

GROWTH AND DEVELOPMENT IN HIV-INFECTED CHILDREN

GROWTH

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Objectives

The purposes of this module are to:

1. Present an overview of normal growth and development in children.
2. Describe how HIV infection impacts growth and development in children.
3. Review the effects of highly active antiretroviral therapy (HAART) on growth and development in HIV-infected children.
4. Discuss changes in bone formation and pubertal development in HIV-positive children.

Key Points

1. Growth and development are important indicators of the health of a child.
2. Health care providers who care for children should evaluate each child's growth and development at every visit.
3. HIV infection can lead to growth problems, developmental delays, and developmental regression.
4. When problems in growth and development are found, the health care provider should attempt to treat the underlying cause of the problem.
5. Bone problems and abnormal pubertal development are more commonly seen in HIV-infected children than in non-infected children.

Overview

Growth and development are important indicators of a child's health. Accurate measurements of weight, height, and head circumference are essential parts of the health evaluations of growing children. Children who are unhealthy tend to grow more slowly and to be smaller than healthy children their age. Likewise, developmental delays often result from health problems.

HIV-infected children are at particular risk for problems related to growth and development. HIV and opportunistic infections often negatively influence the growth and development of young children. The lives of many HIV-infected children are complicated by a lack of nutritious food necessary for normal growth and development. When a child's caretakers are ill or are suffering emotionally from the loss of friends and family members, they may be less available to provide appropriate developmental stimulation.

Health care providers who treat children should understand how to assess whether a child's growth and development are appropriate for the age of the child. By evaluating growth and development at every medical visit, we can learn much about the child's health.

Newborns: Birth-Weight Comparisons

Small size at the time of birth is not clearly associated with HIV infection in full-term newborns. A full-term newborn's birth weight is determined by many factors, including maternal nutrition, placental function, and fetal genetics. Studies examining the role of maternal HIV infection in fetal growth have failed to show a consistent relationship. According to the European Collaborative Study and a study from Durban, South Africa, newborn height and weight of infected and uninfected children born to HIV-positive mothers are not significantly different.^{1,2} In contrast, a study based on a U.S. inner-city population concluded that children born to HIV-infected mothers are at increased risk of low birth weight as well as prematurity.^{3,4} The results of this study were adjusted for confounding factors such as tobacco, alcohol, and other drug use known to affect birth weight. Further studies are needed to clarify the reasons for the inconsistencies seen between these populations. At this time, the evidence does not clearly imply a relationship between HIV infection and infant birth weight.

While full-term newborns who are HIV-infected or HIV-exposed are not typically smaller than term unexposed infants, prematurity is more common among HIV-exposed infants. A study done prior to the implementation of prenatal prophylaxis and the routine use of HAART showed the rate of prematurity associated with HIV infection was as high as 19 percent, more than 30 percent higher than in the uninfected population. The population evaluated in the HIV-positive group was also at increased risk for smoking, alcohol use, and illicit drug use, which can contribute to a higher incidence of premature births. The use of HAART does not decrease the incidence of prematurity among children born to HIV-positive mothers. This has been demonstrated in a multicenter U.S. study of more than 3000 children born to HIV-positive women, in which the incidence of prematurity was 17 percent in the HAART-treated group and 16 percent among those not receiving HAART.⁵

Frontal Occipital Circumference (FOC) and HIV

Head circumference is known to be correlated with brain volume. The brain is one of the primary targets of HIV infection. HIV infection in young children sometimes results in reduced brain growth.⁶ Smaller FOC at birth has been associated with developmental delays and reduced academic achievement in non-infected children. Studies have not shown a statistically significant difference in birth FOC between infected and uninfected children.⁷ The Women and Infants Transmission Study (WITS) did, however, show a trend toward smaller birth FOC in HIV-infected infants. This study also showed that infants infected with HIV had a continued decrement in brain growth as evidenced by persistent microcephaly (FOC <5th percentile for age).

The WITS group also showed an association between early HIV-positive culture and higher risk of neurologic compromise. Since microcephaly has been correlated with adverse developmental outcomes,⁸ FOC measurements may be used as a tool for the identification of infants at risk for these unfavorable outcomes. FOC may also be used as an early predictor of HIV-associated progressive encephalopathy in infants.⁹ FOC measurements are most useful during the first 2 years of life, when head circumference changes most rapidly.

