Module 2: Diagnosis and Staging of HIV Disease

Session 1: Clinical Evaluation for Paediatric HIV Infection

Total Session Time: 1 hour 15 minutes

Learning Objectives

By the end of this session, participants will be able to:
- Describe aspects of a comprehensive history
- Describe principles of a thorough physical examination
- Describe the signs and symptoms/conditions associated with HIV and AIDS in children
- Explain a presumptive diagnosis of HIV infection in children under 18 months

Aspects of a Comprehensive History

Common Clinical Features of Acute Seroconversion Illness
Clinical features of acute seroconversion illness include:
- Fever and sweating
- General tiredness
- Headache
- Cough or sore throat (pharyngitis)
- Enlarged lymph nodes (generalised lymphadenopathy)
- Nausea, vomiting or diarrhoea
- A measles-like rash
- Oral or genital ulcers
- Muscle or joint pains

NOTE that: these symptoms and signs are similar to those found in glandular fever (infectious mononucleosis).

Clinical Evaluation of HIV-Infected Children
Major components of clinical evaluation of HIV infection in children:
- History taking
- Nutritional evaluation
- Developmental assessment
- Physical examination
- Presumptive diagnosis of severe HIV disease

The principle of assessment is the same as other children. A thorough assessment will enable a health care worker to determine disease progression. There will be monitoring of CD4 as per national guideline. The history of the mother's HIV status is important, as is that of other siblings and the father.

Importance of History
Good history leads to trust and rapport, and also to the determination of the best management of the patient's condition, such as:

- Develop clinical profile, including birth history for children;
  - Start ART as per national guideline
- Identify changes in health status since last visit:
  - Assess response to treatment
  - Assess disease progression
- Identify changes in home setting that may affect child's health;
  - Adherence to care and medication regimens
- Identify children at a higher risk of rapid progression
- Identify children at high risk of HIV infection (exposed)
- Identify secondary complications that may impact HIV care and treatment
- Birth History will reveal:
  - Maternal Health Status (CD4, WHO stage)
  - Maternal ART
  - Mode of Delivery
  - Birth weight
  - Neonatal complications
  - Infant ART

The three ways that child can become infected with HIV (during pregnancy, during labor and delivery and during breast feeding).

*Refer to **Handout 2.1.1: History Taking** on **page 57** for more input.*

Past Medical History
Enquire about:

- Prior hospitalizations and surgeries
- HIV-related illness e.g. TB in the past
- Prior HIV tests and result
- Past medications

Follow-up Visit History

- New health problems such as signs & symptoms. *Newly diagnosed children* may require a more comprehensive evaluation upon entry into the program compared with those known since birth. These symptoms should be recorded and all diagnoses should be elicited and noted.
- HIV-related illness
- Diet and nutrition
- Medications:
  - Dosing
  - Frequency
  - Adherence
- Disclosure Status;
  - Encourage disclosure from 5–7 yrs

Information regarding past and current medications, allergies and use of vitamins and other supplements should be obtained. HIV infected children tends to have recurrent infection requiring medical attention.

Routine Growth, Developmental and Nutritional Evaluation
Dietary recall can also help identify those individuals who are making poor food choices, and can serve as an opportunity to discuss more healthy options, for example:

- At every visit:
  - Enquire about diet/feeding history: Any child who is not thriving needs extensive nutritional history including assessment of food security
  - Take anthropometric measurements and examine child
  - Assess developmental milestone
- Use growth curves to monitor growth pattern
- Assess school performance and attendance: Questions about school attendance and performance for older children is important to assess the psychosocial status.

Definitions
Growth: Means increase in size e.g. weight, height.

Development: Describes the acquisition of milestones and new skills. Development is an acquisition of new skills, includes all aspects of human emotional, intellectual, social, perceptual, and personality development.

I**mportance of Using Growth Curves**
The importance of using growth curve in monitoring growth pattern includes:

- Easy and systematic way to follow changes in growth over time for an individual child
- Weight, height/length and head circumference should be plotted at every visit;
  - Head circumference is a good indicator of brain development in children below 2 years of age

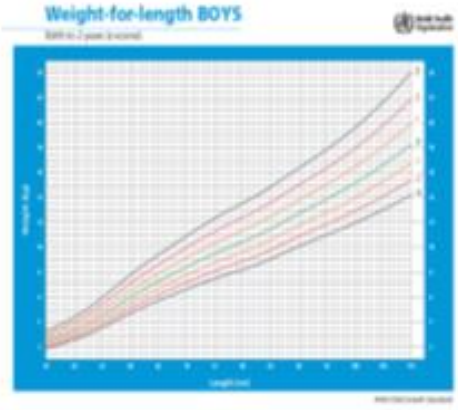
Interpretation of Growth Curves
There are different standard charts for boys and girls. There are charts for: weight for age; height or length for age; and head circumference.

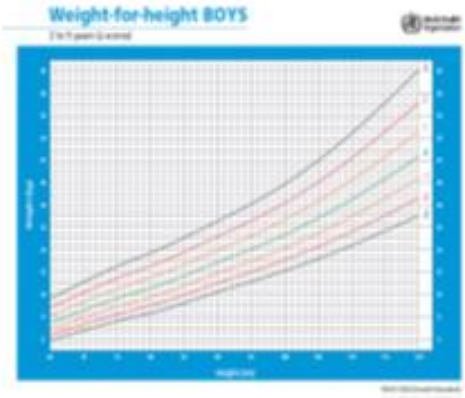
- Measure and weigh a child using same methodology at each visit
- Use age and sex appropriate charts
- Plot measurement (weight, height, head circumference) on the vertical axis against age on the horizontal axis
- Compare growth point with previous points
- Assess growth percentile

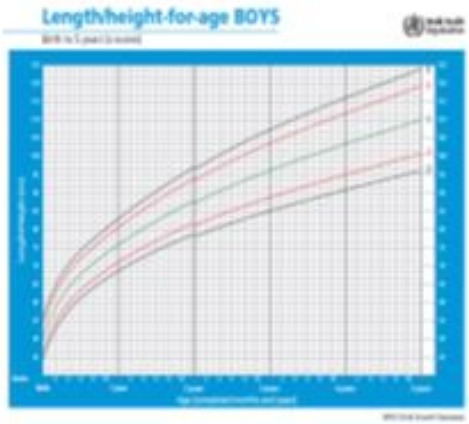
*Refer to **Handout 2.1.2: WHO Growth Curves** on **page 59**.*

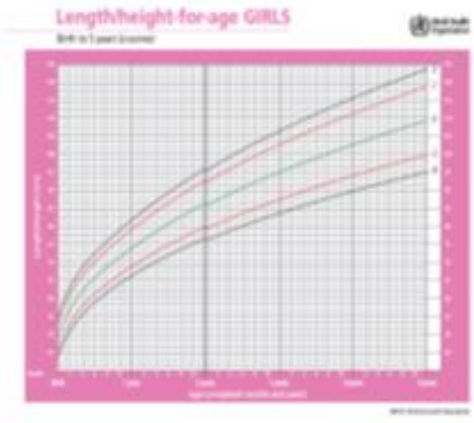
WHO Growth Charts
The WHO Global Database on Child Growth and Malnutrition uses a Z-score cut-off point of <-2 SD to classify low weight-for-age, low height-for-age and low weight-for-height as Moderate malnutrition, and <-3 SD to define severe malnutrition. The cut-off point of >+2 SD classifies high weight-for-age and high weight-for-height as overweight in children.

The following are examples of the new WHO growth charts.

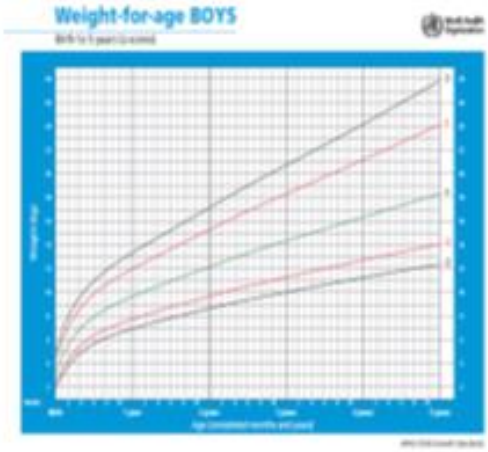




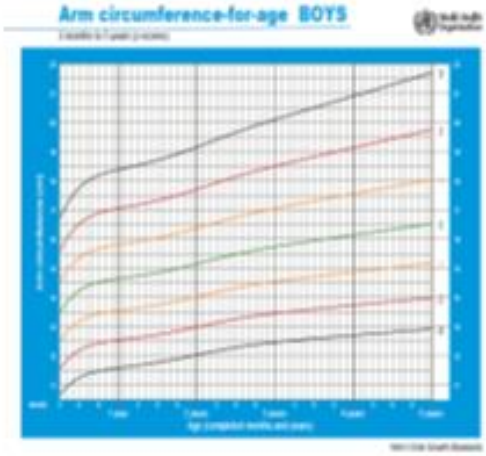




NOTE: This chart above indicates length/height-for age denotes stunting if below -1SD.

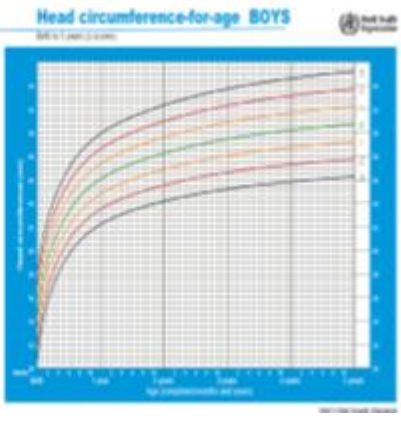


The weight for age denotes underweight if below-1SD in this chart above.

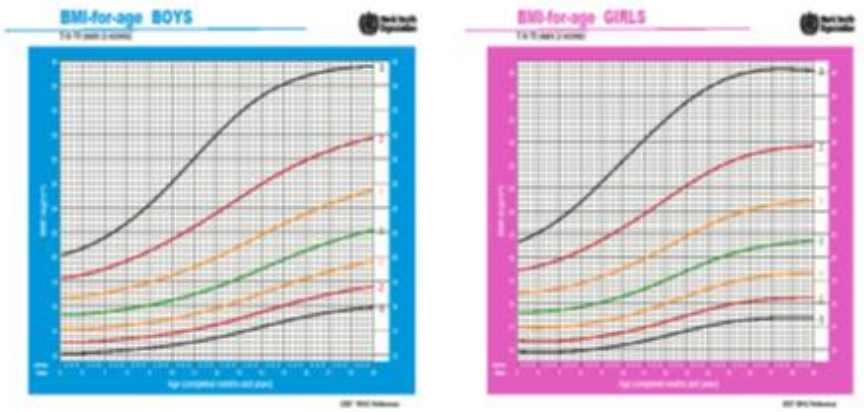


Interpretation of Mid-Upper Arm Circumference (MUAC) indicators for children aged 6 months up to 5 years is as follows:

- MUAC less than 115 mm (11.5cm) indicates Severe Wasting. The child should be immediately referred for treatment.
- MUAC of between 115 mm (11.5cm) and 125mm (12.5cm) indicates Moderate Wasting. The child should be immediately referred for supplementation.
- MUAC of above 125mm (12.5cm) is normal.



