

RECOMMENDATIONS FOR MANAGEMENT OF INFANTS BORN TO MOTHERS WITH HIV INFECTION

ARV PROPHYLAXIS

Infants should be administered antiretroviral prophylaxis to reduce the risk of MTCT. Typical options include:

- single-dose (SD) nevirapine (NVP); or
- zidovudine (AZT) for one week;¹ or
- SD NVP plus AZT for one week.*

The exact ARV prophylaxis regimen and timing of administration depends in part on what therapy (if any) mothers received during antenatal care and during labour and delivery. These regimens are summarised in *Chapter VII: Antiretroviral Therapy in Pregnant Women and Prevention of Mother-to-Child Transmission of HIV*.

DIAGNOSIS OF HIV INFECTION IN INFANTS

HIV DNA PCR (polymerase chain reaction) should be performed at age six to eight weeks followed by serial DNA PCRs. Two consecutive positive DNA PCRs are considered diagnostic of HIV infection.

If this is not available, then all children should have HIV ELISA done at age eighteen months. Prior to diagnosis, all children are to be monitored clinically for any signs or symptoms of HIV infection.

The early diagnosis of HIV infection in infants is challenging in resource-constrained countries, both from a diagnostic and therapeutic perspective. Tests for antibodies to HIV do not establish the presence of HIV infection in infants due to the transfer of maternal antibodies; therefore, a virologic test is required. PCR-based techniques that directly detect the existence of HIV in the plasma allow diagnosis by age one month. Approximately 30% of infants with HIV infection will have a positive DNA PCR result from samples obtained before age forty-eight hours, 93% are detectable by age two weeks, and almost all are positive by age one month. A single DNA PCR has a sensitivity of 95% and a specificity of 97% on samples collected after age one month.

Serial qualitative DNA PCR is currently the accepted standard for diagnosis of HIV infection. Two positive assays drawn at separate time points are considered diagnostic of infection.ⁱ Assays that detect HIV RNA in plasma appear to be as sensitive as HIV DNA PCR, with sensitivities of 90% to 100% by age two to three months. Specificity is also comparable. Some clinicians choose to use an HIV RNA assay as the confirmatory test for infants testing HIV DNA PCR-positive. HIV culture can also be used for diagnosis but is more complex and expensive to perform, and definitive results are not available for four weeks. The use of p24 antigen testing alone is not recommended because of the high frequency of false-positive assays.ⁱⁱ

Although breastfeeding is discouraged in HIV-exposed infants in the Caribbean, if mothers still choose to breastfeed, it should be noted that the risk of HIV infection continues throughout the entire duration of breastfeeding. Therefore, a negative virologic test in early infancy does not negate the possibility of infection occurring subsequently if breastfeeding continues.

Ideally, prenatal HIV testing would identify infants born to infected mothers, and DNA PCR of these infants would identify those who are HIV-infected in early infancy. However, within the developing world, such as the Caribbean, tests that directly measure the presence of HIV itself

¹Consider an extended course (four to six weeks) of AZT therapy for the infant if the mother received less than four weeks of prepartum ART.

(e.g. p24 antigen, or DNA or RNA PCR testing) are expensive and inaccessible to many. When early diagnosis is not possible, clinical parameters are used to assess the possibility of HIV infection. The most common signs of HIV infection in infants include failure to thrive, hepatosplenomegaly, and diffuse adenopathy. HIV-infected children may also present with frequent or chronic diarrhoea, frequent minor bacterial infections such as otitis media and sinusitis, refractory thrush, and severe refractory non-infectious skin manifestations.

The WHO has formulated both a case definition and a staging system for AIDS, given the challenges in resource-poor settings regarding diagnosing HIV infection in children prior to age eighteen months (see *Appendix A* and *Appendix B*).ⁱⁱⁱ The WHO recognises that the current staging system for HIV infection in children has its limitations, and is currently revising its staging system, since many of the clinical symptoms in the paediatric stages are not specific for HIV infection and may overlap those seen in children without HIV infection in resource-limited settings.^{iv} The U.S. Centers for Disease Control and Prevention (CDC) has also developed a surveillance definition for AIDS without laboratory evidence of HIV infection, as summarised in *Appendix C*.^v Despite the possible overlap with other infections, until a definitive diagnosis can be made, the use of these clinical classifications can be useful in helping to define the parameters for initiation of HAART.