Variable Onset of Growth Failure

Children's growth is affected by many factors, including general nutrition, overall health, endocrine abnormalities,¹⁰ and caretaker nurturing. A child is said to be failing to thrive when his or her height and weight are less than the 5th percentile for age or he or she is crossing percentiles downward on standardized growth curves. (U.S. standardized growth charts are provided in the "Nutrition and HIV/AIDS" chapter.) Failure to thrive is a diagnosis that has

multiple etiologies, one of which is HIV infection. According to the European Collaborative Study, at 10-year follow-up, infected children were on average 7 kg lighter and 7.5 cm shorter than uninfected children.

The onset of growth failure in children with HIV has been variable. Some studies have reported growth deceleration as early as the first few months of life. Other studies have shown children with normal growth into and beyond their second year of life.¹¹ Overall, studies have shown that children with HIV infection grow more slowly than uninfected children, a difference that becomes more significant with age. Asymptomatic infected children have similar growth patterns as mildly or moderately symptomatic children. However, children with severe illness tend to have poorer growth.² Increased levels of postnatal viremia have been clearly associated with decreased linear growth.¹²

Nutrition, Growth, and HIV

Even in patients without HIV infection, nutrition plays an important role in childhood growth. The effects of nutrition on patients with HIV have been studied with respect to CD4+ counts and growth parameters. An observational study of nutritional interventions among children with AIDS (giving adequate calories, protein, fat, and micronutrients) determined that attention to these nutritional factors may help restore intestinal absorption and improve CD4 counts. The researchers reported that providing adequate nutrition was most beneficial if started prior to the development of an AIDS-defining illness. Early nutritional interventions play an important role in helping to decrease morbidity and mortality among HIV-infected children, particularly in developing countries without access to antiretroviral therapy.¹³

Growth as a Predictor of Prognosis

Children infected with HIV have been classified in three clinical groups with regard to the timing of

their disease progression. Infants who develop symptoms of AIDS or who die within the first year of life are classified as “rapid progressors.” Children who suffer from an AIDS-defining illness or who die within one to five years of infection are classified as “intermediate progressors.” Those children who do not develop symptoms and who survive past 5 years of age are classified as “slow progressors.” Growth failure in children has been clearly associated with accelerated progression from asymptomatic HIV infection to AIDS. Those children who qualify for classification as “rapid progressors” have the highest incidence of growth failure.⁶

Perinatally acquired HIV infection is sometimes associated with early and progressive decrements in weight and length. Height growth velocity (rate of growth) has been shown to predict survival independently of age, viral load, and CD4+ cell count.¹⁴ Studies in Thailand, Rwanda, and the U.S. have evaluated growth as a predictor of prognosis. The consensus in these studies was that growth failure is highly suggestive of rapid disease progression.¹⁵ Patients who failed to gain 2 kg by 4 months of age, as well as those with low CD4+ counts (maternal and infant) at time of birth and high viral loads at 2 months of age, were most likely to have rapid disease progression.¹⁵

In resource-limited environments, where obtaining laboratory data is sometimes not possible, growth monitoring may be the best available tool for assessing risk of disease progression.

Effects of HAART on Growth

Early studies demonstrated that mono or dual antiretroviral therapies containing zidovudine, didanosine, or zalcitabine led to a temporary increase in weight and linear growth rate. The transitory nature of the benefits seen with mono and dual therapy are related to the frequent occurrence of treatment failure due to drug resistance. Because HAART is less likely to lead to resistance and treatment failure, more

sustainable clinical growth responses are seen among children on HAART.¹⁶

HAART clearly has a positive effect on height and weight in children with HIV-1 infection. According to a study performed in the Netherlands, this effect is sustained for at least 96 weeks (study duration) in patients who respond virologically to HAART. Successful application of HAART was defined as a long-term reduction in viral load of at least 1.5 log copies/ml, or viral load suppression to less than 500 copies/ml, and increased CD4+ counts. The children in this study were divided into virologic responders and virologic non-responders. Virologic responders demonstrated a significant increase in height and weight, whereas virologic non-responders did not.¹⁶

The body mass index (BMI) has been used as a tool to evaluate nutritional status in both adults and children. The BMI is calculated by using the formula

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 \text{ (meters)}}$$

Unlike what has been seen in adult populations, BMIs did not vary significantly between responder and non-responder children. An increase in BMI did, however, correlate inversely with the clinical stage of HIV prior to the initiation of HAART.¹⁶ Children with worse clinical stages at the beginning of therapy had a more significant increase in BMI than children starting at better clinical stages.

