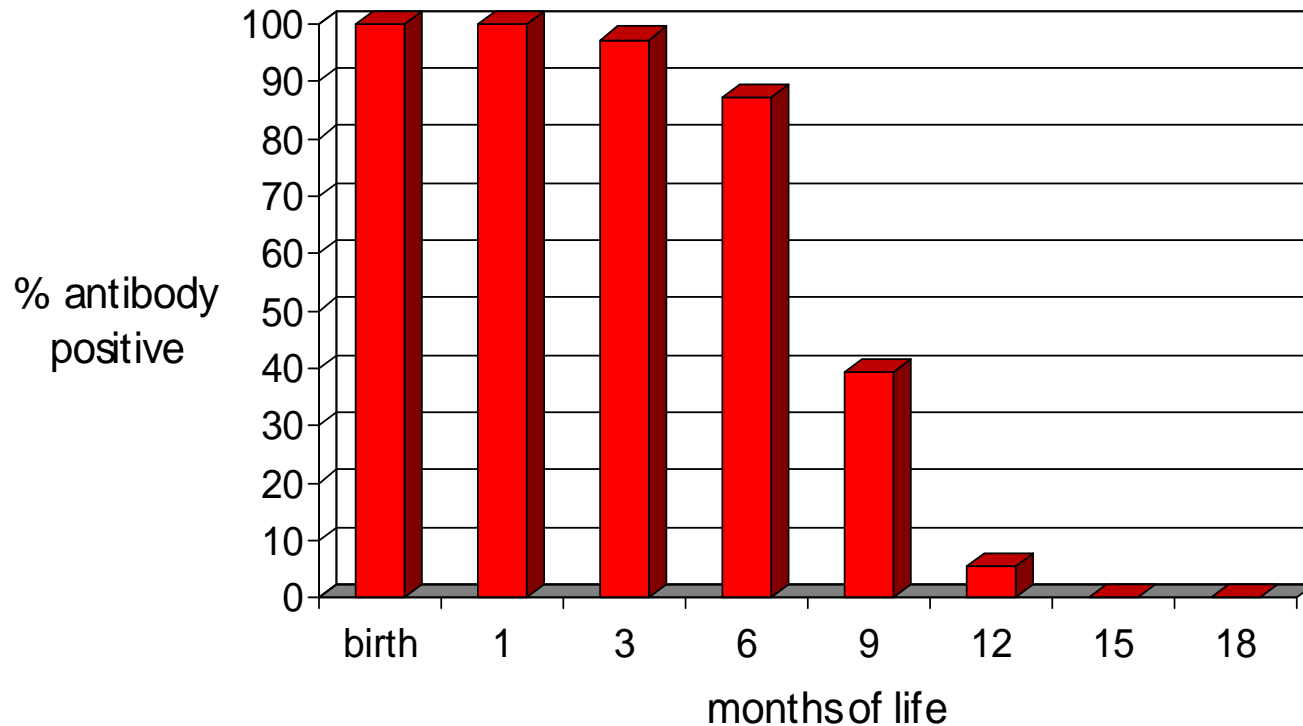
Testing for immune response to the HIV virus	Testing for the HIV virus directly
<b>Rapid ELISA (enzyme linked immunosorbent assay)</b>	<b>PCR – DNA (Qualitative)</b> <ul style="list-style-type: none"><li>• Detects the presence of the virus</li><li>• Only use for diagnostic purposes</li></ul>
<b>Laboratory ELISA</b>	<b>PCR – RNA (Quantitative)</b> <ul style="list-style-type: none"><li>• Determines the quantity of viral copies/ml of blood (viral load)</li><li>• Use for prognostic and monitoring of treatment</li><li>• Can be used as a diagnostic test</li></ul>
<b>Western Blot test</b>	
<b>Oraquick rapid test for saliva*</b>	

# HIV Antibody Tests

- A positive antibody test
  - Cannot confirm HIV infection until the child is > 18 months of age
  - All HIV exposed infants test antibody positive due to the passive transfer of maternal antibody to the fetus during pregnancy
  - These antibodies only “fade” after 6-18 months
- A negative antibody test
  - Exclude HIV infection in children < 18 months of age who have been weaned for at least 6 weeks
  - Remember: An infant who is infected during breast feeding may lose maternal antibodies, test negative, and then develop endogenous antibodies usually within 6 weeks of the “moment” of acquiring HIV infection



