

Diagnosis and management of the HIV-exposed infant

Unit 6.1

Paediatric Antiretroviral Therapy Workshop
Institute for Human Virology-Nigeria ACTION
Abuja
24-28 July 2006

Goals



- Understand the medical and psychosocial needs of the HIV-exposed infant
- Assess the nutritional status of the HIV-exposed infant
- Be able to interpret clinical and laboratory data to determine the HIV infection status in an infant under various circumstances

Needs of the HIV-exposed infant: Goals of the clinic visit



- Nutritional assessment, counseling, and support
- Developmental assessment
- Assessment of adherence to follow up & prophylaxis
- Diagnostic assessment: History, physical exam, laboratory tests, and diagnosis
- Antiretroviral prophylaxis
- Bacterial, malarial, and *Pneumocystis* prophylaxis
- Counseling: Infant status, family voluntary counseling and testing for HIV, and engagement in care

Visit schedule



- At birth
 - Antiretroviral prophylaxis
 - Nutrition counseling and support
 - Arrange follow up for infant, mother, other family
- 0-6 months of age: every month
- 6-12 months of age: every 2-3 months
- 12-18+ months: every 3 months
- Criteria for discharge from HIV clinic
 - HIV infection ruled out
 - No ongoing exposure
 - Nutrition status stable

Nutritional history



- Is the child taking any breast milk?
- What other liquids or solids does child take?
 - Water, teas
 - Cow's or other animal's milk & source
 - Modified milk
 - Infant formula- which and how reconstituted
 - Pap/pounded yam
 - Other solids
- How are substitute or complementary feeds afforded?
- Cup or bottle? How cleaned?
- Is there refrigeration?