Catch-up growth typically affects weight before affecting height.¹⁶ HAART's beneficial effects on a patient's growth likewise are first seen as increases in weight (usually by 48 weeks of therapy) and later as height improvements (usually by 96 weeks of therapy). A group from the Duke Clinical Research Institute is looking at the prediction of treatment failure using height velocity as a marker for treatment response.¹⁷ If validated internationally, this type of prediction could provide an excellent low-cost method for evaluating treatment response in resource-limited settings.

Bone Growth: Osteopenia, Osteoporosis, and Osteonecrosis

Bone mass increases during childhood and adolescence; peak bone mass normally is achieved during the third decade of life.¹⁸ When people have low bone density for their age, they are said to have osteopenia. Those whose bone density is less than 2.5 standard deviations below the mean have the severe form of bone wasting called osteoporosis. Children who fail to form bone normally are at high risk for suffering from fractures during adulthood due to early osteoporosis. HIV-infected children accumulate bone density at a slower rate than non-infected children, and certain HAART regimens may further decrease bone density.^{19,20}

The mechanisms by which bone mass is decreased among HIV-positive children are complicated and incompletely understood. HIV probably affects bone development both directly and indirectly. HIV can infect bone cells directly. The virus also leads to the elevation of several cytokines (IL-1, IL-6, and TNF-alpha) that contribute to increased activity of osteoclasts (cells that break down bone).²⁰ Vitamin D deficiency also contributes to abnormal bone metabolism and has been reported in adults with HIV.²¹ While increased rates of bone fractures are not commonly seen among HIV-infected children, these children are at high risk of fractures later in life due to their early development of osteopenia and osteoporosis.

Children and adults with HIV infection are also at increased risk of osteonecrosis of the hip. In children, this condition is called Legg-Calve-Perthes Disease (LCPD). A study of perinatally HIV-infected children demonstrated a prevalence of LCPD that was more than eight times that of the general population.²² LCPD is diagnosed on the basis of typical X-ray findings in a symptomatic patient. Treatments for LCPD include the use of non-steroidal anti-inflammatory and pain-control medications, temporary cessation of weight bearing, and exercises to maintain

the range of motion. In severe cases, immobilization of the joint or surgery may be required.

Low bone density can be quantified using dual-energy X-ray absorptiometry (DEXA scans) or quantitative CT scans. The appearance of the bones on plain X-rays can also give qualitative evidence for the existence of osteopenia or osteoporosis. Weight-bearing exercises (such as jogging, dancing, and weight lifting) can help children with HIV to maximize their bone development.

Providing a diet that is rich in vitamin D, especially in areas where children have limited exposure to sunlight, will also help to ensure the best possible bone growth. Studies are currently looking at the effects of various bone-building medicines on HIV-infected children with osteopenia and osteoporosis, but no medications are currently recommended for routine use.

Puberty

Delay of sexual maturation is a common occurrence among children with chronic diseases. Children with HIV infection have delays both in the age of onset of

puberty and in their progression through the Tanner stages. The median delay in pubertal onset is two years for girls and one year for boys. Entry into the late Tanner stages is delayed by about 2.5 years in girls and 1.5 years in boys.²³ Children with increased immune-system dysfunction tend to have the most significant delays in pubertal development.²⁴ Therefore, tracking pubertal development may help to clarify underlying disease progression.