These are the WHO head circumference charts. They are for children 0-5 years. Head circumference should be measured until 2 years of age. Occipito-frontal circumference is measured as the maximum circumference of the head to the nearest 0.1 cm with a non-elastic, flexible, measuring tape passing above the supra-orbital ridges and over the maximum occipital prominence.

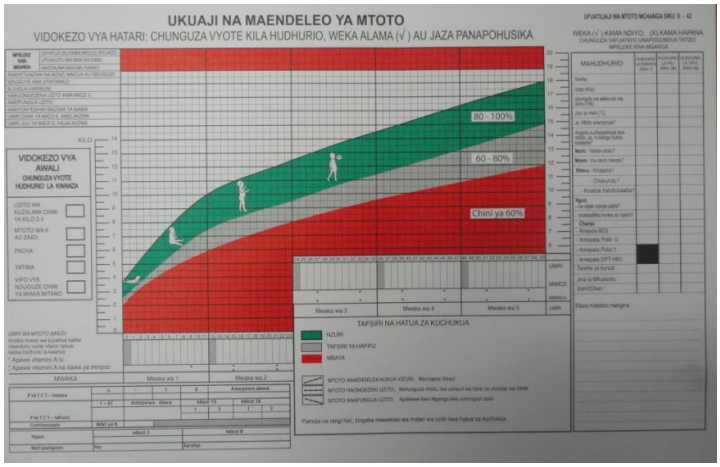


Body mass index (BMI) is a measure of body fat based on height and weight that applies to adult men and women including adolescents. BMI is calculated from the person's weight in kilograms divided by the square of height in meters (Weight (kg) / Height $(m)^2$).
A high BMI can be an indicator of high body fatness. BMI can be used to screen for weight categories that may lead to health problems but it is not diagnostic of the body fatness or health of an individual.

BMI is not accurate enough to be used as a diagnostic tool. However, it is used as a screening tool to identify potential weight problems.

BMI categories include:
- Below 18.5–Underweight
- 18.5-24.9 Healthy
- 25.0-29.9 Overweight
- 30.0 and above Obese

RCH Card No. 1



The RCH card 1 shows weight for age and interpretation has been made easy through colour coding. The card has a lot of other important information such as early neonatal period, HIV status, immunization.

Failure-to-Thrive
It is important to try to assess the reason for failure to grow: intake, vs absorption or losses. Failure to sustain a normal velocity of weight and/or height growth over three subsequent months; this can be quantified using growth curves, often is the most sensitive and reliable measure of disease progression in a child with HIV infection.

Growth can sometimes reflect serious underlying problems and, if unresolved, may result in stunted growth and delayed development. Thus, it is important that all children with slow growth are identified and given support. Growth faltering is not a 'syndrome' or a specific disease, but simply an observation that a child is growing exceptionally slowly.

Developmental Assessment
This is an assessment of the child's development should be done at every visit;
- Take note if the child's behavior is appropriate for the age

Delayed acquisition of developmental milestones or loss of previously acquired skills can be the first sign of HIV encephalopathy.

Can be done through observation during the physical exam and by asking the parent focusing on four domains:
- Cognitive
- Motor
- Language
- Social

An assessment of school performance can be done for older children

*Refer to **Handout 2.1.3: Developmental Assessment** on **page 65** for more input*

Physical Examination
Perform thorough physical examination:
- Initial exam should be comprehensive, both general and systemic examination
- Identify any HIV related physical findings

NOTE that: ALWAYS REMEMBER TO APPLY ETAT

*Refer to **Handout 2.1.4: Physical Examination** on **page 67** for more input.*

Clinical Signs & Conditions Suggestive of HIV Infection in Children & Presumptive Diagnosis of HIV Infection in Children under 18 Months

Clinical Signs & Conditions Suggestive of HIV Infection in Children
AIDS defining conditions are clinical conditions which only occur in children who have a severely damaged immune system due to HIV infection. AIDS defining infections include

conditions which are rare in HIV negative children, such as oesophageal candidiasis and Pneumocystis pneumonia.

The term 'AIDS defining conditions include:
- Unexplained wasting
- Stunting or severe malnutrition
- HIV encephalopathy
- Non-Hodgkin's lymphoma
- Other conditions specific to HIV infection

Conditions specific to HIV infection:
- Pneumocystis pneumonia
- Oesophageal candidiasis
- Extrapulmonary cryptococcosis
- Invasive salmonella infection
- Lymphoid interstitial pneumonitis (LIP)
- Herpes zoster with multi-dermatomal involvement
- Kaposi's sarcoma
- Lymphoma
- Progressive Multifocal Leucoencephalopathy (PML)

Common in HIV infected, but uncommon in HIV uninfected children:
- Recurrent severe bacterial infection
- Persistent or recurrent oral thrush
- Bilateral parotid enlargement
- Generalized lymphadenopathy
- Hepatosplenomegaly (non-malaria areas)
- Persistent or recurrent fever
- Neurological dysfunction
- Herpes zoster of single dermatome
- Persistent generalized dermatitis

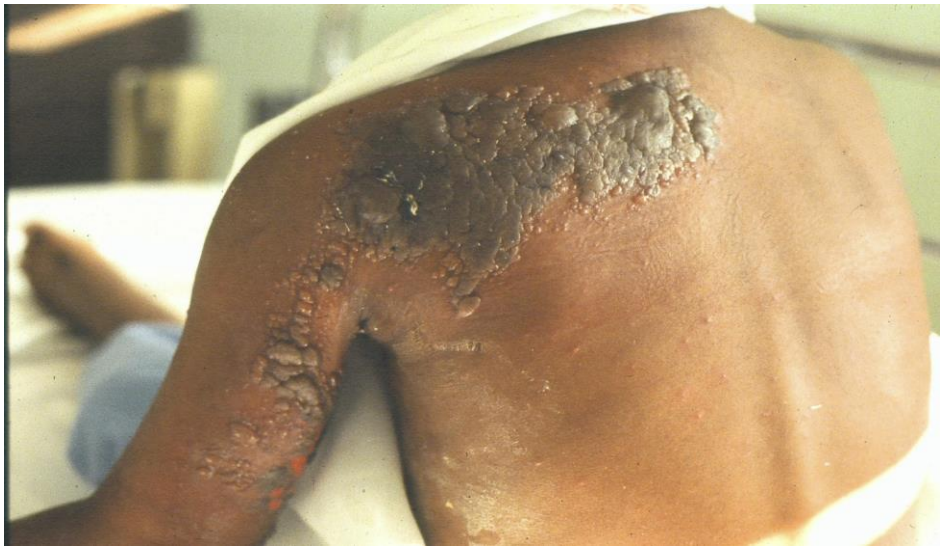
HIV associated infections may be caused by a wide range of organisms such as bacteria, viruses, fungi or protozoa. Many of these infections occur with severe immunosuppression.

The first clinical sign to suggest that a child has a weakened immune system is often the appearance of an HIV associated infection.

Common in both HIV positive and HIV negative children:
- Otitis media - persistent or recurrent
- Diarrhoea – persistent or recurrent
- Severe pneumonia
- Tuberculosis
- Bronchiectasis
- Failure to thrive
- Marasmus

HIV associated infections do not always indicate that the patient is HIV infected. They may also be found in HIV negative children. These infections, however, should always alert one to the fact that the child may be HIV infected. HIV associated infections are therefore an important indicator for HIV screening.

Varicella Zoster



This is an eleven year old with severe advanced HIV showing Herpes/Varicella zoster infection of single dermatome. However, multiple dermatomes may become involved, a condition very specific to HIV in children.

Activity on Presumptive Diagnosis

Refer to ***Worksheet 2.1.1: Presumptive Diagnosis Case Study*** *on* ***page 69*** *for more case studies about the presumptive diagnosis*

Presumptive Diagnosis of Severe HIV Disease

A presumptive diagnosis of severe HIV disease in children under 18 months should be made if:

- The child is confirmed as being HIV antibody-positive AND
- A diagnosis of any AIDS-defining condition(s) can be made OR
- The child is symptomatic with two or more of the following, oral thrush, Severe pneumonia, and severe sepsis.

In accordance with WHO Integrated Management of Childhood Illness guidelines:

- Oral thrush: Creamy white soft small plaques on red or normally coloured mucosa which can often be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender.
- Severe pneumonia: Cough or difficult breathing in a child with chest indrawing, or any of the general danger signs outlined in the WHO Integrated Management of Childhood Illness guidelines: that is lethargic or unconscious, not able to drink or breastfeed, vomiting and presence or history of convulsions during current illness,.
- Severe sepsis: Fever or low body temperature in a young infant with any severe sign, such as rapid breathing, chest indrawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast-milk, convulsions, stiff neck.

Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive child under 18 months include:

- Recent HIV-related maternal death or
- Advanced maternal HIV disease
- Child's CD4 percent <25%

Confirm the diagnosis of HIV infection as soon as possible.

AIDS indicator conditions include some but not all HIV clinical stage 4 conditions seen in children such as Pneumocystis pneumonia, oesophageal candidiasis, cryptococcal meningitis, cerebral toxoplasmosis, unexplained wasting or malnutrition.

Where ART has been initiated on the basis of the presumptive diagnosis of severe HIV disease, efforts should be made to confirm the HIV infection as soon as possible using confirmatory lab tests for viral antigen, if not possible then the latest with HIV antibody testing at 18 months of age. Decisions on further treatment should be adjusted at that time according to clinical staging and immunologic criteria where available.

Key Points

- A comprehensive history and thorough physical examination are fundamental for a quality pediatric HIV care
- Familiarity with common signs, symptoms/ conditions associated with HIV & AIDS in children can enable an early diagnosis and save lives
- In children < 18 months, a presumptive diagnosis of HIV infection can enable early treatment in settings where laboratory confirmation is not possible

Handout 2.1.1: History Taking

***Birth weight*:** Babies with HIV in-utero are likely to be born with low birth weight. Having low birth weight is a risk for HIV infection.

Mode of delivery: Babies born by caesarean section to mothers who are HIV positive have a lower risk of HIV than those delivered vaginally especially when maternal viral load exceeds 1000 copies per ml. Instrumental delivery, early rupture of membranes (>4 hours) are all risk factors for HIV infection. All these can be ascertained by taking a detailed history and looking at the patients medical records.

Maternal health status at the time of conception or delivery is a serious indicator of likelihood of HIV infection. Ask the mother about opportunistic infections around the time of delivery.

It is also important to ask the mother or caretaker about use of ART in pregnancy (PMTCT option B+) or prophylactic ARVs to exposed infants.