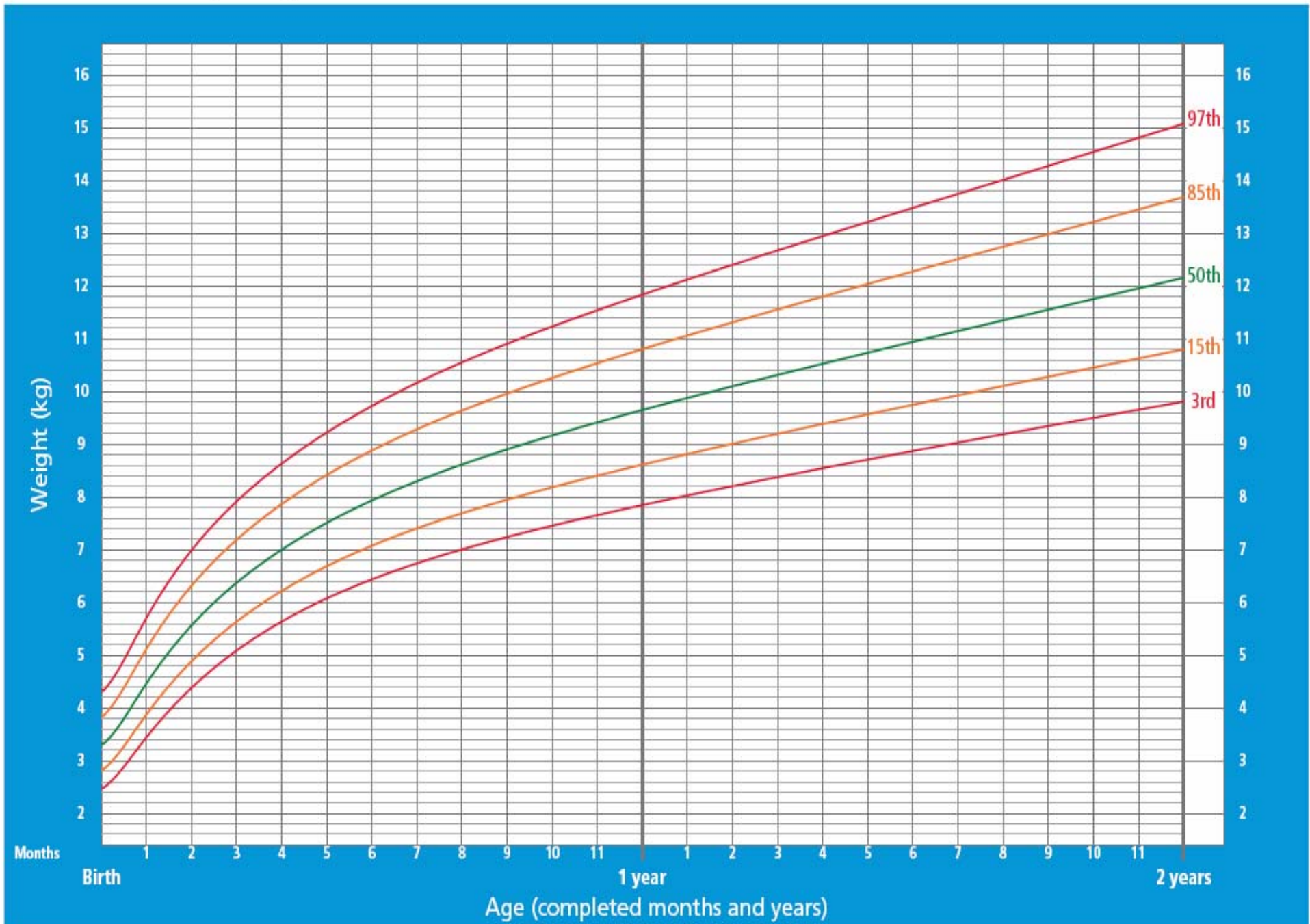
Measures of nutritional status



- Weight for age
 - Measures chronic and acute malnutrition
 - Standard growth chart
 - Express as % of the median (50th percentile)
 - Classified as
- Height for age
 - Measures chronic malnutrition
 - Standard growth chart
- Weight-for-height
 - Measures acute > chronic malnutrition
 - Corrects for normal variation in size
 - Weight for height chart