PROPHYLAXIS AGAINST PNEUMOCYSTIS JIROVECI (FORMERLY PNEUMOCYSTIS CARINII) PNEUMONIA (PCP)

The majority of paediatric PCP cases occur during the first year of life and may occur before HIV infection is documented or a decline in the CD4+ T cell count is observed. PCP prophylaxis is therefore recommended for all HIV-infected infants as well as for those whose HIV status is indeterminate.^{vi} Prophylaxis is initiated at age four to six weeks, following the completion of AZT prophylaxis, and continued until it is established that the child is not HIV-infected.

Trimethoprim-sulfamethoxazole (TMP-SMX; co-trimoxazole) is the agent of choice. Several dosing options can be recommended:

- TMP-SMX, 5mg/kg/day of the TMP component administered orally in divided doses twice daily and administered seven days per week;
- TMP-SMX, 5mg/kg/day of the TMP component administered orally divided twice daily and administered three times per week on alternate days (e.g. Monday-Wednesday-Friday);
- TMP-SMX, 5mg/kg/day of the TMP component administered orally in divided doses twice daily and administered three times per week on consecutive days (e.g. Monday-Tuesday-Wednesday);
- TMP-SMX, 5mg/kg/day of the TMP component administered orally as a single daily dose and administered three times per week on consecutive days (e.g. Monday-Tuesday-Wednesday).

No data from randomised clinical trials exist to guide the clinician in deciding between daily versus thrice-weekly dosing of TMP-SMX. Theoretically, daily dosing has the added advantage of offering the infant more protection against other pathogens such as *T. gondii* and some bacterial infections. However, daily TMP-SMX dosing may result in a higher incidence of bone marrow toxicity than thrice-weekly dosing. United States treatment guidelines endorse the thrice-weekly regimen as the preferred dosing schedule, whereas the WHO generally recommends daily dosing. Current practices in the Caribbean vary as well: the Bahamas uses thrice-weekly dosing, whereas Jamaica reports excellent outcomes using daily dosing (personal communications, P. McNeil and C. Christie).

If TMP-SMX is not tolerated, children age one month or older can be given dapsone, dosed at 2mg/kg (max 100mg) by mouth daily or 4g/kg (max 200mg) by mouth weekly.

IMMUNISATIONS

Immunisations for children who are HIV-infected (or HIV-exposed with unknown status) differ from those who are not immunocompromised. The section entitled *Recommendations for Use of Specific Vaccines in HIV-Infected Individuals* in *Chapter VI: Recommendations for Adult and Paediatric Opportunistic Infections Prophylaxis* summarises the vaccination schedule for HIV-infected and HIV-exposed infants. Live vaccines are generally contra-indicated with the following exceptions: the measles, mumps and rubella (MMR) vaccine is recommended if the child is not severely immunocompromised; the varicella (VZV) vaccine should be considered if the CD4+ T cell percentage is $\geq 25\%$;^{vii} and the oral polio vaccine (OPV) may be used for asymptomatic children if the inactivated polio vaccine (IPV) is not available.

GROWTH AND NUTRITION

Growth failure is a prominent feature of HIV infection; hence, nutritional assessment is important both as a diagnostic marker (when HIV status is unknown) and to maximise growth in infected children.^{viii}

FOLLOW-UP CARE

Close monitoring of HIV-exposed and -infected infants is critical.

Prior to Discharge from Hospital

- Infants should be reviewed prior to discharge by a paediatrician or the most senior available clinician.
- Infants should be docketed and clinic follow-up ensured.
- Mothers should be taught how to administer ARV prophylaxis to their infants.
- Any issues that may prevent adherence to ARVs or to prophylactic medications should be investigated and addressed.
- A supply of replacement feeds should be provided to mothers and a date for an appointment with the nutritionist established.

Follow-Up in One to Two Weeks

- Routine physical examination of infants should be performed, including growth parameters.
- Adherence to ARV prophylaxis should be ensured.
- Any evidence of side effects of ARV prophylaxis should be monitored.
- Mothers should be advised to continue formula feeds and ensure hygienic preparation of same.
- Any concerns of the parents should be accessed and addressed.