Developmental Assessments

It is important that people who provide health care to children understand basic principles of developmental assessment. This is especially important for those providing care to HIV-infected children, because developmental delays are often early signs of disease progression. Many tools are available for the assessment of developmental progression. Table 1 lists some of the most commonly used tools for the screening of child development. Considering a child's age and cultural background can help medical professionals to determine which tool is the most appropriate for each patient's evaluation. Because some

Table 1: Commonly Used Developmental Screening Tools

Tool	Age of Child	Skills Assessed	Special Limitations or Benefits
Ages and Stages Questionnaire	4-60 months	<ul style="list-style-type: none"> • Communication • Gross and fine motor • Problem-solving • Social 	<ul style="list-style-type: none"> • Completed by parent
Bayley Scales of Infant Development II	1-42 months	<ul style="list-style-type: none"> • Mental development (memory, language, problem-solving) • Motor development (coordination, fine motor movement, body control) 	<ul style="list-style-type: none"> • Requires standardized kit • Requires about 45 minutes to administer
Clinical Adaptive Test/Clinical Linguistic and Auditory Milestones Test (CAT/CLAMS)	Under 24 months	<ul style="list-style-type: none"> • Similar to DDII (see below) • Helps to distinguish isolated language delay from mental retardation 	<ul style="list-style-type: none"> • Requires standardized kit
Denver Developmental Screening Test (DDII)	Birth to 6 years	<ul style="list-style-type: none"> • Fine motor • Gross motor • Personal/social • Language 	<ul style="list-style-type: none"> • Requires about 20 minutes to perform • Requires standardized kit • Low sensitivity and specificity
Kaufman Assessment Battery for Children	2.5-12.5 years	<ul style="list-style-type: none"> • 16 subsets of cognitive skills 	<ul style="list-style-type: none"> • Requires 40-90 minutes to administer
McCarthy Scales of Children's Abilities	2.5-8.5 years	<ul style="list-style-type: none"> • Cognitive abilities • Gross and fine motor abilities 	<ul style="list-style-type: none"> • Requires 45-60 minutes to administer • Requires standardized kit
Wechsler Intelligence Scales	3-7 years and 6-16 years	<ul style="list-style-type: none"> • Verbal and nonverbal intelligence 	<ul style="list-style-type: none"> • Time-consuming to administer (>1 hour) • Requires standardized kit

Table 2: Developmental Milestones – The First 24 Months of Life

Age	Psychosocial	Gross Motor	Fine Motor and Visual	Communication and Hearing
1 month	<ul style="list-style-type: none"> Follows faces to the midline 	<ul style="list-style-type: none"> Moves all extremities equally Lifts head when lying on stomach 	<ul style="list-style-type: none"> Opens hands spontaneously 	<ul style="list-style-type: none"> Startled by loud sounds Cries Quiets when fed and comforted
2 months	<ul style="list-style-type: none"> Follows faces past the midline Smiles responsively 	<ul style="list-style-type: none"> Lifts head up 45 degrees when on stomach 	<ul style="list-style-type: none"> Looks at own hand 	<ul style="list-style-type: none"> Makes baby sounds such as cooing, squealing and gurgling
3 months	<ul style="list-style-type: none"> Recognizes mother Smiles responsively 	<ul style="list-style-type: none"> Can support head for a few seconds when held upright 	<ul style="list-style-type: none"> Opens hands frequently 	<ul style="list-style-type: none"> Responds to voices Laughs
4 months	<ul style="list-style-type: none"> Follows an object with eyes for 180 degrees Regards own hand Anticipates food on sight 	<ul style="list-style-type: none"> Bears weight on legs Good neck control when pulled to sitting position Lifts chest and supports self on elbows when lying on stomach 	<ul style="list-style-type: none"> Brings hands together in midline (clasps hands) Grabs an object such as a rattle Reaches for objects 	<ul style="list-style-type: none"> Turns head to sound
6 months	<ul style="list-style-type: none"> Reaches for familiar people 	<ul style="list-style-type: none"> Rolls from stomach to back or back to stomach Sits with anterior support 	<ul style="list-style-type: none"> Plays with hands by touching them together Sees small objects such as crumbs 	<ul style="list-style-type: none"> Responds to name Babbles
9 months	<ul style="list-style-type: none"> Indicates wants Waves “bye-bye” Has stranger anxiety 	<ul style="list-style-type: none"> Can sit without support Creeps or crawls on hands and knees 	<ul style="list-style-type: none"> Looks for a toy when it falls from his/her hand Takes a toy in each hand Transfers a toy from one hand to the other 	<ul style="list-style-type: none"> Responds to soft sounds such as whispers
12 months	<ul style="list-style-type: none"> Has separation anxiety Social interactions are intentional and goal-directed 	<ul style="list-style-type: none"> Pulls self up to standing position Walks with support 	<ul style="list-style-type: none"> Points at objects with index finger 	<ul style="list-style-type: none"> Says at least 1 word Makes “ma-ma” or “da-da” sounds Locates sounds by turning head
15 months	<ul style="list-style-type: none"> Imitates activities Finds a nearby hidden object 	<ul style="list-style-type: none"> Can take steps on own Can get to a sitting position from a lying position 	<ul style="list-style-type: none"> Can stack one cube on top of another 	<ul style="list-style-type: none"> Able to say “mama” and “dada” to respective parents (sounds to identify caretakers)
18 months	<ul style="list-style-type: none"> Initiates interactions by calling to adult 	<ul style="list-style-type: none"> Walks without help 	<ul style="list-style-type: none"> Can take off own shoes Feeds self 	<ul style="list-style-type: none"> Says at least 3 words
2 years	<ul style="list-style-type: none"> Does things to please others Engages in parallel (imitative) play 	<ul style="list-style-type: none"> Runs without falling 	<ul style="list-style-type: none"> Looks at pictures in a book Imitates drawing a vertical line 	<ul style="list-style-type: none"> Combines 2 different words