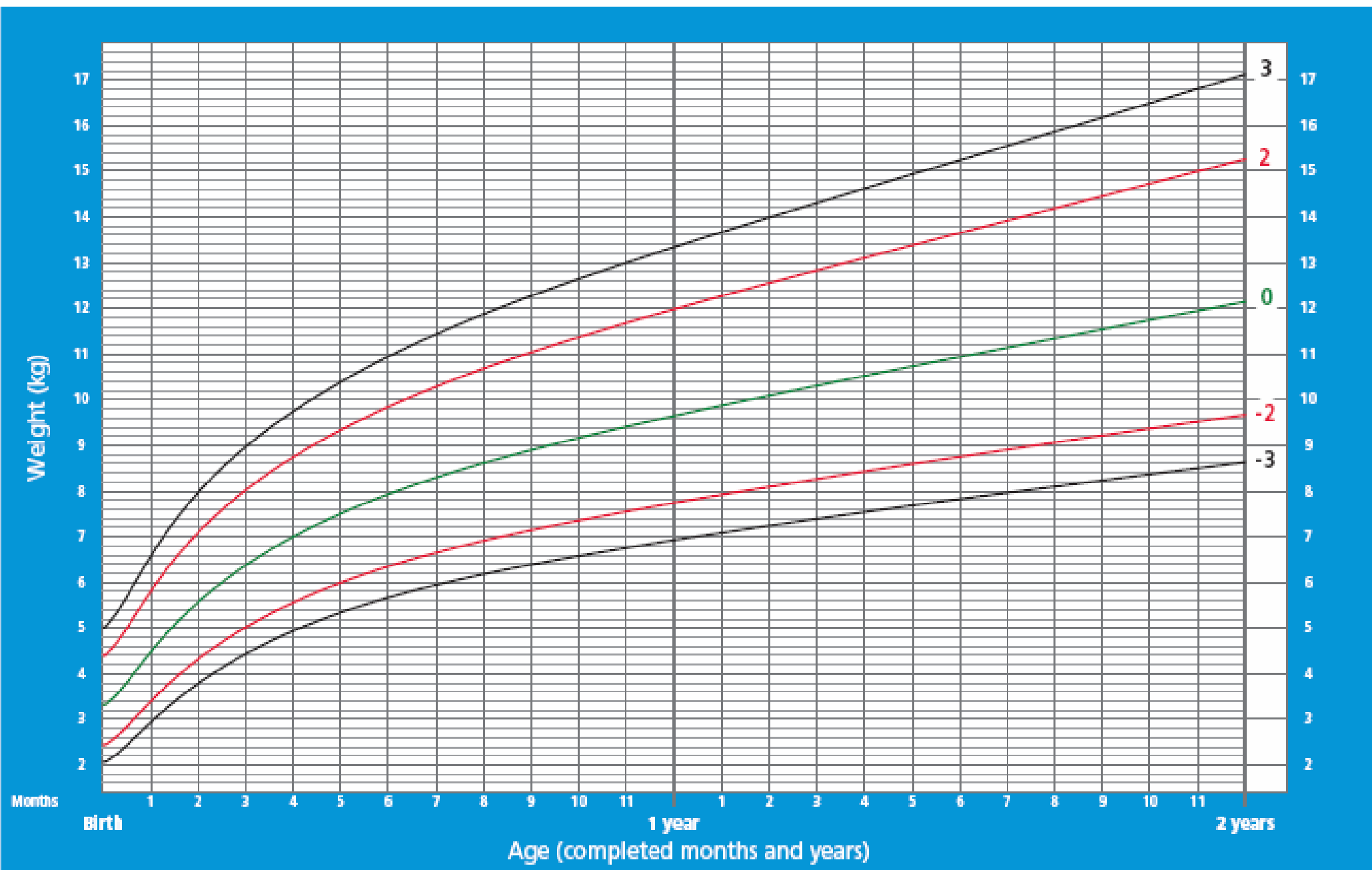
Weight-for-age BOYS

Birth to 2 years (percentiles)



Weight-for-age BOYS

Birth to 2 years (z-scores)