# Antibody Detection in 77 HIV-Exposed, Uninfected Infants in South Africa



Moodley D, Pediatric Infectious Disease Journal 1995;14:850

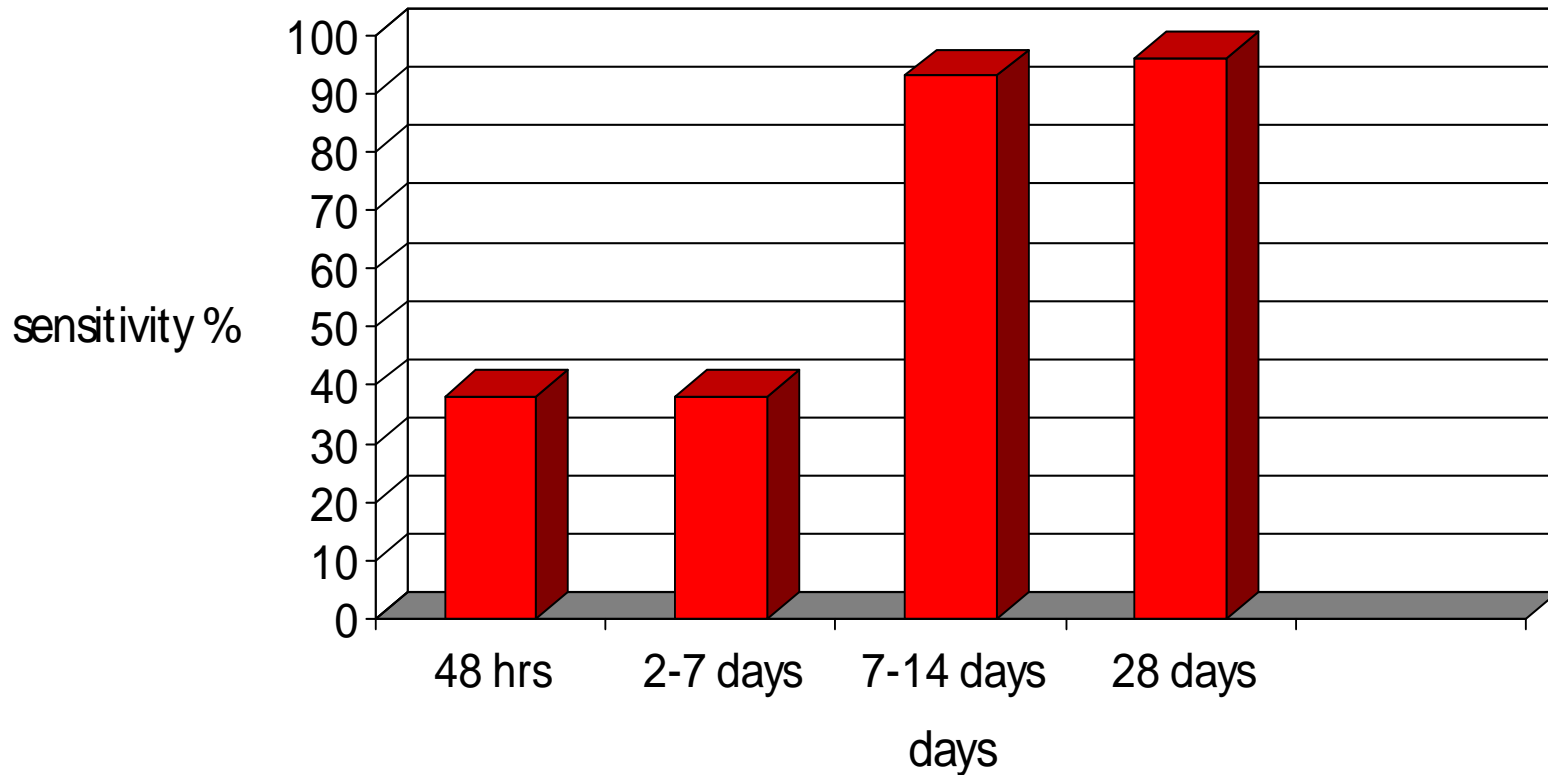
# When to Use Antibody for Infant Diagnostic Testing

- To diagnose HIV infection in an infant  $> 18$  months of age
- To determine HIV exposure status in a baby  $< 18$  months
- To exclude infection in a baby  $> 6$  weeks after weaning
  - A negative antibody suggests that maternal antibody has waned and the infant does not make endogenous antibody

# Virologic Testing - Polymerase Chain Reaction (PCR)

- DNA PCR
  - Used to diagnose infection
  - Detects viral DNA
- RNA PCR (viral load)
  - Generally used to monitor treatment, can be used to diagnose infection
  - Quantitative test that detects viral RNA

# When to Use DNA PCR for Infant Diagnosis



Dunn D, AIDS 1995, 9:F7

# Why Test at 6 Weeks?

- Based on previous graph:
  - If testing infants at birth, only a third of infants will be correctly diagnosed as infected with HIV
  - The vast majority of infants with in utero, intra-partum and early postnatal infection will be identified by 6 weeks of age though
- Most infants have their first visit for vaccine and growth monitoring at 6 weeks
- Remember: Our goal is to identify HIV infected infants as early as possible, rather than confirm the absence of HIV infection in HIV exposed infants
  - This will enable us to identify those infants needing close monitoring for disease progression and assess for antiretroviral treatment

# Virologic Testing

- Every HIV-exposed baby should have at least one DNA PCR test
  - At about 6 weeksOR
  - At first visit\*OR
  - Any child with an initial negative DNA PCR who develops symptoms of HIV infection before 18 months of age
- In infants with early negative DNA PCR, rapid antibody testing should be done 6 weeks post-weaning
  - A negative antibody rules out infections
  - Repeat DNA PCR testing should be done on those who continue to test HIV antibody positive if they are younger than 18 months

# Summary: Which test and when –

3 main groups:

- Children > 18 months of age
- HIV exposed Infants < 18 months of age with virologic testing available
- HIV exposed Infants < 18 months of age where virologic testing is unavailable

# 1. Children > 18 Months of age

In children with and without known exposure:

- Do antibody test
- There is no need for presumptive clinical diagnosis,
  - if antibody test is positive, the child is HIV infected
- A child older than 18 months who tests HIV negative is presumed to be uninfected **unless** he is still breastfeeding



## 2. HIV-exposed infants < 18 months of age

If routine virologic testing is available:

- Virologic test at 6 weeks or at the first encounter thereafter
- If the test is positive, the infant should be considered to be HIV infected, whether or not he/she has symptoms suggestive of HIV infection
- Virologic testing should be used to identify the infected infant before disease progression rather than to exclude infection

# 3. HIV exposed infants < 18 months of age

If virologic testing is unavailable:

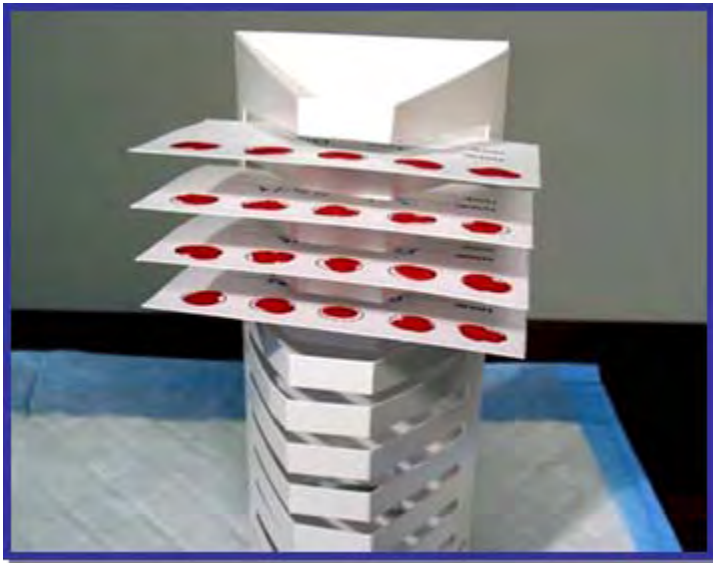
- Monitor closely for any signs of HIV infection or disease progression
- HIV antibody testing at 12-18 months of age or > 6 weeks after weaning, whichever is later, to identify final infection status
- If symptoms suggestive of HIV
  - Refer for virologic testing if available at other site
  - Evaluate for eligibility for ART (Presumptive Clinical Diagnosis)
  - A child with the combination of clinical symptoms (WHO stage II or III) and CD4% (< 20%) should be considered as HIV infected
  - If no CD4 counts available, a total lymphocyte count (TLC) < 3500 can be used

# WHO Clinical Criteria for Presumptive Diagnosis of HIV

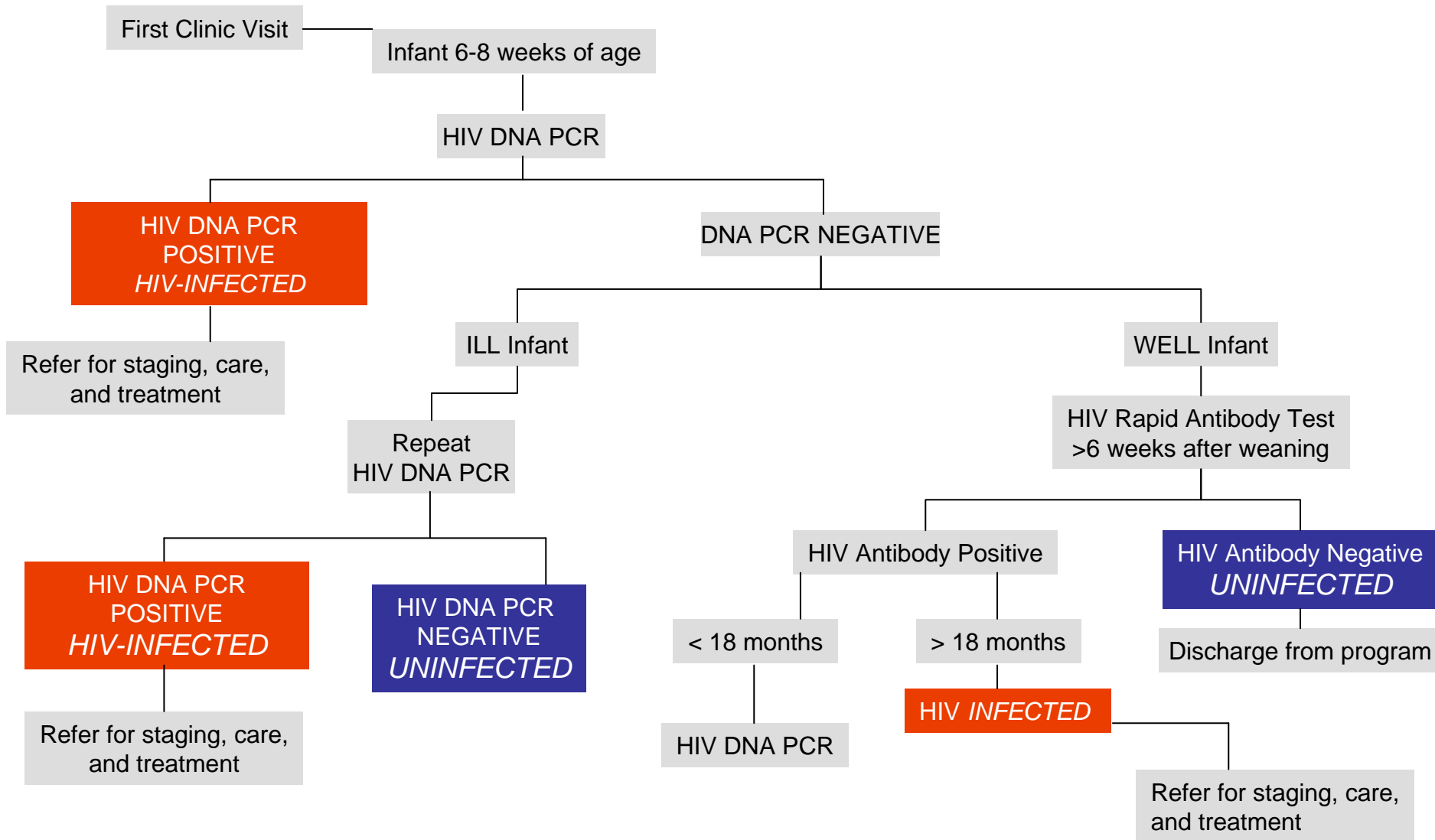
- Confirmed antibody positive *AND*
  - AIDS- indicator diagnosis or stage 4 **OR**
  - 2 or More of:
    - Oral Thrush
    - Severe Pneumonia
    - Severe Sepsis
- Other supportive factors in sero-positive infants are:
  - Infant CD4 < 20%
  - Maternal HIV related death or advanced HIV illness
- For the purposes of initiating ART in an HIV-infected infant
- The antibody test should be confirmed at 18 months