Infants who are infected during pregnancy and those who develop symptoms early are likely to progress rapidly. However, not all children are at the same risk of disease progression. Many of the factors associated with transmission are also associated with risk of disease progression.

Children born to sicker moms are more likely to be sick. Some virus strains are more virulent. HLA factors may also influence disease progression. Use of PCP prophylaxis and early intervention with ART will also influence measured disease progression.

The other important part of the history is the report of medication adherence. Children are likely to be receiving a number of medications including prophylaxis, ARVs, vitamins and treatments for intercurrent illnesses. Providers should routinely ask about adherence to medication and barriers to adherence. This should be part of the routine history each time the child is evaluated.

Focus on particular barriers that may be encountered by the child compared with the adult e.g. palatability. Also, remember that most children will also be taking meds other than ARVs.

The importance of disclosing the HIV infection when the child is able to understand by using language and concepts appropriate to the child's age and developmental stage should be emphasized at each follow-up visit.

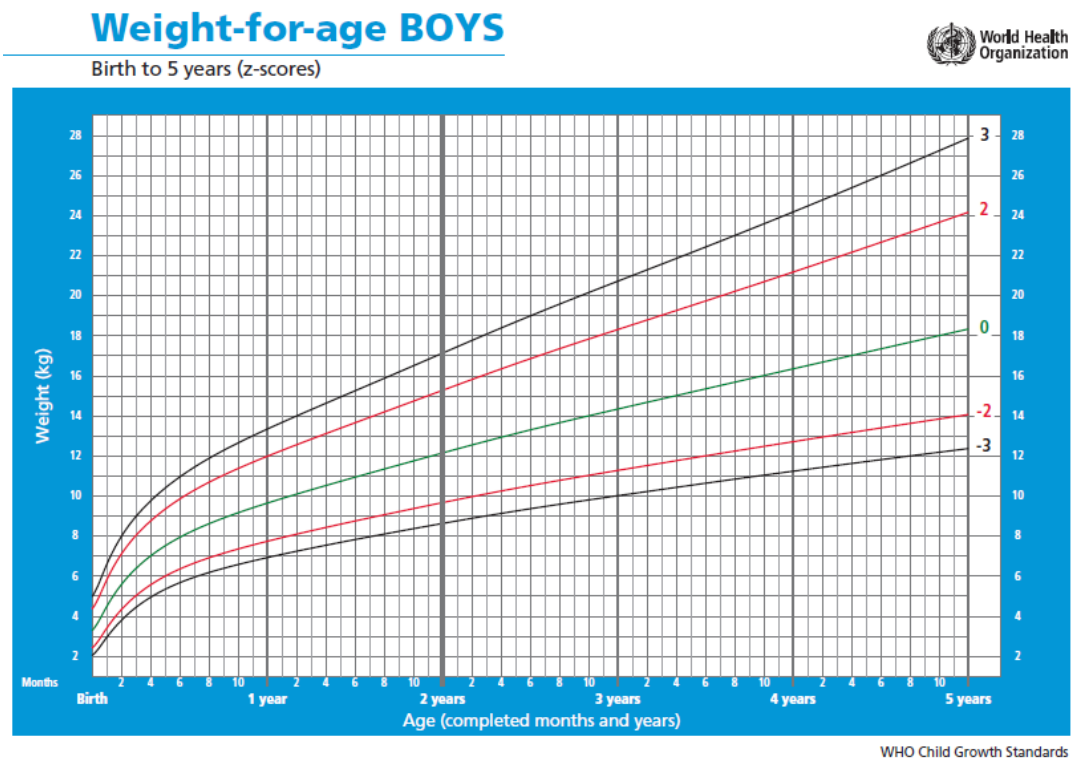
It is essential to collect as much information as possible about their disease course to determine their clinical stage of illness and disability. Also, children with established disease may require a more comprehensive evaluation upon entry into the program compared with those known since birth.

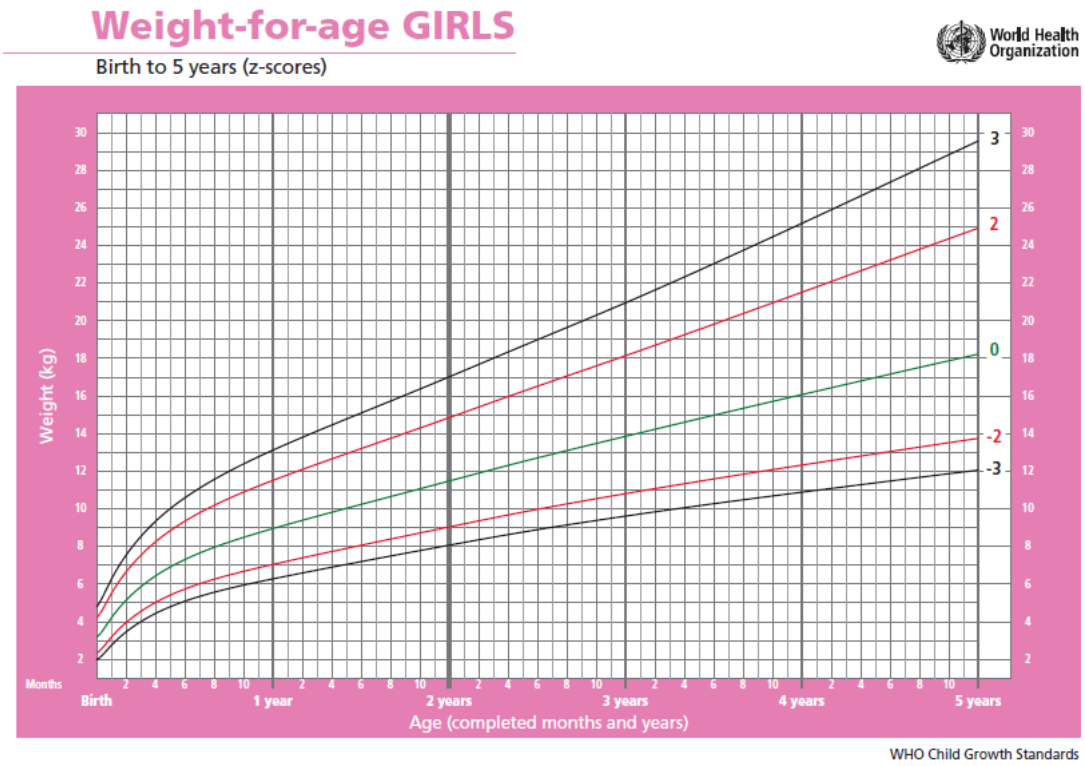
Accurate history of the patient should be obtained at each visit. Information regarding past hospitalization, current medications, allergies and use of vitamins and other supplements should be obtained. Questions about school attendance and performance for older children are important to assess the psychosocial status.

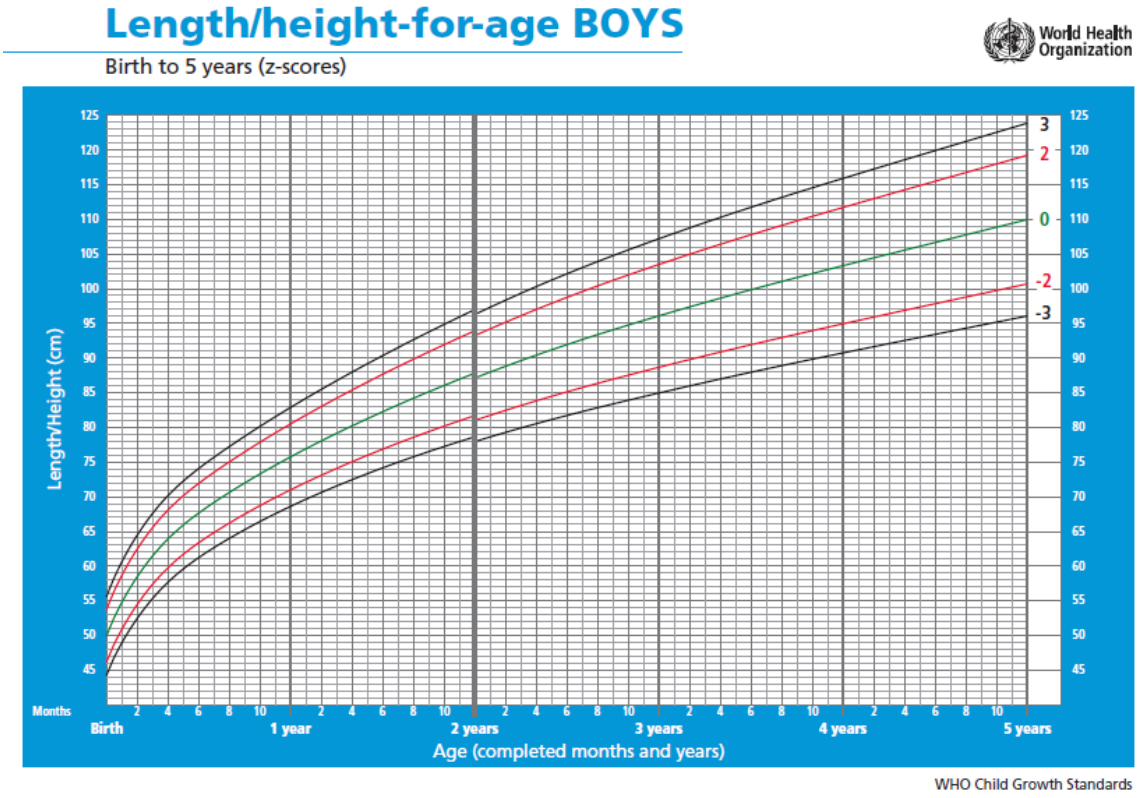
Example of a follow up Check list:

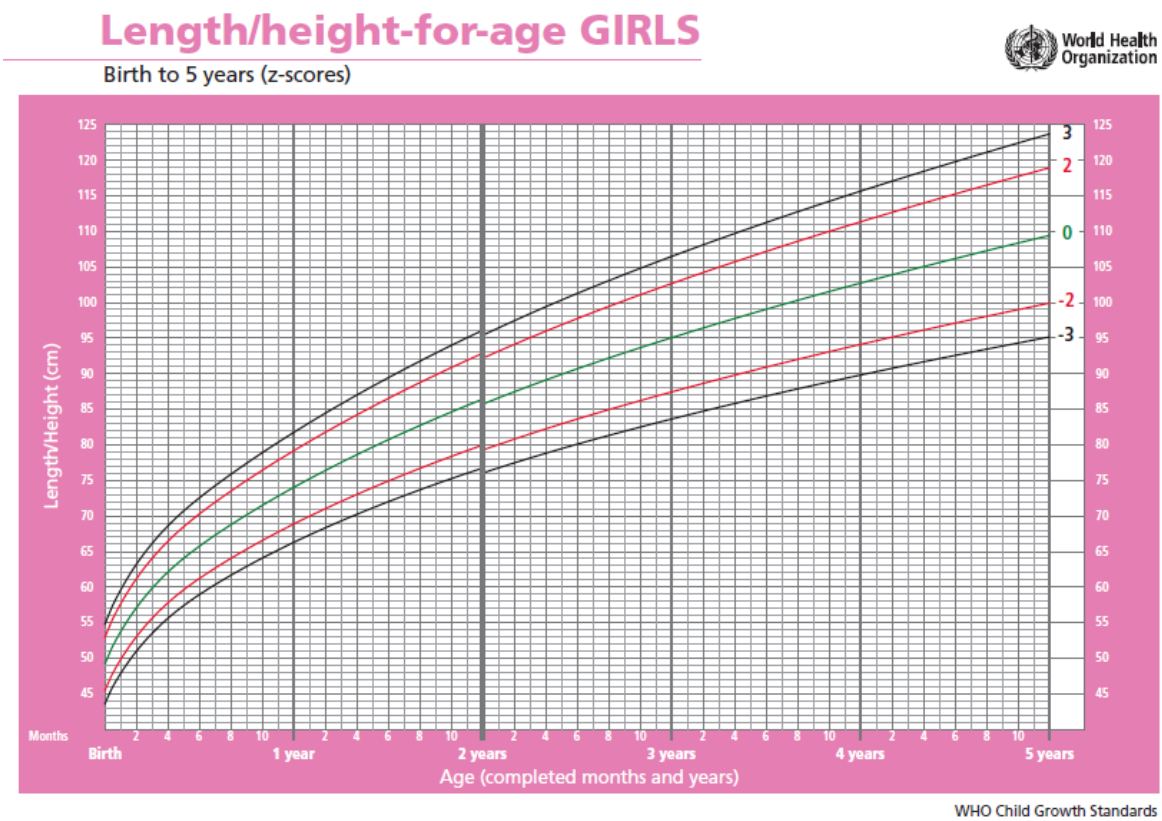
Signs & Symptoms Checklist				
Sign or Symptom	**Yes / No**		**Sign or Symptom**	**Yes / No**
Cough			Pain – muscles	
Mood Changes			Pain – legs/feet	
Diarrhoea			Pain – other Specify: _____	
Difficulty breathing, shortness of breath			Poor Appetite	
Fatigue			Rash	
Fever			Thrush	
Headache			Visual problems (new)	
Memory Problems			Weakness	
Nausea and/or vomiting			Weight loss, failure to thrive	
Night sweats			Other 1 - Specify: _____	
Numbness or tingling in legs and/or feet			Other 2 - Specify: _____	
Pain – abdominal			Other 3 - Specify: _____	