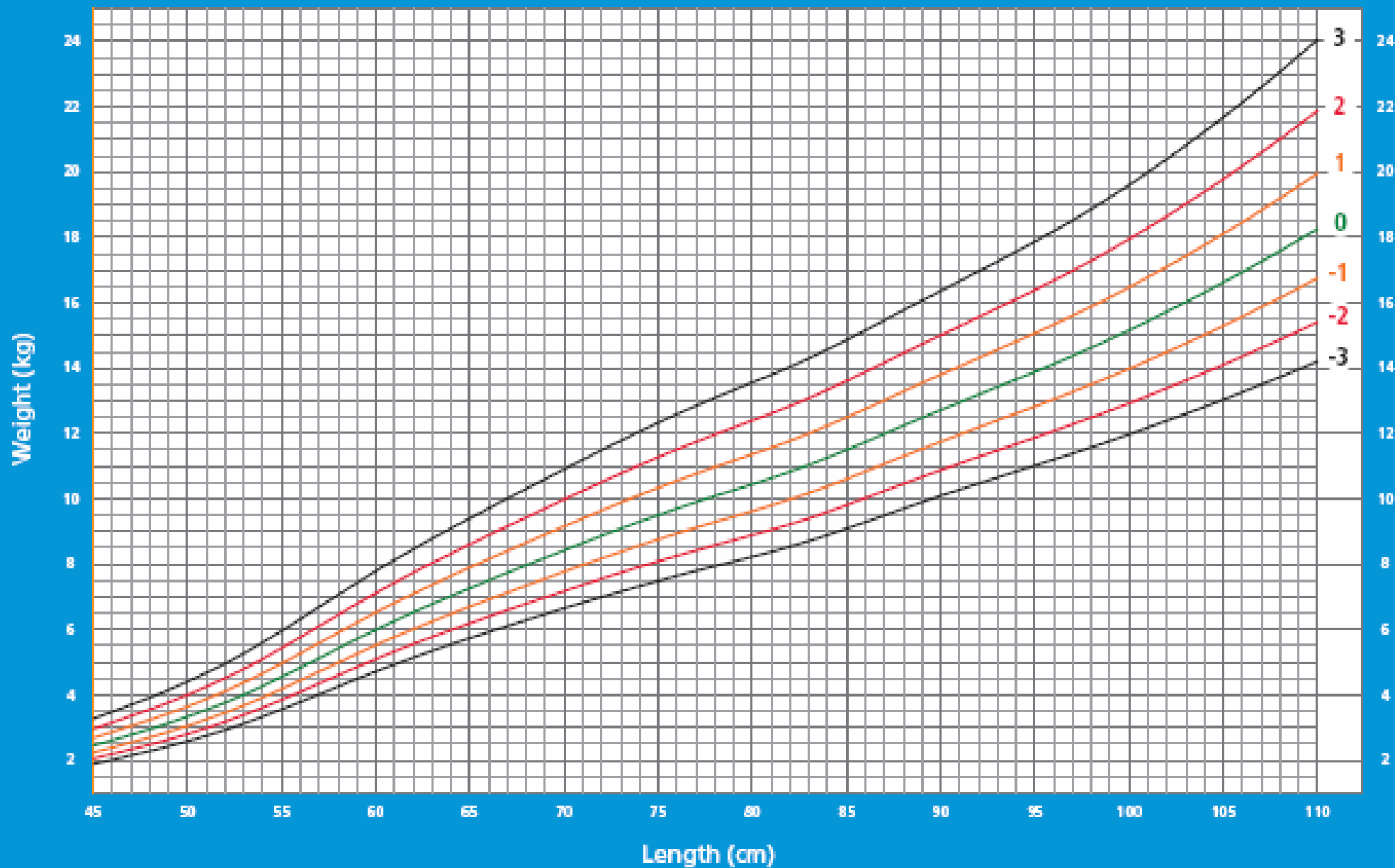
Assessing weight for length/height



- Measure length < 2 years of age and height > 2 years of age using accurate method
- Plot weight and length/height on weight-for length/height curve
- < 2 SD = moderate malnutrition
- < 3 SD = severe malnutrition

Weight-for-length BOYS

Birth to 2 years (z-scores)



Weight gain in the young infant



- Normal loss of ~10% of body weight in the first few days (due to normal diuresis)
- Regain birth weight by 7-10 days
- Thereafter gain ~25 gm/day for first 2-3 months
- Double birthweight by 6 months

Neurodevelopmental assessment



- Check for basic milestones
- Is child's development slow, arrested or regressing?
- Look for spasticity

Age (months)	Key milestones (see Baylor manual for more)
1	Fixes gaze on examiner and follows to midline Lifts head
2	Social smile Lifts chest
3	Coos (vowel sounds) Reaches for object or person
4	Laughs Rolls over
6	Sits in tripod (unsupported by 7 months) Starting to babble (consonant sounds)
9	Pulls to stand Uses pincer
12	1-2 words Takes few steps
15	Follows simple command Walks
18	Runs
24	Puts 2 words together
36	Speaking short sentences

History, systems review, and exam: Symptoms and signs of HIV in the infant



- Growth failure, chronic diarrhea
- Developmental delay
- Frequent or severe bacterial infections
 - Otitis media, pneumonia, sepsis, meningitis
- Fungal infections
 - Thrush, Candida esophagitis (refusal to feed)
 - *Pneumocystis pneumonia*
- Adenopathy, hepatosplenomegaly, parotitis, dermatitis
- Anaemia

HIV diagnostic methods



- Serologic: Detects antibody response to infection
- Virologic: Directly detects virus in cells or plasma
- Immunologic: Measure effect of virus on immune system (drop in CD4 cells)
- Clinical: Observe effects of HIV disease on patient

Infant diagnosis of HIV: serologic methods



- Rapid tests
 - Sensitive, but not completely specific
 - Positive result on second kit is specific
- ELISA: Sensitive, but not completely specific
- Western blot
 - Specific for HIV
 - Becomes indeterminate before ELISA becomes negative