# Remember

- If the picture does not match the test repeat the test!
- A mistake could have been made with labeling and testing or reporting



# Diagnostic Algorithm for Infants < 18 months of Age



# Making Early Infant Diagnosis possible

- Clinical evaluations
  - Good history and physical assessment at each visit
  - Document growth, head circumference, developmental milestones and clinical events
  - CTX prophylaxis from 6 weeks until HIV infection has been definitively ruled out
- Early virologic testing
  - Testing should be done in the context of ongoing family education and support, including infant feeding counseling
  - Use of Dried Blood Spots (DBS) for sample collection
  - Commercially available test kit for DNA PCR testing

# Making Early Infant Diagnosis possible cont.

- Good communication with family
- Team members should emphasize importance of:
  - Determining HIV status
  - Adherence to visit schedule
  - Identifying signs and symptoms
  - Administering Cotrimoxazole prophylaxis

# Summary

- Clinical reasoning is critical to diagnosing infants with HIV
  - Excellent evaluation and care remains the corner stone
- Use virologic tests in a children < 18 months
  - Early use will identify the infants at highest risk for progression
- Use antibody testing to
  - Identify the at-risk infant,
  - Diagnose HIV in infants > 18 months of age,
  - Exclude infection in the weaned infant
- The MDT has numerous critical roles in this process
- The parent or caretaker is the key player, and must be educated and supported on this logistically, emotionally, socially and medically complicated path



# Infant Diagnosis - cases

# Case 1

- A HIV infected mom is referred to the pMTCT program
- She is 34 weeks gestation
- During intake you learn that she has a 13 month old male child at home
- You arrange for her to bring the child to her next visit for evaluation.

# Case Continuation

- Mom brings the child to see you in clinic.
- What are the questions you might want to ask?

# Case Continuation

- Mom reports that the child is still breast feeding, but only 2-3 times per day. She remembers beginning to add water and food to his diet when he was 2 months old. Now he eats everything.
- He has been a well child, but was hospitalized once for an infection in his chest and sometimes he gets white discharge from his ears.
- He has received all of his immunizations but mom didn't bring his record.

# Case Continuation

- Mom was only just diagnosed with HIV during the current pregnancy
- She did not receive pMTCT treatment when she was pregnant with her 13 month old
- Mom is waiting to receive her CD4+ cell count test results

# Clinical Question

- What would you look for on physical examination to help determine the 13 month old child's HIV status?

# Case Continuation

- The child appears well
- Weight, height, and head circumference are on the 25%, 10%, and 10% percentiles, respectively (no old growth data are available)
- There are scars on his tympanic membranes but his examination is otherwise normal
- He says a few words and takes steps alone