Handout 2.1.2: WHO Growth Charts



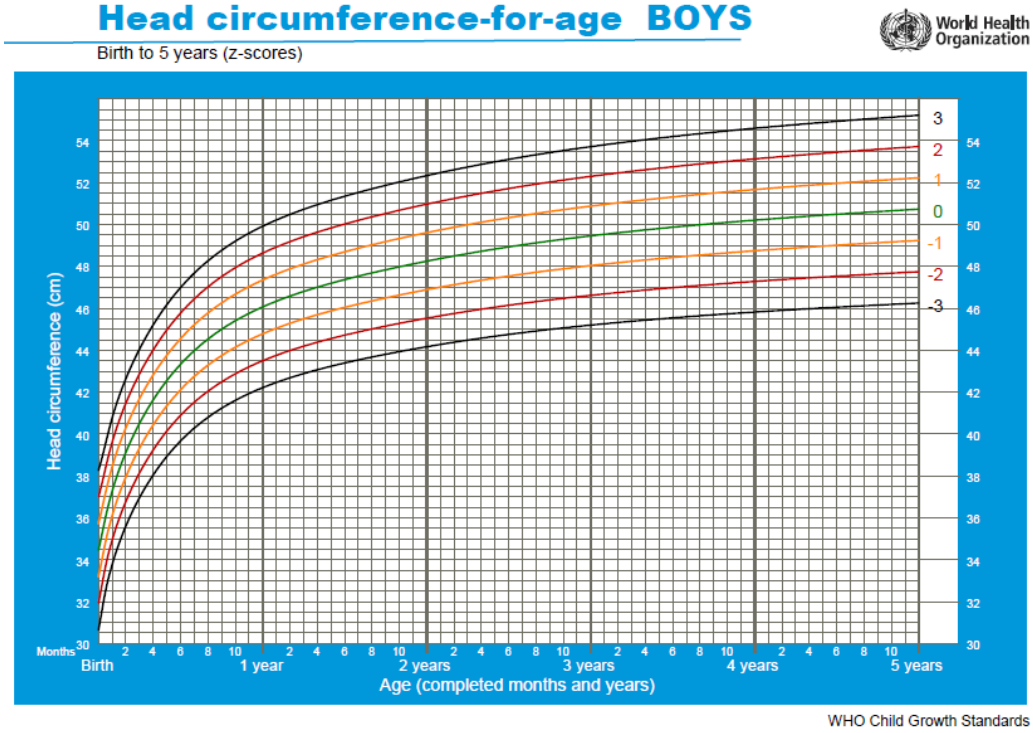


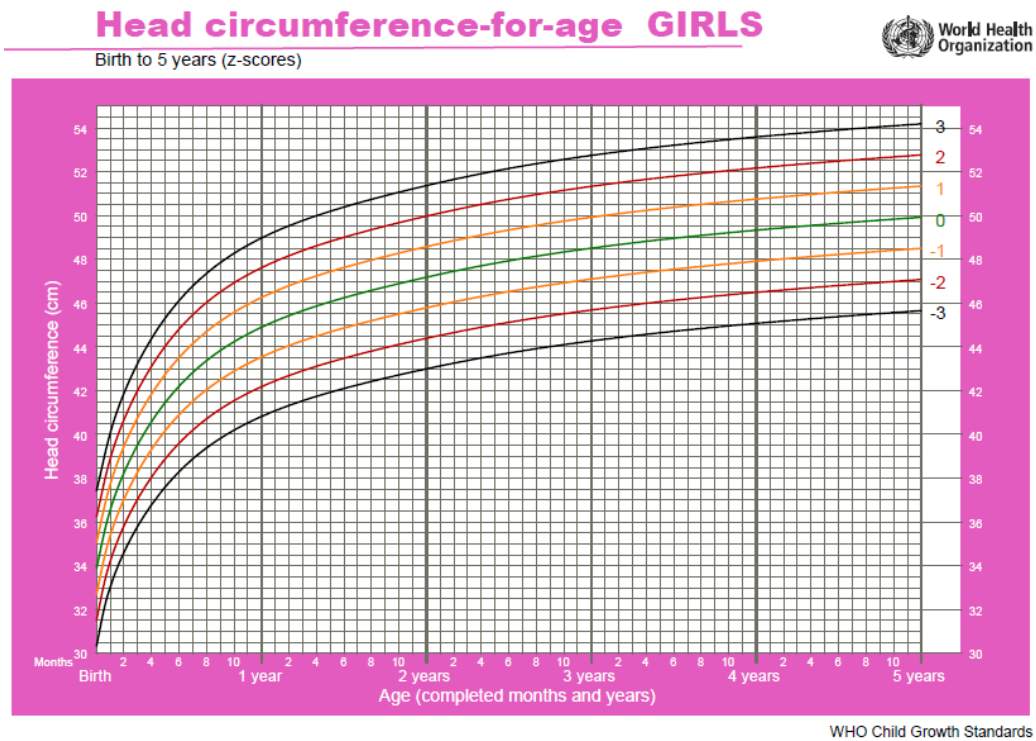


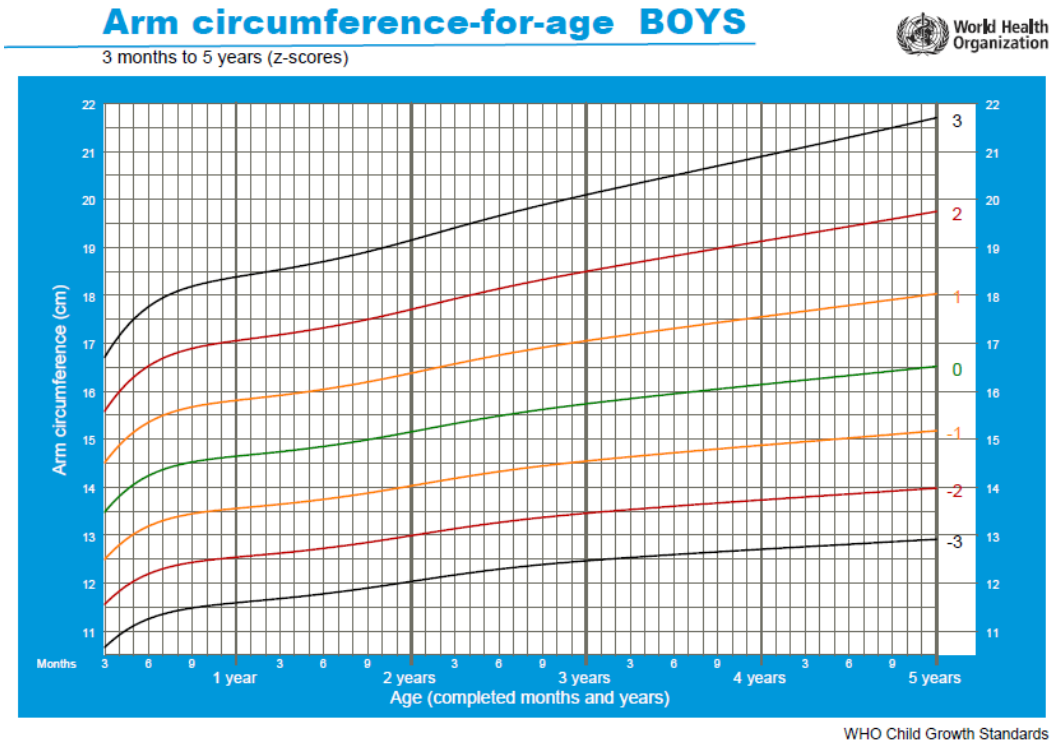


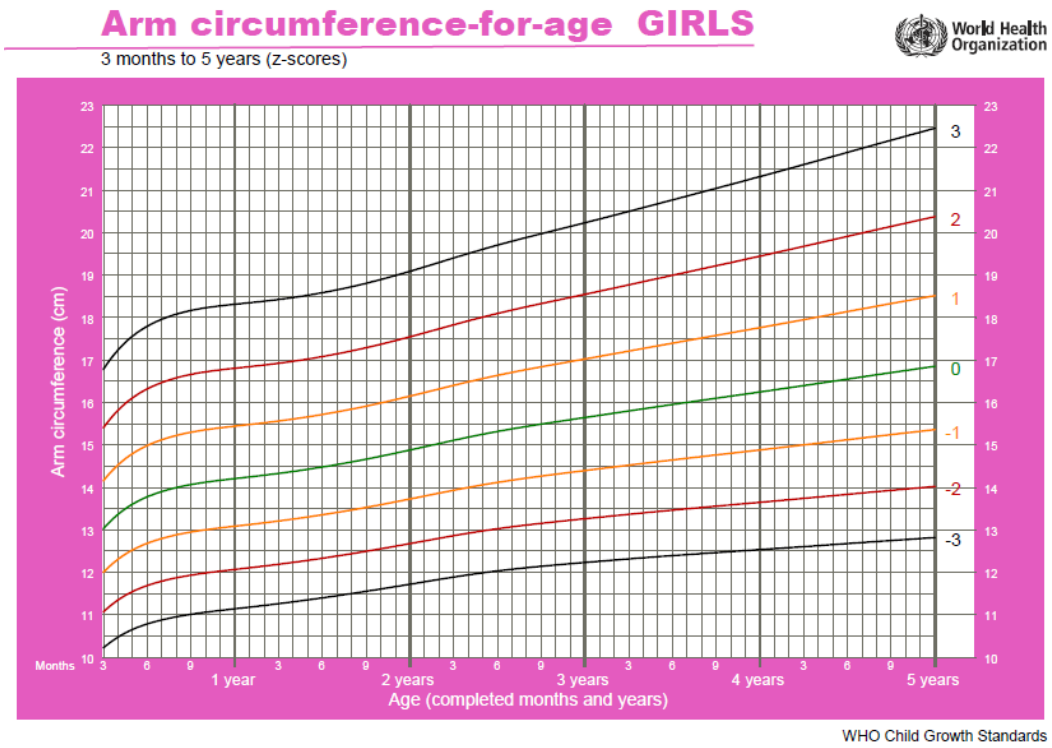
The curved lines on the growth chart show selected percentiles that indicate the rank of the child's measurement. The 95th percentile (or 3 SD) line for weight for-Age, it means that only 5 of 100 children (5%) of the same age and gender in the reference population have a

higher weight for-Age. If the percentile rank indicates a nutrition-related health concern, additional monitoring and assessment are recommended.









During routine screening, health care providers assess physical growth using the child's weight, length or height and head circumference. When plotted correctly, a series of accurate weights and measurements offer important information about a child's growth pattern.

Step 1: Obtain accurate weights and measures using standard methods and equipment.

Step 2: Select the appropriate growth chart to use based on the age and gender of the child.

Step 3: Plot measurements for the current visit on the appropriate growth chart.

- *When plotting weight-for age, find the age on the horizontal axis. Use a straight edge or right-angle ruler to draw a vertical line up from that point.*
- *Find the appropriate measurement (weight, length or head circumference on the vertical axis. Use a straight edge or right-angle ruler to draw a horizontal line across from that point until it intersects the vertical line. Make a small dot where the two lines intersect.*

Step 4: Interpret the plotted measurements

- *Determine the percentile rank and determine if it suggests that the anthropometric index is indicative of nutritional risk based on the percentile cutoff value.*
- *Compare today's percentile rank with the rank from previous visits to identify any major shifts in the child's growth pattern and the need for further assessment.*

The Z-score or standard deviation classification system

There are three different systems by which a child or a group of children can be compared to the reference population: Z-scores (standard deviation scores), percentiles, and percent of median. For population-based assessment—including surveys and nutritional surveillance—the Z-score is widely recognized as the best system for analysis and presentation of anthropometric data because of its advantages compared to the other methods.

The Z-score system expresses the anthropometric value as a number of standard deviations or Z-scores below or above the reference mean or median value. A fixed Z-score interval implies a fixed height or weight difference for children of a given age. The formula for calculating the Z-score is:

Z-score (or SD-score) = (observed value - median value of the reference population) / standard deviation value of reference population

$$\text{Z-score (or SD-score)} = \frac{\text{(observed value-median value of the reference population)}}{\text{standard deviation value of reference population}}$$

For consistency with clinical screening, prevalence-based data are commonly reported using a cut-off value, often <-2 and >+2 Z-scores. The rationale for this is the statistical definition of the central 95% of a distribution as the "normal" range, which is not necessarily based on the optimal point for predicting functional outcomes.

The WHO Global Database on Child Growth and Malnutrition uses a Z-score cut-off point of <-2 SD to classify low weight-for-age, low height-for-age and low weight-for-height as moderate and severe undernutrition, and <-3 SD to define severe undernutrition. The cut-off point of >+2 SD classifies high weight-for-age and high weight-for-height as overweight in children.

Reference: *Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. WHO Technical Report Series No. 854. Geneva: World Health Organization, 1995.*

Handout 2.1.3: Developmental Assessment

One of the first and most important clinical features of symptomatic HIV infection in children is a delay in developmental milestones. Children with advanced HIV disease may also have a slowing of head growth (head circumference).

While examining the baby it is important to notice whether the child's behavior is appropriate for the age.

Cognitive Development
Refers to development in the way a baby thinks. This includes his language, communication and exploration skills. Examples of cognitive activities include learning to talk, interacting with toys, identifying faces and socializing with other people. Infant's cognitive growth is stimulated by specific activities practiced on a regular basis.

Motor Development
There are two types of motor development:

- Gross motor development: development of skills using large movements that involve the whole body e.g. walking
- Fine motor development: development of skills involving the hands and fingers and using smaller, more precise movements.

Developmental Assessment Checklist	
1 month	Raises head, makes crawling movements, alerts to sounds, follows faces at midline
2 months	Follows faces past the midline, lifts chest off table, smiles socially
4 months	Rolls front to back, laughs
6 months	Sits unsupported, babbles
9 months	Pulls to stand, says "mama"
12 months	Walks alone, uses two words together
18 months	Can remove garment of clothing, scribble, use 6 words, run
24 months	Can wash hands, jump up, combine words
36 months	Can put on shirt, speech is understandable, can balance on one foot
48 months	Can dress alone, draw a person, use complex speech (adjectives, prepositions) hop

Handout 2.1.4: Physical Examination

Physical examination or clinical examination is a process where the physician examines the patient's body to look for signs of disease. Physical examination of a child with HIV is the same as a physical examination of any other child.

The clinical expression of HIV infection in children is highly variable. Some HIV-positive children develop severe HIV-related signs and symptoms in the first year of life. Other HIV-positive children may remain asymptomatic or mildly symptomatic for more than a year and may survive for several years.

Beforedoing physical examination you have to introduce yourself to the mother and older children if any.
Before touching the child, explain to the parent what you are going to do during the physical exam. Be sure to also explain this as you are going through the exam. Explain that you will need to touch the child. Do not be afraid to touch the child
The following are some of the emergency and priority signs as discussed in ETAT.

- Obstructed breathing
- Severe respiratory distress
- Cyanosis
- Convulsions
- Coma
- Confusion
- Shock
- Severe dehydration

Priority signs are signs which should alert you to a child who needs prompt, but not emergency assessment. These signs can be remembered with the symbols **3 TPR –MOB:**

- **T**iny baby: any sick child aged under two months
- **T**emperature: child is very hot
- **T**rauma or other urgent surgical condition
- **P**allor (severe)
- **P**oisoning
- **P**ain (severe)
- **R**espiratory distress
- **R**estless, continuously irritable, or lethargic
- **R**eferral (urgent)
- **M**alnutrition: Visible severe wasting
- **O**edema of both feet
- **B**urns

Worksheet 2.1.1: Presumptive Diagnosis Case Study

Instructions:

- In small groups, read the case study below and answer the questions.
- You will have approximately 10 minutes to complete the case study.
- Be prepared to share and discuss your responses in plenary.

Case Study

Grace is 14 months of age when brought to your hospital with fever, difficulties in breathing and diarrhea on and off for the last three months. Before she was fine. Only received symptomatic treatment.

O/E: Looks wasted and dehydrated, Temp 37.7o C, skin changes on the buttocks, generalized lymphadenopathy, high RR with some crackles heard

1. What is your preliminary and differential diagnosis?

2. What else would you ask for?

Anthropometric measures:

- Height 67 cm
- Weight 5.5 kg
- Head Circumference 44 cm

3. What are your comments?

Session 2: Diagnosis and Staging for Children with Confirmed HIV Infection

Total Session Time: 1 hour 30 minutes

Learning Objectives

By the end of this session, participants will be able to:
- Describe HIV diagnosis in children<18 months and≥18 months
- Outline importance of WHO clinical staging in children
- Describe the WHO clinical staging of paediatric HIV

HIV diagnosis in children<18 months and≥18 months

Diagnosis of HIV in children
Laboratory evaluation includes:
- HIV diagnosis such as:
  - Antibody Tests: Rapid Tests (according to national HTC algorithm)
  - Virological Test: HIV viral tests are the tests for detecting presence of virus, such as DNA PCR test.

There are two types of Polymerase Chain Reaction (PCR) tests:
- DNA PCR: Detects the presence of virus
- RNA PCR: Measures the amount of virus in the blood, also known as the viral load

NOTE: The antibody test looks for the presence of antibodies specific for HIV while Virological tests looks for the presence of viral material (the DNA, or RNA).

Diagnosis in Children < 18 Months
Children born to HIV infected women can be classified in several ways depending on when HIV testing is done and what method is used. HIV status should be confirmed as soon as possible. If the child is symptomatic, a positive antibody test can be used to make a presumptive diagnosis and initiate treatment until HIV diagnosis is confirmed.

Maternal HIV antibody is passively transferred to infant across the placenta and remains positive up to 18 months:
- The antibody test is therefore positive at birth in children born to HIV infected women, including those children that are NOT infected
- Virological tests are required in order to diagnose HIV

Diagnosis in Children ≥ 18 Months
Definitive HIV diagnosis in children aged 18 months and more (with known or unknown HIV exposure) can be made with antibody tests, such as rapid antibody tests following standard national testing algorithms.

In children ≥18 months diagnosis of HIV infection is determined by the detection of antibodies; thus rapid antibody tests are used. The use of rapid antibody tests for diagnosis has the advantage that the results become available at the time of the clinic visit.

*Refer to **Handout 2.2.1 Diagnosis of HIV in Children >18 months and adults** on **page 81** for more information on the diagnosis of HIV in children older than 18 months and Adults.*

Laboratory Evaluation
In interpreting laboratory results, the health care provider needs to know:

- The child's Age
- Breastfeeding Status such as;
  - Is child currently breastfeeding?
  - When did child stopped breastfeeding?

Window Period is the time from infection to development of positive test:

- Antibody Test: 6 weeks
- DNA PCR: 4 weeks

Assays that detect the virus or its components (i.e. virologic tests) are required in order to positively diagnose HIV infection in children < 18 months of age. The two most commonly used tests for such a diagnosis are DNA PCR or RNA PCR. However, DNA PCR is the preferred method of choice used for early detection of HIV infection. Most people can get an accurate test reading three to four weeks after a suspected infection.

Most people have a **"window period"** (usually 3 to 6 weeks) during which antibodies to HIV are still being produced and are not yet detectable.
This early period of infection represents the time of greatest infectivity, but transmission can occur during all stages of the infection.
If someone has had a recent possible HIV exposure, retesting should be done after 6 weeks to confirm test results, which enables sufficient time to pass for antibody production in infected individuals.