Interpretation of HIV serology in infant



- Serologic tests reflect maternal serology at term
- Time course of seroreversion in exposed, uninfected infants
 - Seroreversion as early as 7 months
 - 50% seronegative by 10 months
 - 95% seronegative by 12 months
 - 100% seronegative by 15-18 months
 - *These are rough guides- depends on sensitivity of particular kit used*
- A POSITIVE result at <15-18 months indicates *HIV exposure (may or may not be infected)*
- A POSITIVE result at >18 months indicates *HIV infection*
- A NEGATIVE result at > 18 months indicates *No HIV infection*
- A NEGATIVE result <6 months indicates *no prenatal exposure*

Virologic and immunologic methods



- PCR
 - DNA: Stable sample; simpler and less expensive
 - RNA: Viral load; very slightly more sensitive
- Other virologic methods
 - P24: detects viral antigen in plasma
 - Reverse transcriptase assay
 - These methods promising but not in commercial kits and proven
- CD4
 - Most infected infants do not have low CD4
 - If CD4 < 20%, HIV infection is likely

DNA PCR for infant diagnosis



- Detects latent viral DNA integrated in host cell genome
- Detectable 2-4 weeks after infection
- Sample stable in ACD tube at room temperature with no processing for 3 days
- Has been adapted for use on dried blood spots on filter paper
 - Simple storage and shipment
 - Can be done on capillary blood
 - Sensitivity may be less than whole blood if sample taken too early

PCR sensitivity for HIV diagnosis in untreated, non-breastfed infant



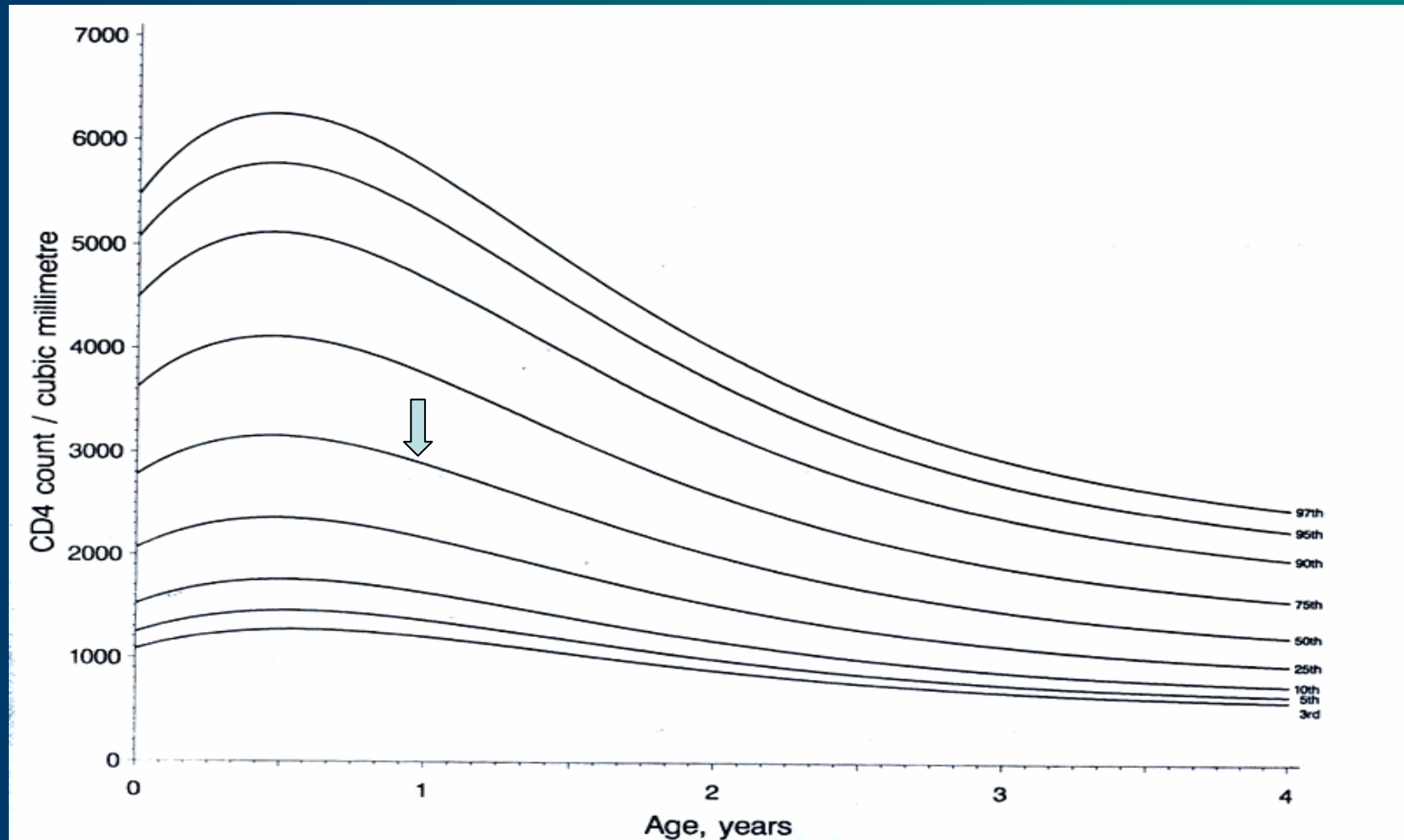
<u>Time</u>	<u>Sensitivity</u>
Birth	~30%
2 weeks	~60%
4 weeks	>95%
8 weeks	100%