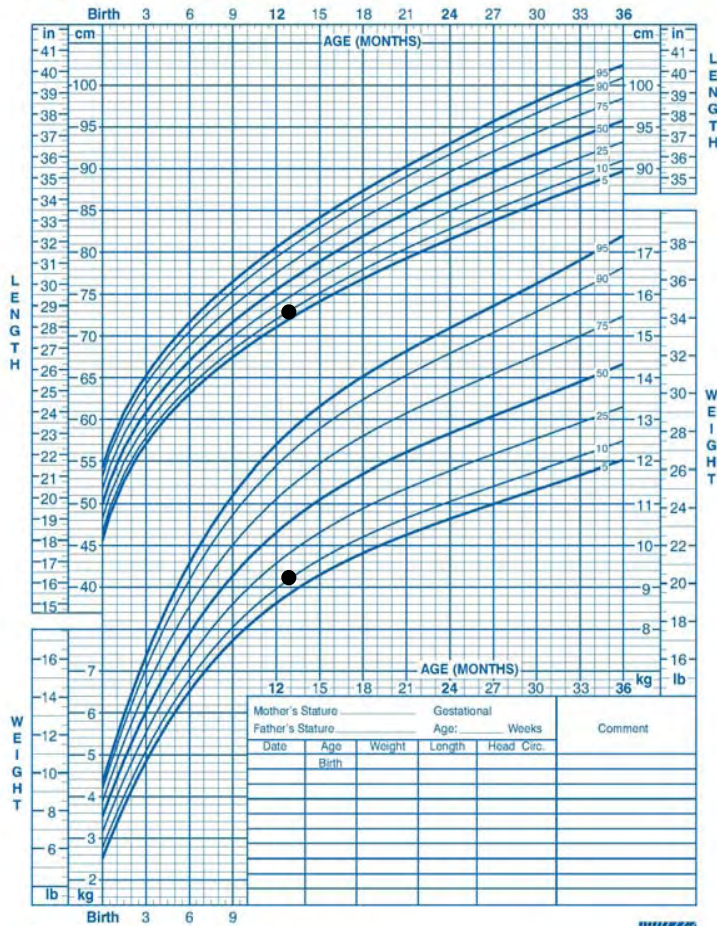
# The Growth Chart

Birth to 36 months: Boys

Length-for-age and Weight-for-age percentiles

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



- What laboratory test(s) would you do, if any?





# Different Diagnostic Tests

## Advantages and Disadvantages

- HIV Rapid Test/Antibody
  - If positive,
    - not definitive at 13 months
    - may still be maternal antibody
  - If negative,
    - Rules out early perinatal infection (in utero, intrapartum)
    - Still at risk because of ongoing breast feeding exposure. Need to repeat >6 weeks after discontinuation of breast feeding

# Different Diagnostic Tests

## Advantages and Disadvantages

- HIV DNA PCR
  - If positive, highly likely to be infected if lab is reliable
  - If negative, still at risk because of BF. Need to repeated > 6 weeks after discontinuation of breast feeding

# Case Continuation

- You decide to send a rapid HIV antibody test. The results are available within an hour and you learn that the child tests positive

# Clinical Question

- How do you explain the test results to mom?

# Clinical Questions

- Given that the antibody test is positive, which of the following options would you now choose?
  - Do DNA PCR or RNA PCR testing?
  - Repeat HIV antibody at >18 months
  - Repeat HIV antibody >6 weeks after discontinuation of breast feeding

# Case 2

- Mom brings her 10 week old back for care to the clinic
- She has been receiving cotrimoxazole since 4 weeks of age
- She is breast feeding and receiving additional foods and water from an aunt
- Mom works several days each week
  
- She had a blood test on the last visit and mom is anxious to know the results

- Baby appears well. She smiles, makes good eye contact, and reaches out
- Growth following the 25<sup>th</sup> centiles for height and weight
- DNA-PCR results were reported as negative

# Clinical Question

- Given the laboratory result and the clinical findings, do you think this child is HIV-infected?



# Clinical Question

- How will you manage the child?

# Case Continuation

Since the baby is thriving you decide not to change clinical management, but you do:

- Continue CTX
- Close, regular follow-up
- Explain to mother that a repeat HIV test will be required

# Case Conclusion

- Mom weaned the baby at 6 months
- Baby continued to be followed
- How would you go about confirming the diagnosis?

# Case 3

- A 10 week old baby girl is brought to the clinic by her paternal grandmother.
- Her mother enrolled in PMTCT during pregnancy at 35 weeks gestation.
- Mom usually brings the baby to clinic but she is back at work now so grandma is caring for the child.
- DNA PCR testing was done when the baby was last at the clinic at 6 weeks of age. The result was positive.
- The team had planned to tell mom the results at this visit

