

Recommendations on the Management of HIV Infection in Infants and Children

**Scientific Committee on AIDS
of
Hong Kong Advisory Council on AIDS
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About the Scientific Committee on AIDS

The Scientific Committee on AIDS (SCA) works on the scientific, technical, professional and surveillance aspects of HIV/AIDS. It was renamed from the former Scientific Working Group on AIDS in 1990 to give it equal status to the other two committees under the Advisory Council on AIDS (ACA). It is now in its fourth term of ACA (1999-2002), with its first meeting held on 19 November 1999.

SCA has the following terms of reference:

- (a) to evaluate the HIV/STD surveillance system in Hong Kong;
- (b) to develop and recommend technical and professional guidelines/protocols on HIV/AIDS prevention, management and control;
- (c) to provide scientific and clinical input to the process of planning and development of services in HIV/AIDS prevention, management and control, and the training of health and community care workers; and
- (d) to recommend and coordinate researches on the clinical, scientific, epidemiological and sociological aspects of HIV/AIDS with special reference to Hong Kong.

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INTRODUCTION

1. In Hong Kong, the number of known infections in children has remained small. A majority of the infected children in the mid- and late- nineteen eighties were haemophiliacs or recipients of contaminated blood. Mother-to-child transmission is now the single most important mode of HIV infection in children in Hong Kong. Worldwide, it accounts for over 90% of all paediatric HIV infections.

2. Early identification of human immunodeficiency virus (HIV)-infected pregnant women prior to delivery could effectively reduce perinatal transmission of the infection. However, treatment of HIV-infected women will not completely eliminate all mother-to-child infections. The proportion of infections occurring in utero is estimated to be approximately 25% to 40% among children who are not breast-fed. (1) Mathematical modelling suggests that much of this in utero transmission occurs relatively late in gestation. (2) The absolute risk for in utero transmission is estimated to be 5% or 6%, and for intrapartum transmission, approximately 13% to 18%. Therefore, a small number of infants may still be infected before the diagnosis of the mother. Another reason of perinatal infection is that not all HIV-infected pregnant women may be diagnosed and can receive therapy in time.

3. Advances in HIV treatment are changing the landscape of HIV/AIDS in the clinical setting. Prior to effective viral suppressive therapy, a majority of the infected infants developed marked immunosuppression and AIDS-defining conditions by approximately seven years of age. Pneumocystis carinii pneumonia (PCP), HIV encephalopathy, developmental delay, failure to thrive and recurrent bacterial infections were commonly observed problems. Today, children receiving antiretroviral agents often have different clinical and pharmacokinetic profiles, and have slightly different side effects as compared to adults.

4. The current set of recommendations is developed by the Scientific Committee on AIDS (SCA)* to suggest a standard approach in the management of infants and children perinatally exposed and/or infected with HIV, based on scientific evidence and a review of international experience and recommendations. (3,4,5). However, since HIV research in children usually lags behind that in adults, some recommendations have been extrapolated from adult data. A local perspective is nevertheless adopted in the preparation of the document. This document supersedes the SCA Guidelines on Management of HIV infection Children published in 1995.

PRINCIPLES

* Dr Susan Chiu of the Department of Paediatrics, The University of Hong Kong assisted in the preparation of the recommendations, in association with the clinical team of the Integrated Treatment Centre, Department of Health, Hong Kong. This publication supersedes the previous version dated July 2001.

5. The guiding principles in the following recommendations are:
- (a) HIV-exposed or infected children should be evaluated as soon as possible after birth for the diagnosis of HIV infection.
 - (b) Postnatal antiretroviral treatment should be completed according to the perinatal prophylaxis regimen chosen for the mother.
 - (c) Prophylaxis against PCP should normally be commenced at 6 weeks of age for an infant born to an HIV-infected mother.
 - (d) Early treatment of HIV-infected infants regardless of clinical and immunologic parameters is the preferred approach for achieving viral suppression. Other options exist and shall be considered in clinical context and in consideration of issues relating to adherence.
 - (e) Childhood immunisation is an important part of the clinical management for HIV infected children, the practice of which is similar to that for healthy infants and children with slight adjustment.
 - (f) Highly Active Antiretroviral Therapy (HAART) is the standard in management of HIV-infected children, if antiretroviral therapy is indicated.
 - (g) A multispecialty, multidisciplinary approach involving the following expertise is needed for the comprehensive care of HIV-infected children: paediatric infectious disease, paediatric neurology, paediatric cardiology, nursing, social work, psychology, nutrition, and pharmacology. Life-long continuous care is recommended.
 - (h) Recommendations for therapy and management will have to be updated frequently as the management of HIV infection in infants, children and adolescents is rapidly evolving and becoming increasingly complex.
 - (i) A mechanism shall be in place to enhance the local knowledge-base in HIV management in children, and the exposure (infection or otherwise) of children to antiretroviral treatment.