Follow-Up at Six Weeks to Two Months

- Routine physical examination of infants should be performed.
- Growth and development should be assessed.
- ARV prophylaxis should be discontinued.
- TMP-SMX prophylaxis should be commenced, using one of the dosing options outlined on page VIII-5. TMP-SMX prophylaxis should be continued until it is established that the child is HIV-negative.

- Iron and vitamin supplementation should also be commenced.
- Blood samples for HIV DNA PCR testing should be drawn.
- Blood samples for other tests should be drawn, e.g. CBC and differential, TORCH screen, VDRL, and Hepatitis BsAg and HTLV-1 serology, as appropriate.
- Vaccination with pentavalent (DPT, Hib, and Hepatitis B (HBV)) and polio should be started. IPV is preferred, but if IPV is not available, OPV may be administered to asymptomatic infants.
- Continuation of formula feeds should be advised.
- Any medical problems should be treated.
- Any concerns of the parents should be accessed and addressed.

Follow-Up at Four Months

- Routine physical examination of infants should be performed.
- Growth and development should be assessed.
- Second dose of vaccinations should be given.
- Blood sample for second HIV DNA PCR testing should be drawn.
- TMP-SMX prophylaxis should be continued.
- Iron and vitamin supplementation should be continued.
- Continuation of formula feeds should be advised.
- Any medical problems should be treated.
- Any concerns of the parents should be accessed and addressed.

Follow-Up beyond Four Months

Ideally, HIV-exposed children should be followed up by a comprehensive team of paediatricians, nurses, and nutritionists. The routine follow-up schedule is similar to that of children who are not exposed to HIV. Subsequent to the four-month visit, patients should be seen again at age six months, then at three-month intervals or more frequently if indicated.

At Each Visit:

- Routine physical examination of infants should be performed.
- Growth and development should be assessed.
- Appropriate diet should be ensured.
- Adequate vaccination coverage should be ensured.
- TMP-SMX prophylaxis should be continued.
- Iron and vitamin supplementation should be continued.
- Any evidence of HIV or opportunistic infections (OIs) should be monitored.
- Any medical problems should be treated.
- Any concerns of the parents should be accessed and addressed.

Baseline follow-up physical examinations include temperature; measurement of weight, height, and head circumference (monitor on growth charts); and examination for thrush, adenopathy, skin

eruptions, ear, nose, and throat infections, chest infections, abdominal organ enlargement, and neurological and developmental abnormalities.

ⁱAAP. 2000. 2000 Red Book: Committee on Infectious Diseases, 25th Edition. Elk Grove Village, IL: American Academy of Pediatrics **and** The Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the use of antiretroviral agents in paediatric HIV infection. November 26, 2003. Available at: <http://AIDSinfo.nih.gov>. Accessed 2004.

ⁱⁱThe Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, 2003.

ⁱⁱⁱPan American Health Organisation. Case definition: acquired immune deficiency syndrome (AIDS) *Epidemiological Bulletin* June 2001;22(2):about 2p. Available at: <<http://www.paho.org/English/DD/AIS/beindexe.htm>>. **and** World Health Organisation. Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach: 2003 revision. Geneva: World Health Organisation, 2003.

^{iv}WHO, 2003.

^{vv}PAHO, 2001.

^{vi}Pavia A. Primary Care of Infants and Children with HIV. In *HIV InSite Knowledge Base*, 1 Peiperl, P Volberding (eds.). Online textbook of HIV disease from the University of California San Francisco and San Francisco General Hospital. July 2001. Available at <http://hivinsite.ucsf.edu/InSite.jsp?doc=kb-03-01-14> **and** Working Group on PCP Prophylaxis for Children. 1995 revised guidelines for prophylaxis against *Pneumocystis carinii* pneumonia for children infected with or perinatally exposed to human immunodeficiency virus. *MMWR Wkly* [serial on the Internet] 28 Apr 1995 [cited 2004] 44(RR-4):1-11. Available at <<http://wonder.cdc.gov/wonder/prevguid/m0037275/m0037275.asp>>.

^{vii}AAP, 2000.

^{viii}Pavia, 2001.