Early Infant Diagnosis (EID)
Every HIV-exposed baby should have a DNA PCR test:

- At 4-6 weeks of life Or
- At first visit* (if >6 weeks of age)

Testing at these 4-6 weeks of age should identify all babies infected during pregnancy, labor & delivery and during early breast feeding. Early diagnosis of HIV allows health-care providers to offer optimal care and treatment of HIV infected children, assists in decision-making on infant feeding, and avoids needless stress in mothers and families.

Most infants have their first visit for immunizations and growth monitoring at 6 weeks. CTX prophylaxis should be stated at this visit. The sensitivity of the DNA PCR test is > 96%.

If the child presents at 9-18 months of age first screen with a rapid antibody test. If rapid test is positive confirm with the DNA PCR test.

*Refer to **Handout 2.2.2: Entry Points for Promoting Early Diagnosis** on **page 83** for more information on virological testing.*

*Refer to the algorithm in **Handout 2.2.3: HIV Testing of Infants and Children** on **page 85.***

HIV Diagnosis in Children 0-9 Months

Infants of HIV-positive women should be diagnosed using **DNA PCR**: DNA PCR can be performed on specimens of whole blood collected onto filter paper as DBS without significant loss of sensitivity or specificity. That is, all HIV-exposed infants should have specimen collected using SOPs for Dried Blood Spot (DBS) at 4-6 weeks of age.

Positive DNA PCR means the child is HIV-positive and need to start ARV treatment. Infants that have negative DNA PCR who are still breastfeeding (or stopped < 6 weeks before the test was done) need repeat testing 6 weeks after complete cessation of breastfeeding.

HIV Diagnosis in Children 9-18 Months

Infants 9-18 months of age can be diagnosed with a rapid antibody test:

- A positive antibody test means the child is HIV-exposed and the child needs DNA-PCR for definitive diagnosis
- If the antibody test is negative and the child is still breastfeeding or recently stopped breastfeeding the child needs repeat testing 6 weeks after last breast feeding

HIV Test Results & Breastfeeding

For any test result, it is important to explain to the patient and the caregiver/parent what the test results mean. The clinician is responsible for this as well as the counsellor. Therefore, breast feeding will provide the baby with nutrients and antibodies from breast milk.

The use of ARVs for PMTCT (mother and/or infant) does not affect interpretation of a DNA PCR test.

- If the PCR is positive, encourage mother to continue breastfeeding
- If the PCR is negative, encourage mother to continue EXCLUSIVE breastfeeding until 6 months of age, then introduce complementary foods
- Repeat the PCR test or if the child is ≥ 18 months do antibody test 6 weeks after complete cessation of breast-feeding

Presumptive diagnosis of HIV infection

A presumptive diagnosis of HIV infection in children <18 months must be made based on clinical findings:

- Good clinical reasoning can identify children at high risk for HIV disease & rapid progression

The purpose of making a presumptive diagnosis is to initiate ART in the sick child:

- Children with severe manifestations of HIV infection should not be denied treatment because their diagnosis cannot be confirmed

NOTE: presumptive diagnosis is applied when laboratory confirmation is not available.

- Virological tests may not always be available.
- Therefore, it is important to understand that sick infants still need to be treated.
- Providers will have to make a presumptive diagnosis based on clinical findings.
- The diagnosis will be confirmed when the child is 18 months or older.
- Treatment should not be withheld if there is reasonable evidence that the child has HIV.

Importance of WHO Clinical Staging in Children & Paediatric HIV

Importance of WHO Clinical Staging

In a child with diagnosed HIV infection, the clinical staging system helps to recognize the degree of damage to the immune system and to plan treatment and care options. The stages determine the likely prognosis of HIV, and are a guide when to start, stop or substitute ARV therapy in HIV infected children. Staging is informative for assessment at baseline or entry into HIV care and can also be used to guide decisions on when to start CPT in HIV-infected children and other HIV-related interventions. The clinical staging is for use where HIV infection has been confirmed (i.e. serological and/or virological evidence of HIV infection).

Some of the importance of WHO clinical staging include:

- To determine disease severity
- To decide when to start cotrimoxazole prophylaxis
- As a criteria for monitoring diseases progression
- To determine eligibility criteria for children ≥ 15 yrs

The advantages of having CD4 count include:

- To monitor the immune system
- To help in monitoring the effectiveness of ART

Classification of HIV-Associated Clinical Disease

World Health Organization (WHO) Clinical staging is categorized into FOUR stages:

- Stage 1 – Asymptomatic
- Stage 2 – Mild
- Stage 3 – Advanced
- Stage 4 – Severe

NOTE that: WHO clinical staging of HIV disease should only be used once HIV infection has been confirmed (serological and/or virological evidence of HIV infection).

*Refer to **Handout 2.2.4: WHO Clinical Staging in Adults, Adolescents, and Children** on **page 87** for more information about classification of WHO clinical staging.*

WHO Clinical Stage 1

This stage is characterized with:

- Asymptomatic
- Persistent generalized lymphadenopathy (PGL)

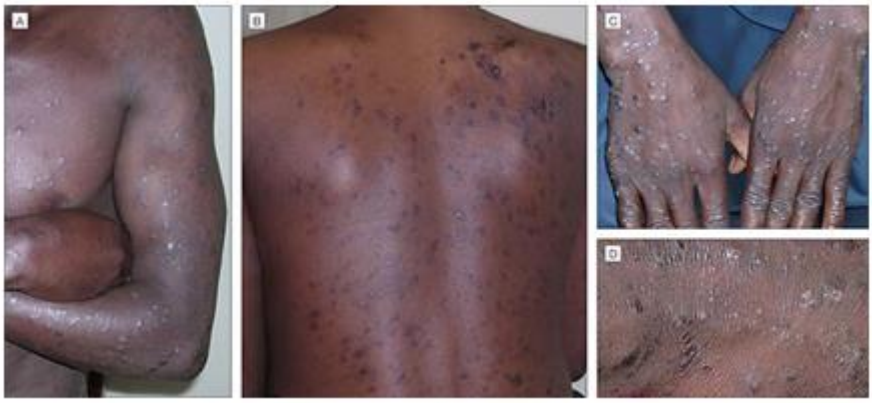
WHO Clinical Stage 2 (Mild)

In stage 2 featured by:

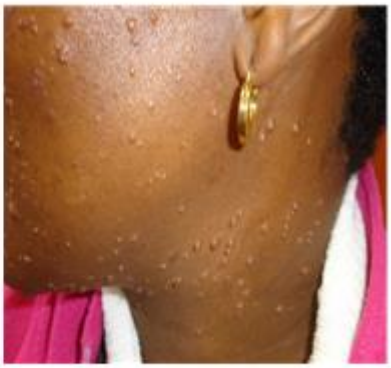
- Unexplained persistent hepatospleenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Fungal nail infections
- Angular cheilitis
- Lineal gingival erythema
- Unexplained persistent parotid enlargement

- Herpes zoster
- Recurrent or chronic URTIs (otitis media, otorrhea, sinusitis, tonsilllitis) (**URTI** means Upper Respiratory Tract Infections).
- Recurrent oral ulcerations

WHO Stage 2: Papular Pruritic Eruptions

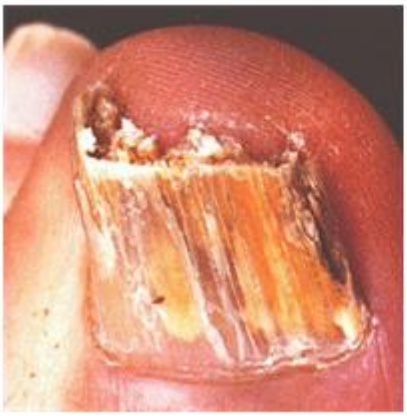


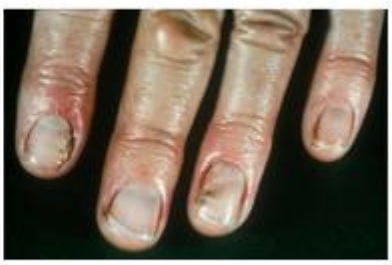
Verruca Planus



Molluscum Contagiosum

WHO Stage 2: Fungal Nail Infections





Recurrent Oral Ulcers

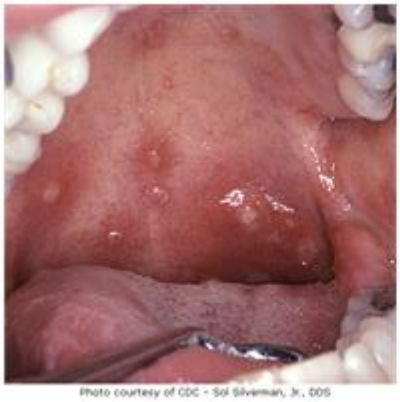
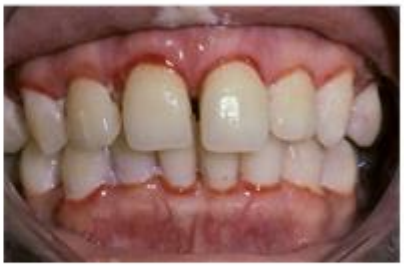


Photo courtesy of CDC - Sol Silverman, Jr., DDS

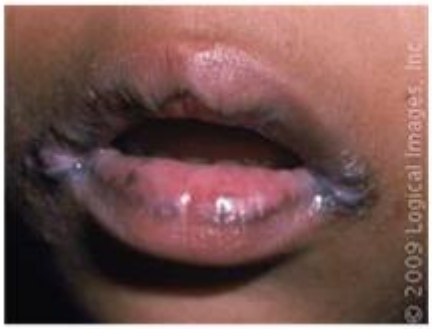
Lineal Gingival Erythema



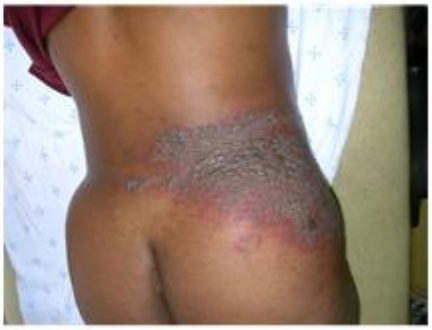
NOTE that:

- Linear gingival erythema appears as a distinct band of erythema of the gingival margin which may extend to the alveolar mucosa.
- The erythema does not respond to removal of local factors or improved plaque control. Although a relationship to candidiasis has been reported, the cause is not known.
- This entity may be self-limiting or may progress on to necrotizing ulcerative periodontitis

Angular Cheilitis



Herpes Zoster



Angular cheilitis frequently accompanies intraoral candidiasis and may persist if topical antifungal treatment is used intraorally. Angular cheilitis appears as erythema and/or fissuring at the corners of the mouth. This is a common lesion and is seen frequently in dental patients unrelated to HIV infection.