# Case Continuation

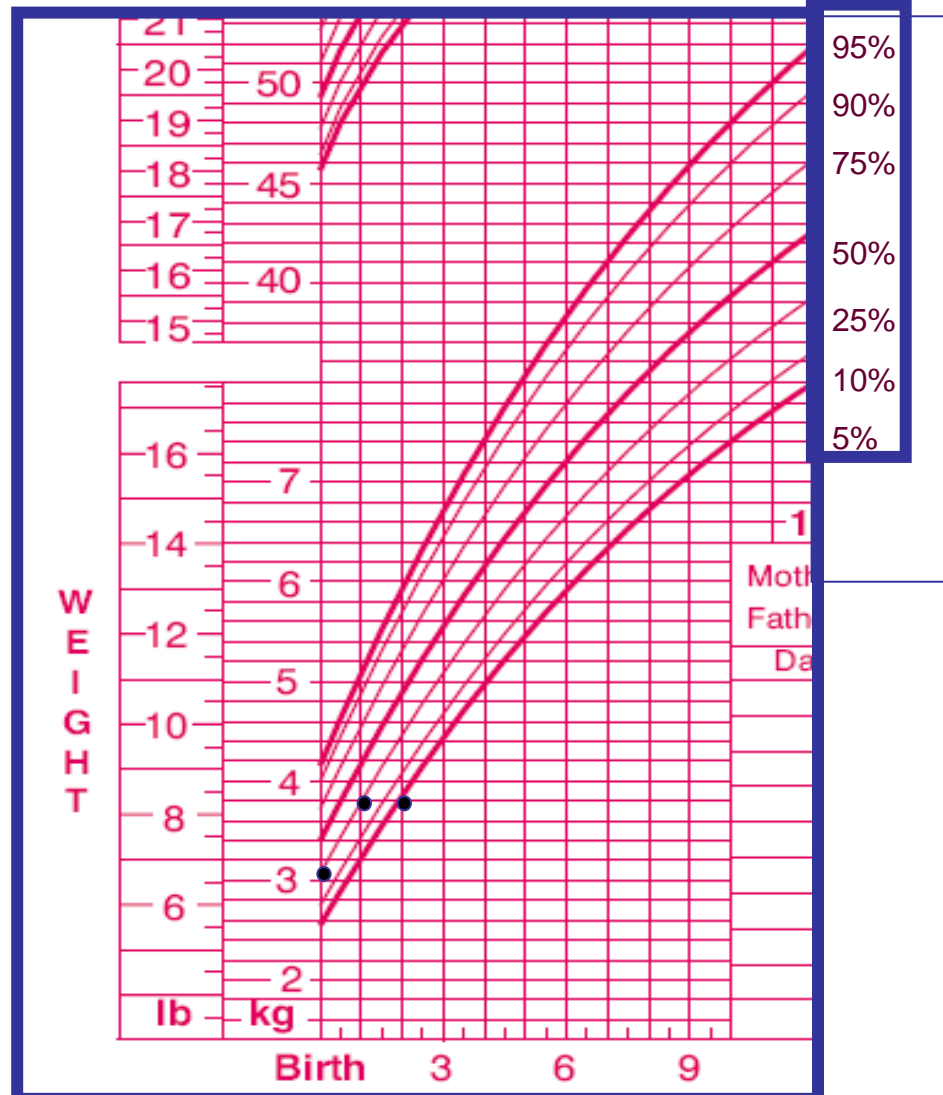
- Grandma reports that the baby is doing fine.
- She feeds her some porridge and mashed banana with a little milk and water during the day.
- Mom is breast feeding when she is home.
  - The baby is a good eater.
- She had some loose stools last week
  - This got better after grandma gave her some herb tea.
- Grandma doesn't give her any medicine. She is sure that she doesn't receive anything from her mother or she would have told her. She asks if something is wrong with the baby?

# Case Continuation

- The baby is well appearing, but has not gained any weight since the last visit.
- The exam is notable for
  - dermatitis
  - oral thrush
  - small palpable lymphadenopathy.
- The baby has one large, loose stool during the evaluation.

# Case Continuation - Growth Chart

- Birth Weight- 3.0 kg
- Weight at 1 month- 3.8 kg
- Weight at 2 months.- 3.8 kg



# Clinical Question

- What do you want to do next?



# Case Continuation

- The clinicians decide that further evaluation and treatment is required.
- Since grandma didn't know about the CTX, the nurse is worried that grandma doesn't know about the mother's or the baby's HIV status.

# Clinical Questions

- How would you assess what grandma knows?
- Do you want to discuss the child's HIV status with grandma?
- Do you want to tell her the results of the DNA-PCR test?

# Case Continuation

- The team quickly decides that the child's condition is not an emergency and does not warrant disclosure to the grandmother.
- The decision is made to schedule another appointment for the mother and child.
- You tell grandmother that the child needs medicine and a blood test

# Case Continuation

- 10 days later mom comes to clinic with the baby.
- The baby has not been feeding well and has been having diarrhea.
- Her weight is now below the 5th percentile and the thrush has worsened.
- Liver enlargement and splenomegaly are also noted on exam.

# Clinical Question

- What do you want to say to mom?

# Clinical Question

- The team tells the mom in a supportive manner about her child's diagnosis.
- Now, how do you want to proceed with the baby?

# Case Continuation

- The baby is admitted to the hospital for nutritional rehabilitation.
- The CD4 is available the next day:
  - CD4 750, 6%.

# Clinical Questions

- Is the child eligible for ART? Would you begin treatment?
- How will you explain your decision to her mother?