DIAGNOSIS OF HIV INFECTION IN CHILDREN

6. Diagnosis of HIV infection in perinatally exposed children can be made by the culture of peripheral blood mononuclear cells (PBMC) or HIV DNA polymerase chain reaction (PCR). International literature has recommended DNA PCR as the virologic method for early diagnosis of HIV infection in infants. The test, if available, should be performed within the first 48 hours of life. This method has very good sensitivity and specificity for detecting the presence of the virus within PBMCs. The sensitivity of the HIV DNA PCR has been studied: 38% of infected infants were positive within 48 hours of life, 93% were positive by 14 days of age, and 96% were positive by 4 weeks of age. Infants with 2 positive results can be determined to be infected. (6) Infants with negative tests during the first 6 weeks of life should be re-tested between 1 to 2 months of age, and again between 4 to 6 months of life. (4) Initially there was concern that prophylactic antiretroviral treatment of the infant might interfere with the early diagnosis of

HIV infection. However, to date, zidovudine (ZDV) has not been shown to decrease the sensitivity and predictive values of virologic assays. (4,7)

7. Currently, both HIV culture and HIV DNA PCR are not available as routine diagnostic tests. In clinical practice, HIV RNA PCR assay is recommended as the alternative for diagnostic purpose in Hong Kong. The latter assay is available in clinical laboratories and can be used to test for plasma virus. There has been concern about potential false-positive results near the assay's limit of detection. (8,9,10) In all circumstances, clinical correlation and the advice of virologist should be sought in the interpretation of the results.

8. A child born to an HIV-infected mother is considered uninfected if
- (a) there is no clinical evidence of HIV infection, and
 - (b) in the absence of breastfeeding, 2 or more virologic determinations (culture or PCR) are persistently negative, both of which are performed at 1 month of age or older, and one of which is performed at 4 months of age or older, or
 - (c) 2 negative HIV antibody tests at least 1 month apart, performed at greater than 6 months of age.(6)

CARE OF INFANT BORN TO AN HIV-INFECTED MOTHER

Antiretroviral therapy

9. All infants born to HIV-infected women who have been started on the ACTG 076 prophylaxis regimen should receive a 6-week course of oral ZDV. ZDV is also recommended for the infant born to an HIV-infected woman who has received no antiretroviral therapy during pregnancy or delivery.(11) Alternatives include the use of nevirapine or ZDV/ lamivudine (3TC) combination or ZDV/nevirapine combination. If the mother is not diagnosed until labour and has received an alternative antiretroviral prophylaxis regimen, the infant should receive the same antiretroviral agent according to the regimen. Breastfeeding by their HIV-infected mothers is contraindicated in Hong Kong since there are safe alternatives to breast milk. (refer to the Scientific Committee on AIDS Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission published in April 2001) (12)

Laboratory monitoring

10. Complete blood picture (CBP) and differential count should be performed on the newborn as a baseline evaluation before administration of ZDV. Anaemia is the primary short-term complication of the 6-week ZDV regimen in the neonate. Repeat measurement of haemoglobin is required during and after the completion of the regimen. Infants who have anaemia at birth or who are premature warrant more intensive monitoring.

11. CD4+ lymphocyte count and percentage should be monitored at 1 and 3 months of age and then continued at 3-month-interval until HIV infection in the infant can be ruled out.

12. Quantitative immunoglobulins should be measured when the infant is 4 to 6 months of age.

Prophylaxis for *Pneumocystis carinii* pneumonia (PCP)

13. PCP used to be the most common AIDS presenting illness in children before the days of effective antiretroviral therapy. It occurs most often between 3 and 6 months of age when many HIV-exposed infants have not yet been identified as being infected. In 1995, CDC revised the recommendation for PCP prophylaxis in HIV-exposed infants. (13) (Table 1) All infants born to HIV-infected women should begin prophylaxis at 6 weeks of age, following completion of the ZDV prophylaxis regimen, regardless of CD4+ lymphocyte counts or percentage. The drug regimens are shown in Table 2.