HIV diagnosis and CD4 counts in infants



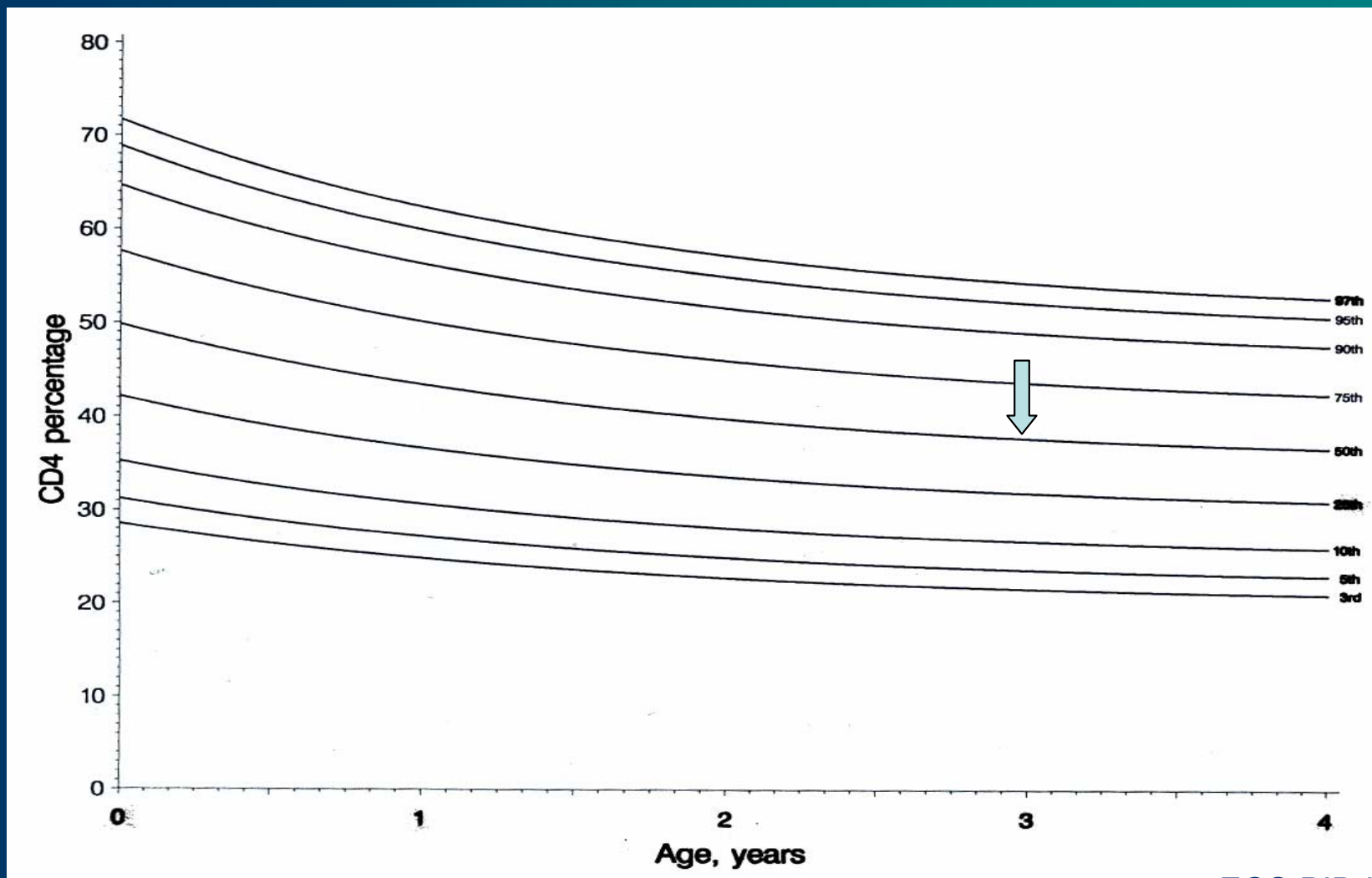
- CD4 count and percentage can be *normal* in infants with HIV, including symptomatic HIV: a normal CD4 count does *not* exclude diagnosis of HIV
- CD4 count and percentage can be affected by acute infections
- Most infants with moderate to severe symptoms have depressed CD4 counts
- CD4 < 20% of total lymphocytes is highly suggestive of HIV and *in the presence of symptoms* leads to *presumptive* diagnosis of HIV