Table 3: Developmental Red Flags

Age	Developmental Problem
Birth to 3 months	<ul style="list-style-type: none"> Failure to alert to environmental stimuli Rolling over before 2 months (indicative of hypertonia) Persistent fisting at 3 months
4-6 months	<ul style="list-style-type: none"> Poor head control Failure to smile Failure to reach for objects by 5 months
6-12 months	<ul style="list-style-type: none"> No baby sounds or babbling Inability to localize sounds by 10 months
12-24 months	<ul style="list-style-type: none"> Lack of consonant production Hand dominance prior to 18 months (indicates contralateral weakness) No imitation of speech and activities by 16 months
Any age	<ul style="list-style-type: none"> Loss of previously attained milestones

children may not have regular exposure to elements of the standardized screening tools, these tools may underestimate the knowledge and abilities of children in certain cultures. Cultural practices may influence the “normal” age of development of even basic motor tasks such as crawling and walking. Therefore, whenever possible, a tool that has been researched and validated for use among children of similar backgrounds should be used.

When standardized screening tools are not available, health care providers should at least keep a record of the developmental milestones that have been achieved by their pediatric patients. By identifying children who are not achieving age-appropriate milestones, providers can better recognize those patients who need more intensive evaluations and therapies. Not achieving key milestones by certain ages can be considered “red flags” that should alert medical practitioners to the need for further interventions. Tables 2 and 3 provide basic guidelines regarding normal milestone progression in young children.

Children who fail to reach age-appropriate milestones should be evaluated for conditions that lead to developmental and neurological deficits. Sustained developmental regressions (loss of the ability to perform previously acquired skills) are never normal and should prompt appropriate interventions.

Developmental Delays in HIV-Infected Children

HIV-infected children, especially those with other serious HIV-related symptoms, have a higher

incidence of developmental delays than their non-infected peers. Uninfected children born to HIV-infected mothers, however, achieve developmental milestones at the same rate as children born to uninfected mothers. Significant cognitive and motor deficits have been shown to occur with increased frequency among HIV-infected children, beginning in infancy.²⁵⁻³¹ These abnormalities cannot be accounted for by other biological or environmental risk factors.²⁷⁻²⁹ Children with other serious HIV-related symptomatology are at greatest risk of significant developmental impairments.^{25,30} It has been demonstrated among HIV-infected children in the U.S. that those children with the lowest rates of neuropsychological functioning are at highest risk of rapid HIV disease progression.^{26,31,32} It is not yet known whether developmental deficits would be similarly predictive of HIV disease progression in low-resource populations where factors such as poor nutrition would be expected to further complicate the clinical picture.

While HIV-infected children with the most systemically advanced HIV disease tend to have the most profound developmental delays, significant delays can also be seen in HIV-infected children with otherwise stable clinical conditions.³³ The reasons for discordant control of HIV disease outside and inside the central nervous system are not yet understood. In a few case studies, improvements in functioning were seen when antiretroviral regimens were altered to include drugs with better CNS penetration.³³ Further studies are needed to clarify the best interventions to optimize the care of HIV-infected children with developmental delays.