# Clinical Question

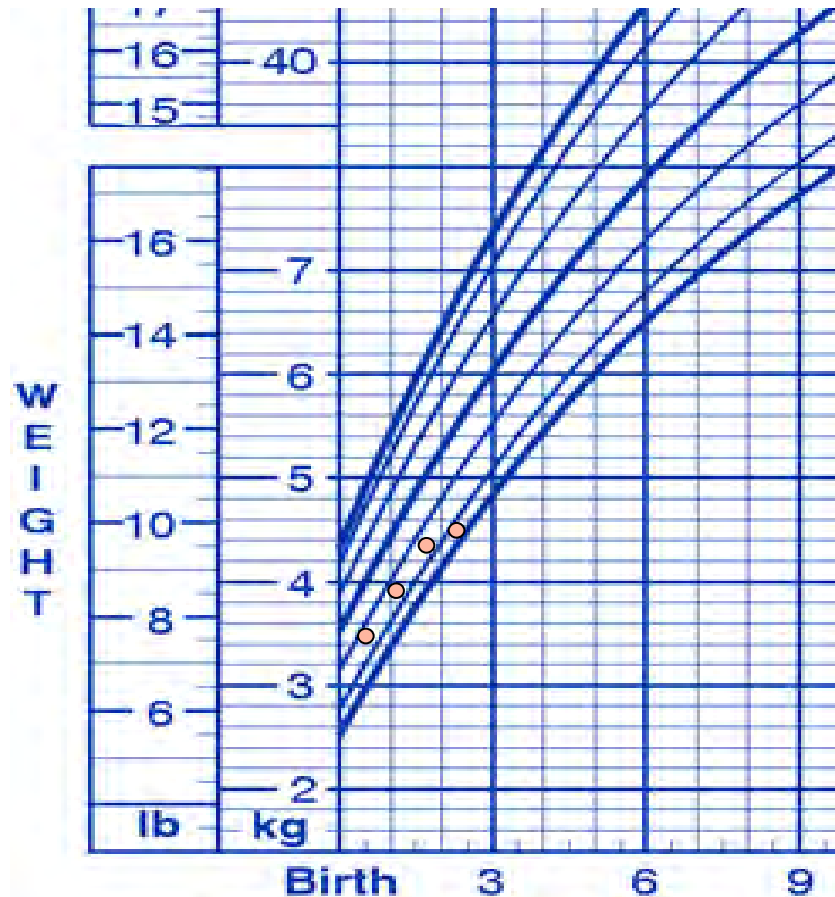
- Grandma arrives at the hospital the next day and wants to know what is wrong with the child.
- The staff initially avoid her, but realize that they must address her questions.
- What should be said to grandma?

# Case 4

- 14 week old infant is brought to clinic for his first visit
- He has a short history of shortness of breath and struggling to feed
- Mom refused an HIV test in pregnancy

# During your assessment

- You find oral thrush
- The baby is extremely distressed
- You hear nothing on auscultation



Published May 30, 2000 (modified 4/20/01).

SOURCE: Developed by the National Center for Health Statistics and the National Center for Chronic Disease Prevention and Control.  
<http://www.cdc.gov/growthcharts>

# You suspect PCP

- You admit the child and institute care
- You do counseling for an HIV test
  - Which test would you perform?

# The HIV EIA is positive

- What would you tell the mother?
- What would you do next?

# You do a PCR

- The lab calls you and say that they will only be able to do the test after 6 weeks because the machine is broken
- What now?

# Case 5

- A 6 month old boy is well know at your clinic
- Mom was diagnosed antenatally with HIV
  - Clinical stage III (oral thrush)
  - CD4 250 cells
  - Vaginal delivery ROM 8 hours
- Baby and mother took Nevirapine
- Baby started on Cotrimazole prophylaxis at 6 week
- Breastfed till now, with introduction of solids at 4 months
- DNA PCR negative at 6 weeks

# Questions

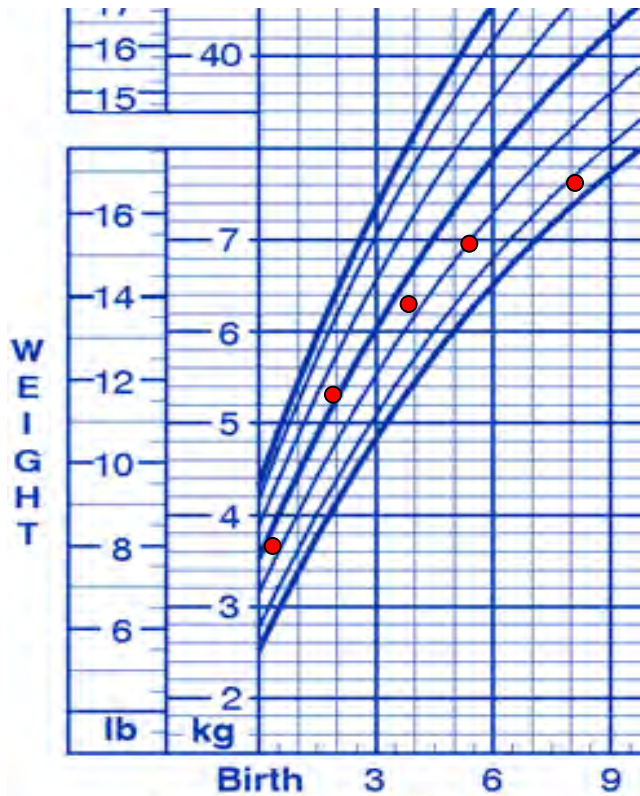
- Identify the risk factors for transmission in the history
- What are the complicating factors in the infant diagnosis