Selected Centiles for CD4 Count by Age, Europe



ECS PIDJ 1992;11:1019

Selected Centiles for CD4% by Age, Europe



ECS PIDJ 1992;11:1021

Assessment of HIV-exposed infant (1)



- What is feeding type and is it appropriate?
 - Exclusive breast feeding
 - Exclusive substitute feeding
 - Mixed feeding
- Nutrition: Adequate, malnourished, severely malnourished?
- Are there any acute or chronic illnesses? TB, malaria, anemia, etc?
- What counseling needs are there?

Assessment of HIV-exposed child (2)



- What is HIV status?
 - HIV exposure status unknown
 - HIV exposed, status indeterminate
 - HIV exposed, status indeterminate, ongoing exposure
 - HIV exposed, presumed infected
 - HIV infected
 - HIV ruled out, no ongoing exposure

DNA PCR for HIV diagnosis* in non-breastfed infant at IHVN/ACTION sites



- Is the infant really non-breastfed?
- DNA PCR at 6-8 weeks of age
- Repeat DNA PCR at 4 months of age
- Confirm with serology at 18 months (?)
 - Often recommended, but yield low to nil and difficult to achieve

* DNA PCR was initiated in 2006 at ACTION sites but is currently available at only a few hospitals at this time

DNA PCR for HIV diagnosis* of breastfed infant at IHVN sites



- DNA PCR at 6-8 weeks
- If weaned before 7 months of age, repeat DNA PCR 6-8 weeks after weaning
- If weaned after 7 months of age, perform rapid test 6-8 weeks after weaning (at 9 months of age or greater)
 - If rapid test negative 6-8 weeks after weaning, HIV ruled out
 - If rapid test positive and age < 18 months, then do PCR
 - Perform rapid at 18 months or 6-8 weeks after weaning, whichever ever comes later

* DNA PCR was initiated in 2006 at ACTION sites but is currently available at only a few hospitals at this time

HIV diagnosis- all infants



- Confirm all positive PCRs with immediate repeat PCR
- For any infant symptomatic infant
 - Rapid test if exposure status unknown
 - Rapid test on exposed infant 9 months of age or greater
 - PCR on exposed infant < 9 months of age
- If first DNA PCR positive and repeat negative, discuss diagnostic plan with laboratory director

How does a child get HIV when mother tests negative in pregnancy?