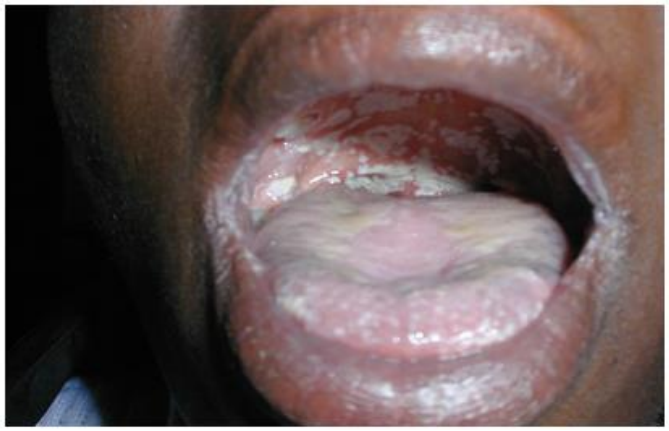
WHO Clinical Stage 3 [Advanced]

Conditions of WHO clinical stage 3 include:

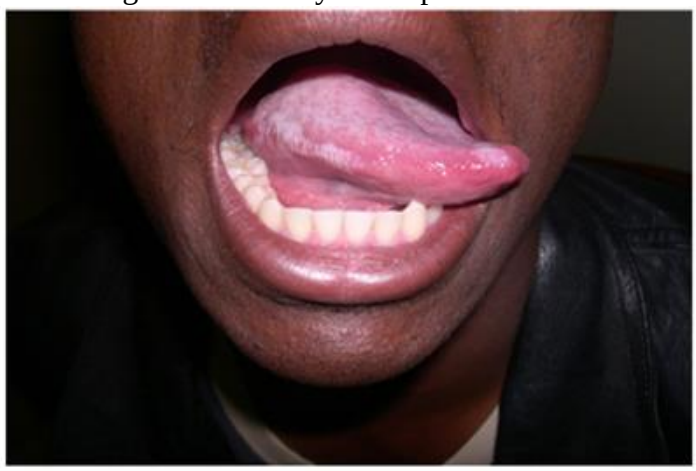
- Moderate unexplained malnutrition
- Unexplained persistent diarrhoea (>14 days)
- Unexplained persistent fever (intermittent or constant, >1 mo)
- Oral candidiasis (outside neonatal period)
- Oral hairy leukoplakia: Oral Hairy Leukoplakia is a raised white lesion of the oral mucosa usually seen on the lateral margin of the tongue that cannot be scratched off and that does not respond to antifungal therapy.
- Acute necrotizing ulcerative gingivitis/periodontitis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia

- Unexplained anaemia (<8 g/dL), neutropaenia (<1,000/mm3), or thrombocytopaenia (<30,000/mm3) for >1mth
- Lymph node tuberculosis
- Chronic HIV-associated lung disease including bronchiectasis
- Symptomatic Lymphoid Interstitial Pneumonitis (LIP)

WHO Stage 3: Oral Candidiasis



WHO Stage 3: Oral Hairy Leukoplakia



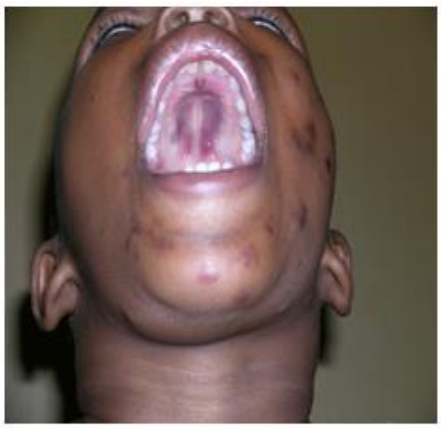
NOTE that:

- Hairy leukoplakia appears as a white corrugated lesion on the lateral border of the tongue. It is usually asymptomatic and may become prominent enough in some patients to be of cosmetic concern.
- The lesions may extend on to the dorsal and ventral tongue. Hairy leukoplakia is caused by Epstein-Barr virus.
- Hairy leukoplakia generally does not require treatment.
- Antiviral treatment (Acylovir/Valacyclovir) and topical Podophyllum resin have been used to treat hairy leukoplakia.
- The result is temporary and lesions generally recur.
- Hairy leukoplakia may wax and wane spontaneously.

WHO Clinical Stage 4 [Severe]

- Unexplained severe wasting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (excluding pneumonia)
- Kaposi's sarcoma
- Oesophageal candidiasis
- Extrapulmonary cryptococcosis including meningitis
- Any disseminated endemic mycosis, this can include:
  - Extra-pulmonary Histoplasmosis
  - Coccidiomycosis
  - Penicilliosis
- Cryptosporidiosis
- Isosporiasis
- Candida of trachea, bronchi or lungs
- Cerebral or B-cell non- Hodgkin Lymphoma
- Progressive Multifocal Leukoencephalopathy (PML)
- Extrapulmonary TB
- Chronic HSV infection (lasting >1 mo)
- HIV-associated cardiomyopathy or
- HIV-associated nephropathy
- HIV encephalopathy
- CMV infection
- CNS toxoplasmosis (> 6 weeks of life)
- Disseminated non-tuberculous mycobacterial infection

WHO Stage 4: Kaposi Sarcoma



Activity: On a case study on Diagnosis of HIV in children older than 18 months and adults.

*Refer to **Worksheet 2.2.1: Case Study** on **page 89** for more information and scenario for the case study.*

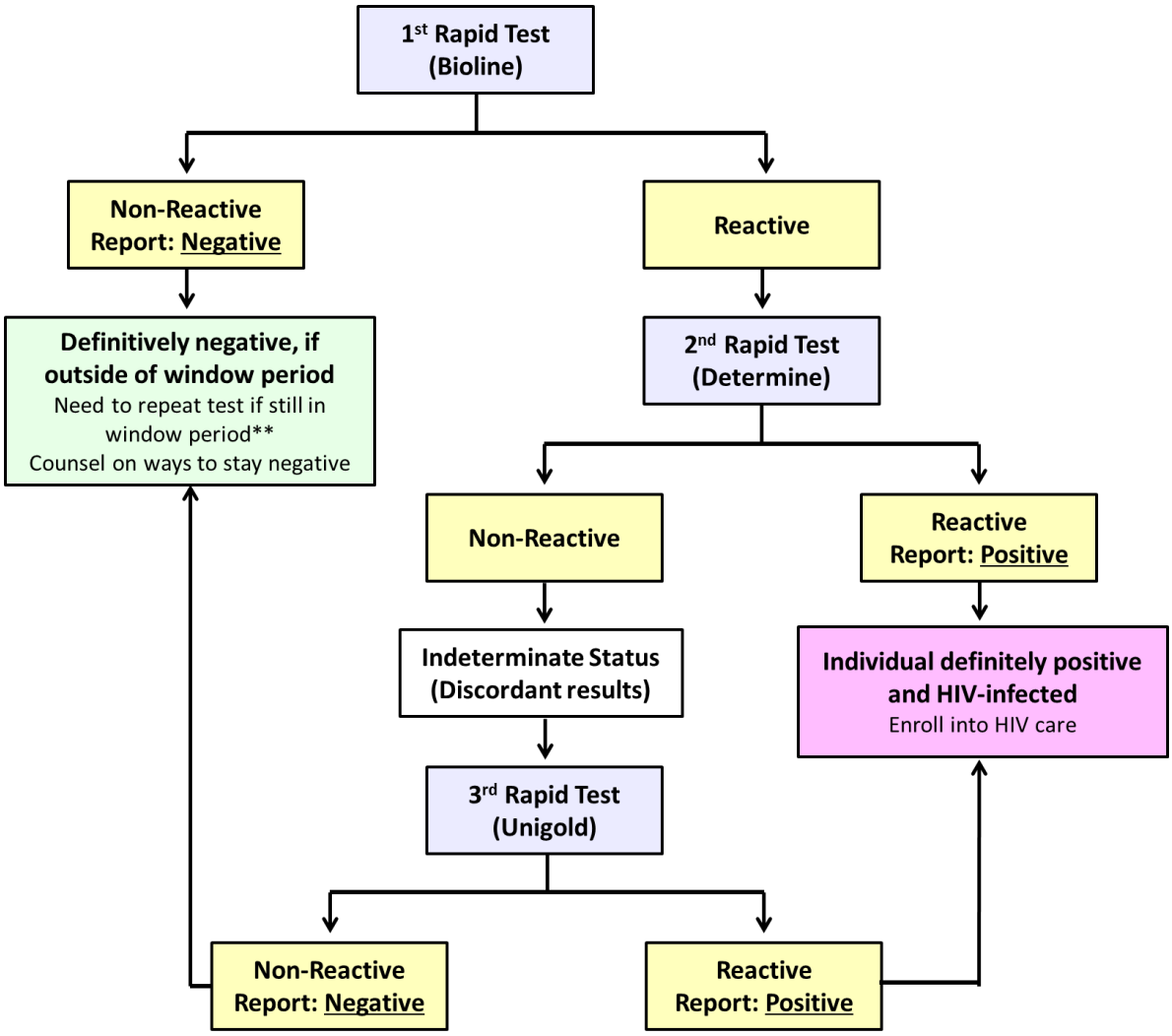
Key Points

- Laboratory confirmation of HIV diagnosis in children depends on age:
  - < 9 months PCR is needed for diagnosis
  - 9 – 18 months start with antibody test, if positive, PCR is needed for confirmation
  - In the absence of PCR for children <18 months, do a presumptive diagnosis to diagnose severe HIV infection
  - If ≥ 18 months antibody test (rapid tests, ELISA) confirms or exclude diagnosis unless the child is breastfeeding
  - If the child is breastfeeding repeat HIV test 6 weeks after complete cessation of breastfeeding
- WHO Clinical staging is done after laboratory confirmation of HIV infection
- WHO clinical staging is used to determine disease severity and progression.