Review Questions

1. What changes in birth measurements would you expect to see in children born with HIV infection?
2. Why are developmental delays and regressions considered to be important indicators of prognosis in HIV-infected children?
3. What are some ways in which children's development can be assessed by their health care providers?
4. What bone-related problems are seen more frequently in HIV-infected children?
5. What pubertal changes are common among HIV-infected girls and boys?

Exam Questions

1. Assessments for developmental delays in children include all of the following EXCEPT:
 - a. Administering an age-appropriate standardized developmental assessment tool
 - b. Evaluating the child for developmental "red flags"
 - c. Tracking developmental milestones
 - d. Measuring the head circumference
2. Which of the following is true regarding the effects of HAART on growth and development?
 - a. In patients who have shown a significant viral load decrease, HAART has no effect on weight or height.
 - b. Patients on HAART tend to have developmental regression secondary to drug interactions.
 - c. Patients who show a virologic response to HAART usually have an increase in weight and a subsequent increase in height.
 - d. HAART provides no improvement in long-term growth parameters when compared to mono-therapy.
3. Skeletal problems related to HIV infection include which of the following?
 - a. Frequent fractures in young children
 - b. Unusually tall stature
 - c. Low bone density
 - d. Osteonecrosis of the hip
 - e. Both a and c
 - f. Both c and d

Answers: 1d, 2c, 3f

Case Studies

Case Study #1

A mother brings her 16-month-old daughter, Lupita, to clinic for evaluation. Lupita's family is poor and frequently does not have enough nutritious food to eat. Lupita's head circumference is at the 50th percentile for her age. Her height is at the 5th percentile for her age. Her weight is far below normal for a child her age. When you draw a line on the growth chart, you see that Lupita's weight would be at the 50th percentile for a 9-month-old child.

Question: Which of the following would be appropriate to tell the child's mother at this time?

- Her head is too big, and tests need to be done to see why her head is growing so fast.
- You are concerned about her weight and want to see her frequently to make sure that she is gaining weight appropriately.
- It is important to make sure that she is getting enough nutrition to gain weight appropriately.
- If she is sick, treating her illness will help her to gain weight.
- b, c, and d

Answer: e. Children who are sick and malnourished commonly have low weight and height and relatively good head growth. Ensuring that they are getting good nutrition and treating any illnesses they have will help them to grow well. When possible, evaluating growth-delayed children more frequently than normal children will help you to ensure that the delayed children are receiving the best nutrition available to meet their needs.

You question the mother and observe the same 16-month-old child to assess her development. She first began rolling over at 5 months of age. Currently she can sit without support and can pull herself up to a standing position. Occasionally she takes a few steps without support, but she falls down frequently. She

transfers toys from hand to hand and can pick up small objects such as crumbs between two fingers. Although she makes some sounds, she does not babble using consonant sounds, and she does not turn her head when her mother calls her name.

Question: Which of the following assessments and recommendations correspond best with the information provided regarding Lupita's development?

- Her development is remarkably delayed in all areas, and her parents should anticipate that she will never walk well.
- She is meeting all age-appropriate milestones; no further evaluations are needed.
- While her motor skills are appropriate for her age, her communication skills should be better; her hearing should be tested.
- Her gross motor skills are delayed due to malnutrition, and intensive nutritional rehabilitation should be instituted to allow her to catch up with her peers developmentally.

Answer: c. This question demonstrates the importance of evaluating all aspects of a child's development. While children who are malnourished do often have gross motor delays, Lupita does not. Her failure to respond to voices and her immature verbalization skills should alert the clinician to the likelihood of a hearing problem or other communication disorder.

Case Study #2

Lupita's cousin, Maria, is also 16 months old. Maria is HIV-infected but was generally healthy during her first year of life even though antiviral therapy was not available for her. Maria's height and weight are similar to those of her cousin. Her head circumference, however, is far below normal for a child her age. At birth, Maria's head circumference was normal, but her

head seems to have stopped growing over the past six months.

Question: Which of the following is true regarding Maria's head circumference?

- Her poor head growth is a concerning sign and indicates that she is at high risk of poor neurodevelopmental outcomes.
- Because her weight is also low, you can be certain that her small head circumference is due to malnutrition.
- HIV-infected children always have small heads.
- Because her head size was normal at birth, she must have been infected with HIV after birth.