HIV in child of seronegative mother



- Do you have DOCUMENTATION of mother's test results?
- Lab/clerical error
- Infection near term: Very high risk of transmission due to high maternal viral load
- Infection while nursing: 10% of seronegative women will get infected while nursing if partner is infected-high risk of transmission to infant
- Sexual abuse
- Other unsafe practices, unqualified "medical" treatment

Mortality of HIV in children



- In resource-rich setting in pre-HAART era
 - 25% AIDS by 1 year & 50% AIDS by 3 years
 - 50% Dead by 6-7 years
- In Africa
 - 35% Dead by 12 months
 - 52% Dead by 2 years
 - Mortality higher in congenitally infected children than in children infected later from breast milk
 - Mortality associated with maternal mortality
 - Exposed (not necessarily infected) children have higher mortality than unexposed children

Presumptive diagnosis of HIV in infant (no PCR) (WHO 2006 paediatric guidelines)



Infant seropositive
and either

Paediatric stage 4 diagnosis
or

2 or more of:

- Oral thrush
- Severe pneumonia
- Severe sepsis

Supporting evidence:

- Death or advanced HIV in mother (implies high VL)
- $CD4 < 20\%$

Infant diagnosis: Case 1



- A 6 month old infant is brought in by her grandmother
 - Mother died 4 months ago of unknown cause
 - Child weighs 4.1 kg. Alert. Decreased subcutaneous fat. Several pea-sized lymph nodes are palpable.
 - HIV rapid test is positive
 - CD4 count is 1200/ μ l (31%)
1. Based on this information, what is this child's HIV status?
 2. What is basis for your answer?
 3. What other information do you want?

Infant diagnosis: Case 2



- An 11 month old boy, whose mother is HIV-infected, is admitted to hospital for lobar pneumonia
 - PCR is not available
1. Will serology help in determining if this child has HIV infection?
 2. Is there any value to getting a CD4 count? When? How will it affect what you do?

Infant diagnosis: Case 2 (cont.)



- A rapid test for antibodies to HIV is negative
 - CD4 count cannot be done until next week
1. Has HIV infection been ruled out?
 2. Is there any other information that needs to be obtained?
 3. Does any other HIV testing need to be done?
If so, what?

Infant diagnosis: Case 3



- 4 month old infant presents with severe pneumonia. There is extensive thrush and hepatosplenomegaly
 - Rapid test for antibodies to HIV is positive
 - CD4 = 800 (24%)
1. Does this infant have HIV infection?
 2. How confident are you of this diagnosis?
 3. What additional testing will you do?

Co-trimoxazole (TMP-SMX, Septrin) prophylaxis in HIV-exposed child



- Very effective for prevention of *Pneumocystis jiroveci* pneumonia (PCP)
 - PCP common in infants, even with *normal* CD4 count (>1500 at < 6 months) or CD4 750-1500 at 6-12 months (mildly suppressed)
- Prophylaxis against *P. falciparum* malaria
- Prevents bacterial infections (efficacy may depend on local sensitivities)
- Reduces mortality by 1/3 in *symptomatic* Zambian children over 12 months with HIV infection
 - Effect on mortality in *exposed infants* not known

Counseling needs of the family with an HIV-exposed infant



- Nutrition counseling of breastfeeding infant
 - Is BF exclusive?
 - Are there difficulties?
 - Are complementary feeds needed (i.e. after 6 months)?
 - Is BF still AFASS, or can infant be weaned and given BMS safely?
- Nutrition counseling of substitute fed infant
 - Obtaining, preparing, storing, giving appropriate BMS
- Diagnostic counseling: what is infant's status?
- Adherence counseling
 - Purpose of follow up visits
 - Adherence to prophylaxis
- Family counseling
 - Is mother in HIV care?
 - Has father been tested?
 - Have all siblings been tested?

Immunizations in HIV-exposed infant



- All national EPI immunizations should be given
- BCG
 - Risk of local adenitis or disseminated disease
 - Benefit outweighs risk in TB-endemic area
 - Can be treated with anti-TB drugs
- DTP, Hepatitis B: Give as usual
- OPV
 - Theoretical increased risk of vaccine polio
 - Until polio eradicated from Africa, benefit outweighs risk
- Measles
 - May withhold vaccine if advanced HIV disease and measles not active in community

Age, CD4 count, and PCP risk in children