Sources/Bibliography

- Tanzania Ministry of Health and Social Welfare. *Prevention of Mother-to-Child Transmission of HIV: Pocket Guide.* 2013. Dar es Salaam: MOHSW. (pages 21-22)

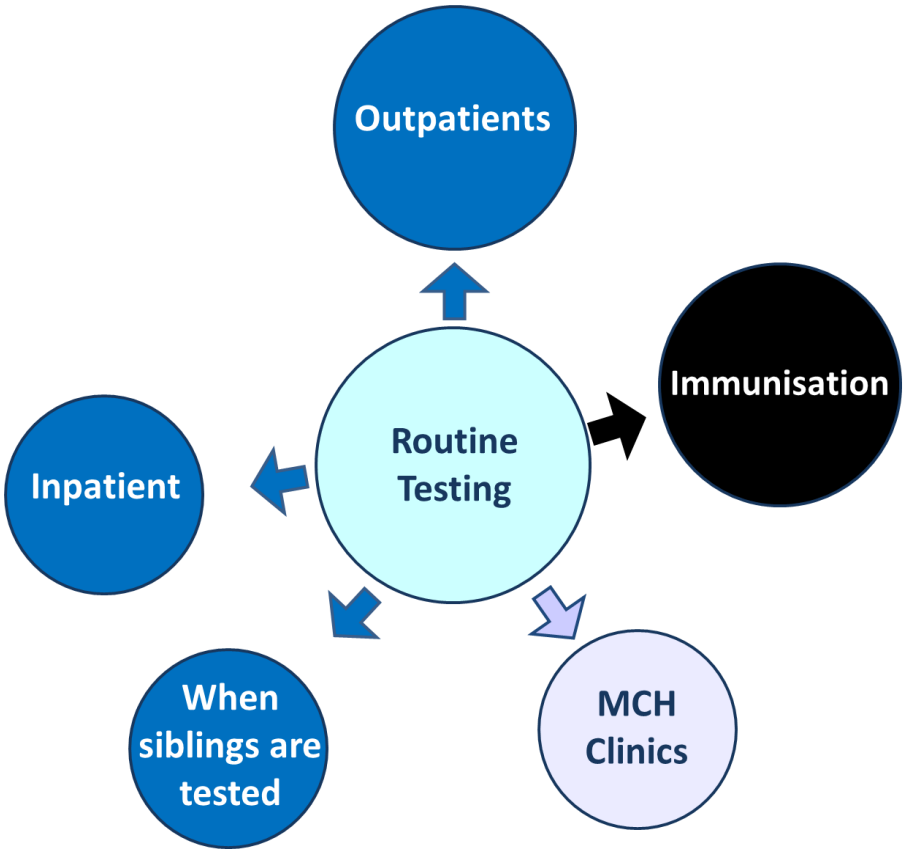
Handout 2.2.1: Diagnosis of HIV in Children Older Than 18 Months and Adults



Notes:
**** A child who has not breastfed from an HIV-infected mother within 3 months of the rapid test is considered to still be in the window period and repeat testing must be performed.**
**** An adult who has engaged in unprotected sexual activity within 3 months of the rapid test is considered to still be in the window period and repeat testing must be performed.**
Counselling on remaining negative should be provided.

NOTE that the risk of HIV transmission remains if breastfeeding continues beyond 18 months of age.In children older than 18 months antibody testing is definitive.

Handout 2.2.2 Entry Points for Promoting Early Diagnosis

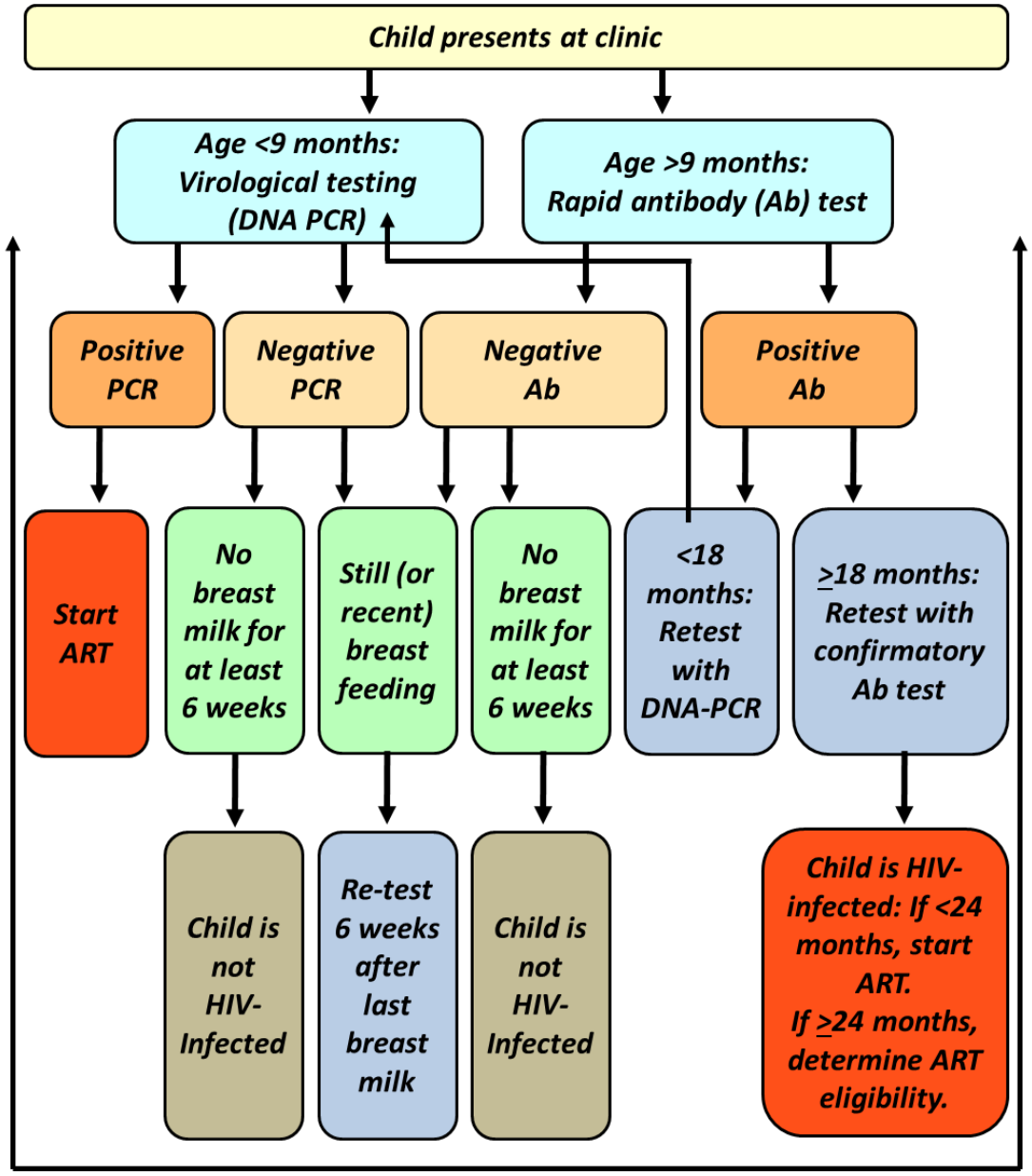


Routine offer of testing is ideal for children attending:

- Outpatient clinics
- RCH clinics
- In-patient clinics/hospitals (admitted children) and
- Provider-initiated routine testing

Routine testing should also be offered to children of adults who are seeking services, including at
PMTCT programmes and hospitals for treatment of HIV, TB, STIs

Handout 2.2.3: Diagnosis of HIV in Infants and Children Less Than 18 Months of Age



Source: Tanzania Ministry of Health and Social Welfare. *Prevention of Mother-to-Child Transmission of HIV: Pocket Guide.* 2013. Dar es Salaam: MOHSW. (pages 21-22)

Why virological testing at the age of 4-6 weeks?

Virological testing at 4-6 weeks of age will identify more than 95% of infants infected intra- and peripartum. However, some flexibility in implementation of this recommendation may be required based on current national or local postpartum and infant follow-up practices and service configuration. Delaying testing beyond this time will delay diagnosis and put HIV infected infants at risk of disease progression and death

If virological testing is not available, presumptive clinical diagnosis in accordance with nationally defined algorithms will be required.
If maternal HIV status is unknown the infant should be screened with rapid antibody first. Also for infants older than 9 months of age at the first clinic visit, screen with a rapid antibody test first. If antibody is positive then perform DNA PCR.
If antibody test is negative and infant is still breastfeeding, repeat rapid antibody 3 months after cessation of breast feeding.

Handout 2.2.4: WHO Clinical Staging of HIV disease in Adults, Adolescents and Children

Source: World Health Organization, 2013. *Consolidated Guidelines on the use of Antiretroviral Drugs for Treating and Preventing HIV Infection.* Geneva, Switzerland: WHO.

Adults and Adolescents[1]	Children
Clinical Stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	
• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Seborrhoeic dermatitis	• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Herpes zoster • Lineal gingival erythema • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Extensive wart virus infection • Extensive molluscumcontagiosum • Unexplained persistent parotid enlargement
Clinical Stage 3	
• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month • Unexplained persistent fever (intermittent or constant for longer than 1 month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) and/or chronic thrombocytopaenia (<50 x 10^9/l)	• Unexplained moderate malnutrition[2] 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 1 month) • Persistent oral candidiasis (after first 6 weeks of life) • Oral hairy leukoplakia • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Acute necrotizing ulcerative gingivitis or • periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) or chronic thrombocytopaenia (<50 x 10^9/l)

Adults and Adolescents[1]	Children
Clinical Stage 4[3]	
• HIV wasting syndrome • *Pneumocystis (jirovecii)* pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Extrapulmonarycryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Recurrent septicaemia (including nontyphoidal*Salmonella*) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis	• Unexplained severe wasting, stunting or severe malnutrition[4] not responding to standard therapy • *Pneumocystis (jirovecii)* pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extrapulmonarycryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis • Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • HIV-associated nephropathy or cardiomyopathy

Notes:

1. In the development of this table, adolescents were defined as 15 years or older. For those aged less than 15 years, the clinical staging for children should be used.
2. For children younger than 5 years, moderate malnutrition is defined as weight-for-height <–2 z-score or mid-upper arm circumference ≥115 mm to <125 mm.
3. Some additional specific conditions can be included in regional classifications, such as penicilliosis in Asia, HIV-associated rectovaginal fistula in southern Africa and reactivation of trypanosomiasis in Latin America.
4. For children younger than 5 years of age, severe wasting is defined as weight-for-height <–3 z-score; stunting is defined as length-for-age/height-for-age <–2 z-score; and severe acute malnutrition is defined as either weight for height <–3 z-score or mid-upper arm circumference <115 mm or the presence of oedema.

Worksheet 2.2.1: Case Study

Instructions:

- In small groups, read the case study below and answer the questions.
- You will have approximately 15 minutes to complete the case study.
- Be prepared to share and discuss your responses in plenary.

Scenario 1:

A 3 year old HIV infected child presents with lymphadenopathy, severe oral candidiasis and severe pneumonia. Her CD4 is 25%.

1a. She has WHO Stage 1 disease: True or False?
1b. She is severely immunosuppressed: True or False?
1c. She has WHO Stage 3 disease: True or False?
1d. She qualifies to start antiretroviral therapy: True or False?
1e. Further evaluation reveals severe wasting; this pushes her stage to WHO Stage 4: True or False?

Scenario 2:

- Absolute (total) CD4 count
- CD4/CD8 ratio
- CD4%

2a. Which of the above tests should be used for monitoring disease progression in adolescents?

2b. Which one should be used for children <6 yrs of age?

Scenario 3:

A 25 year old woman who was started on ART therapy during her pregnancy (option B+) comes to the CTC for a routine follow up visit. Upon inquiring if her partner or child has been screened for HIV, you learn that the child now 9 months old had never been screened. The woman thinks that the child is well and she does not need HIV testing now. She is planning to check her with an ELISA at the age 18 months.

3a. What can you recommend to the woman
3b. What can you do now?