CARE OF THE HIV-INFECTED INFANT OR CHILDREN

14. The following recommendations apply to all newly diagnosed HIV infected children. Once HIV infection is established in a child, the following initial steps should be taken:

Complete and detailed medical history and physical examination

15. Depending on the individual situation, baseline assessment of the child and family may be done in the inpatient setting. This approach has several advantages: more time can be spent during the initial encounter between the family and the medical team; the family can familiarise themselves with the medical team and the hospital; doctors and nurses can observe the social dynamics of the family; and the initiation of antiretroviral drugs can be supervised and monitored.

16. Attention should be paid to clinical symptoms commonly seen in HIV infection, e.g., failure to thrive, developmental delay, lymphadenopathy, hepatomegaly, splenomegaly, candidiasis. The clinical categorisation of paediatric HIV infection is detailed in Table 3. If the child is the first member of the family diagnosed with HIV infection, both parents and other siblings should also be counselled and evaluated for HIV infection.

Baseline and follow-up investigations

17. The main investigations are T cell subset enumeration and viral load measurement. Other investigations are also included in this section.

(a) T-cell subsets

Absolute CD4+ lymphocyte number and percentage are surrogate markers of disease progression in HIV infection and should be monitored. Profound decrease in CD4+ lymphocyte counts in the first year of life signifies rapid progression of HIV disease and indicates the immediate need for highly active antiretroviral therapy (HAART). The immunological classification system for HIV infection in children is in Table 4.

(b) HIV virus load

Quantification of free virus in plasma can be performed using HIV RNA assays. The dynamics of HIV RNA burden observed in infants is very different from that of adults. Perinatally infected infants exhibit primary HIV viraemia in the first month of life when they have a relatively immature system. They exhibit an extremely high plasma virus load, commonly greater than 10^6 copies/ml plasma by HIV RNA PCR. Over time the virus load tends to fall. In general, elevated HIV RNA viral load after the first month of life correlates with rapid disease progression, although some children with high HIV RNA levels in the first year do not progress as rapidly. (14,15,) Due to considerable inpatient biologic variability in HIV RNA levels, only changes greater than 0.7 log in HIV RNA viral load in children under 2 years and those greater than 0.5 log in children older than 2 years should be considered significant.

(c) Other laboratory investigations

Baseline assessment includes CBP with differentials, liver and renal function tests, amylase, lipid, lipase levels, lactate dehydrogenase and quantitative immunoglobulins. Baseline antibody titres should be considered for toxoplasma, cytomegalovirus (CMV), Epstein-Barr virus, varicella-zoster virus, herpes simplex virus (HSV) and hepatitis viruses. Initial titres drawn at the neonatal period would reflect the immune status of the mother. Repeat testing should be done at 12 months of age and then annually if they are negative. The results provide information about these children's exposure and susceptibility to specific infection. For example, CMV negative HIV infected children should receive CMV negative blood in the case of transfusion and if unavailable, leukofiltered blood should be used if possible. For older children, functional antibodies against common antigens could be assessed. This is usually achieved by measuring their immune status after routine immunisation, e.g. IgG against measles and tetanus. Since primary CMV infection in the first months of life has been associated with an increase in HIV replication, urine culture for CMV may also be obtained in the first 6 months of age.

(d) Other evaluations

i) Chest X-ray – A baseline chest X-ray (CXR) should be obtained and then annually even in asymptomatic children. This test identifies mediastinal enlargement, lung lesions, lymphoid interstitial pneumonitis (LIP) and cardiomegaly. Patients with chronic lung changes should also have oxygen saturation measured at every visit.