# You see him in clinic today

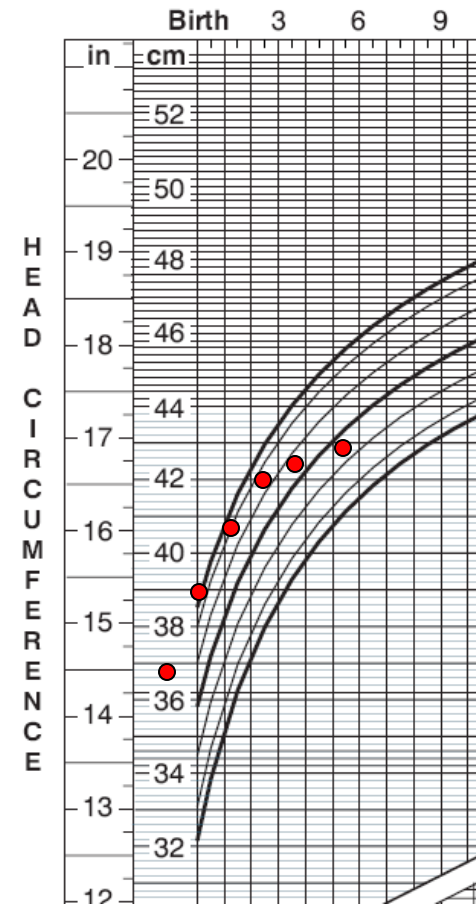
- Mom has no new complaints

# Centile charts



Published May 30, 2000 (modified 4/20/01).  
SOURCE: Developed by the National Center for Human Growth and Development, the National Center for Chronic Disease Prevention and Control, and the National Center for Health Statistics.  
<http://www.cdc.gov/growthcharts>

Growth chart



Head circumference chart

- What is worrying you?
- Why?

# On examination

- No acute illness
- No lymphadenopathy
  
- No head control
- Unable to sit
- Increased tone in lower limbs with brisk ankle reflexes

# Question

- What is your diagnosis?
- Do you need special investigations to confirm your suspicions?

# How would you proceed

# Investigations

- Repeat DNA PCR positive
- CD4 38%

# Management

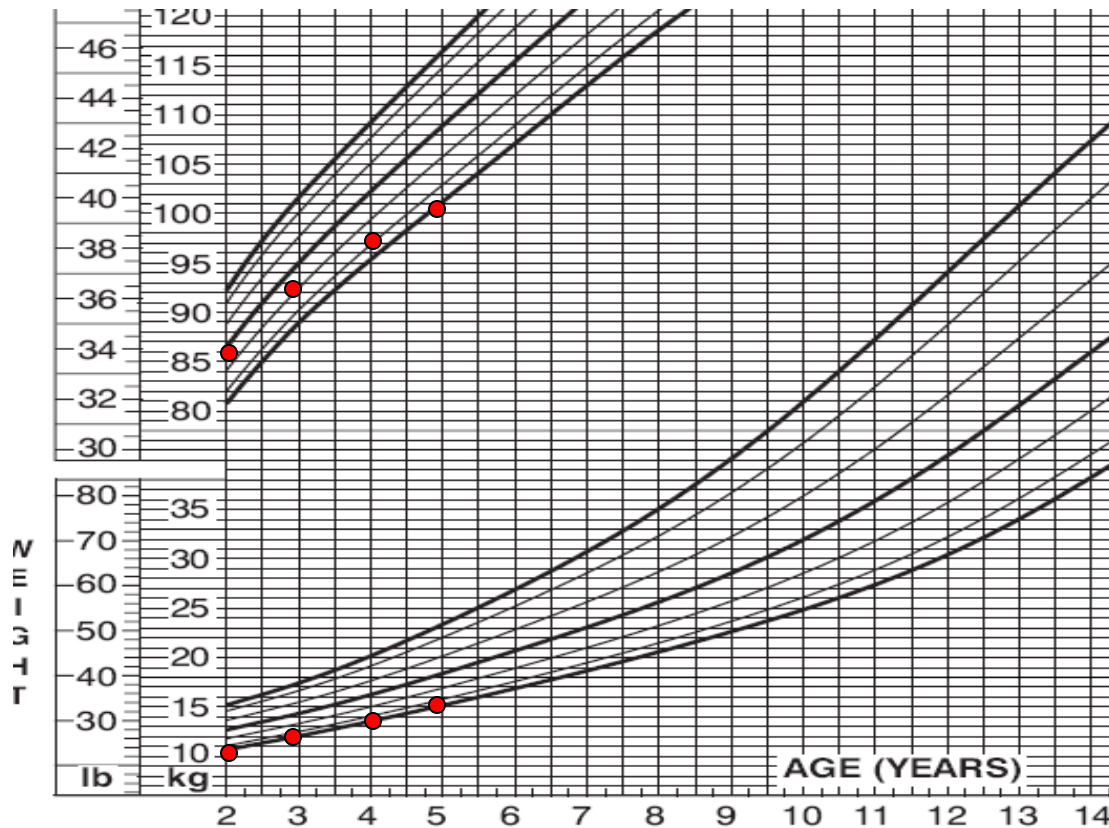
- Stage 4 CNS disease
  - Needs HAART
- You initiate the child with the first line available to you
  - What is your first line
- What are you going to tell the mother?
- When are you going to see the child again?



# Case 6

- Vusi is 5 years old
- He was recently diagnosed with HIV.
- He was tested because his brother Thabo presented with PJP pneumonia
- His only complaints were of recurrent otitis media and scattered molluscum contagiosum on the face
- He has just received his final vaccination

# Your assessment



## Physical examination:

- Bilateral perforations of the tympanic membrane
- Molluscum lesions on the face

## Lab results:

- CD4 10% 195 cells

# What should we consider

- How would you stage him clinically?
- How would you stage him immunologically?
- Does the child need HAART?

After preparation you initiate with D4T, 3TC and NVP

- What is the dose of NVP you are going to prescribe?
- How would you monitor the child?
- What do you tell the mother before sending him home?

- Vusi is doing very well, gaining weight and developing normally
- Mother is happy and you are happy
- Success story!



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