Answer: a. HIV-infected children usually have normal head sizes at birth. The failure of a child's head to continue growing at a normal rate, particularly during the first two years of life, corresponds with an increased risk of developmental delays, regressions, and other neurological problems.

At 1 year of age, Maria's motor skills were normal. She liked to imitate sounds and was able to call her mother and father by name (Mama and Dada). She has lost the ability to do some of the things she was able to do before. She no longer can pull herself to a standing position or sit without support.

Question: All of the following are true regarding Maria's development EXCEPT:

- Developmental regressions are never normal and should always prompt additional evaluations.
- Her development is likely to improve soon without any interventions.
- Her poor head growth may have been an early warning sign that she was at high risk of developmental problems.
- It is likely that her developmental problems are related to her HIV infection and will improve with the institution of HAART.

Answer: b. The recent poor growth and development of this HIV-infected child also indicate that she is at high risk of HIV-disease progression.

Case Study #3

François, a 6-year-old HIV-infected boy, is being followed in your clinic. He has had a number of opportunistic infections, including diarrheal illnesses, dermatitis, and candidiasis. For the past year his height and weight have not increased, but he is not losing weight. You are unable to check his CD4+ count or viral load and are trying to make a decision regarding whether to start this child on HAART.

Question: Which of the following statements provides the best support for an appropriate therapeutic decision for this patient?

- There is no reason to start HAART until the child begins to lose weight.
- HAART should be started because the child has had oral candida.
- HAART should be started because the child has growth failure.
- If his head circumference is normal, then HAART should not be started.

Answer: c. Growth failure is a strong predictor of early demise for HIV-infected children. Head circumference increases rapidly during the first two years of life. A child with later growth failure is not likely to have measurable deficits in head size.

Case Study #4

Vu, a 9-month-old boy, is brought to your clinic for the first time by his maternal grandmother. His mother died of an unknown illness. The grandmother states that the child has been doing well. When questioned further about the development of the child, she says he is unable to sit up without support and cannot roll from front to back. During your examination, you notice that the child is not reaching for toys and cannot bring his hands to the midline. He also has

poor neck control when pulled to a sitting position. The child seems to recognize his grandmother and smiles appropriately.

Question: Which of the following statements best represents the child's developmental assessment?

- a. The child has a significant developmental delay. Evaluations, including HIV testing, need to be started.
- b. The child is at an appropriate developmental stage.
- c. The child is exceeding age-appropriate milestones and needs no further workup.

Answer: a. According to Table 2, the patient is not meeting any of the milestones expected for a 9-month-old child. A child with a significant delay in milestones should have HIV testing as part of the evaluation, especially in areas of high disease prevalence and in cases in which the history is suggestive of exposure.

Case Study #5

Alexandra, a 6-month-old girl known to be HIV-infected, is brought to the clinic for a checkup. Her grandfather tells you that they have been unable to obtain any of her antiretroviral (ARV) medicines, and therefore she has not been taking them. After measuring her head circumference, weight, and height, you notice that her head is <3 percent for age, her weight is 50 percent for age, and her height is 50 percent for age. Looking at her previous growth parameters, you notice that her previous head

circumferences were 25 percent and 10 percent at 2 months and 4 months respectively. Your examination shows that the child is able to roll from front to back, can sit up with support, and babbles.

Question: The best statement concerning the patient's head circumference is that:

- a. Alexandra's head size is appropriate for her age, and there is no reason to be concerned about her development.
- b. Alexandra's head circumference is significantly microcephalic, and she is at higher risk of having abnormal development when compared to children with normal head circumference for age.
- c. Because Alexandra's development is adequate for a 6-month-old child, there is no further need to monitor head growth at follow-up visits.
- d. Alexandra's head circumference is significantly microcephalic, but she is at no increased risk of having abnormal development because she has reached normal developmental milestones up to this point.

Answer: b. Patients infected with HIV who have an abnormally small head circumference have an increased risk of developmental problems and other signs of HIV-related CNS disease. Helping the caretaker obtain the ARVs is of special importance for this patient with falling head circumference. Close monitoring of this patient's development is necessary to ensure timely interventions.

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