- ii) Cardiac assessment – HIV cardiomyopathy starts early in life. When patients are examined by ECG or during autopsy, cardiac abnormalities are detected more often than expected from physical examination. A study on HIV-infected children using ECG has shown that subclinical cardiac abnormalities are common, which may be persistent and often progressive. (16) A baseline and annual cardiac assessment that includes at least a CXR and an ECG is recommended.
- iii) Visual screening - Children who can cooperate with the examiner should have an annual ophthalmology examination. Children with immune category 3 (table 4) should preferably be examined by an ophthalmologist every 6 months, especially if they are seropositive for toxoplasmosis or CMV.
- iv) Neurodevelopmental assessment - For older children, as well as young infants with neurologic deficits, imaging of the brain (MRI or CT) should be performed at baseline for evaluation of possible brain atrophy. Older children are referred for a baseline neurodevelopmental assessment by a neurologist. Infants can be referred after 6 months of age if there are no neurologic symptoms, and earlier if they are symptomatic.
- v) Psychosocial assessment - The diagnosis of HIV infection in a child is very devastating for a family. Since the care of an HIV-infected child is a chronic issue, clinicians should aim to establish a long-term relationship with the patient and the family. The establishment of trust and rapport greatly improves adherence to medical treatment. The family should be assessed by the medical social worker to address the needs for social service or financial support. Members of the family should be offered referral to the clinical psychologist as appropriate.

Antiretroviral Therapy

18. The goals of antiretroviral therapy include:

- (a) Life prolongation
- (b) Prevention of disease progression
- (c) Maintenance or improvement of quality of life.

19. Based on our current understanding of the viral dynamics and disease pathogenesis, the best way to achieve these goals is to suppress HIV replication to very low levels indefinitely. Since drug resistance and virologic failure may be inevitable if viral replication persists in the face of therapy, the immediate goal of therapy should be complete viral suppression. With the implementation of universal testing of pregnant women for HIV infection, most HIV infants can be diagnosed in the first month of life. With the commitment of child carers to adherence to long-term therapy, early treatment of these recently infected infants offers the best chance for complete viral suppression. Initiating therapy very

early in primary infection may also prevent the spread of HIV to long-lived reservoirs like memory CD4+ T lymphocytes.

20. Since the selection for resistant virus by non-adherence may be worse than ongoing replication of untreated wild type virus, the caregivers need to have a good understanding of the importance of adherence before initiating therapy. It is usually a struggle to administer medications to young children and it is not uncommon that they spit out unpalatable medications. Caregivers should be advised to contact the clinicians immediately if the child repeatedly vomits the antiretroviral drugs. It must be emphasised that the effectiveness of an antiretroviral regimen is directly related to adherence.

21. The following are the recommended principles in the use of antiretroviral treatment in infants and children, and the rationale involved.

- (a) Early treatment of all infants under 12 months of age recently diagnosed of HIV infection is recommended.

Although only limited data are available on the effectiveness of early combination antiretroviral therapy in children, studies on primary infection in adults have demonstrated that early aggressive treatment might preserve immune function, decrease viral seeding, lower the viral set point. Recent data from a multicentre observational cohort study suggest that infected children exposed to ZDV during pregnancy or birth had more rapid disease progression if effective multidrug therapy was not initiated.⁽¹⁷⁾ These studies lend support to the early treatment of HIV infected infants

- (b) All HIV infected children with clinical symptoms of HIV infection (clinical categories A, B or C) or evidence of immune suppression (immune categories 2 or 3) (Table 3 and 4) should be treated, regardless of age or virus load. ⁽¹⁸⁾

It is recommended that all immunologic and clinical symptomatic HIV-infected children be treated as soon as possible.⁽⁴⁾

- (c) Antiretroviral therapy should be initiated in infected children aged ≥ 1 year regardless of age or symptom status.

One option (the preferred approach) is to initiate therapy in all HIV-infected children, regardless of age or symptom status. Such an approach would ensure treatment of infected children as early as possible in the course of disease with the highest chance of intervening before immunologic deterioration.

- (d) Although early initiation of antiretroviral therapy is favoured, there are situations when deferment of treatment can be considered.

In asymptomatic children aged ≥ 1 year with normal immune status and a low viral load in whom the risk for clinical disease progression is considered low, and when other factors including the issues of drug safety and concern for adherence due to unreliable caregivers, postponing treatment may be justified. When treatment is deferred, antiretroviral therapy should be initiated when i) HIV RNA levels increase significantly (> 0.7 log in

children under 2 years and >0.5 log in children over 2 years), ii) CD4+ decline into category 2, iii) development of HIV related symptoms, iv) HIV RNA $>10^5$ copies/ml in any child or v) in children older than 30 months who have HIV RNA levels $> 10^4$ copies/ml.

- (e) The regimen should be effective in achieving a sustained viral suppression and the side effects should be tolerable.

Antiretrovirals will need to be administered for many years, if not life-long. The choice of initial therapy needs to take several issues into consideration. Potential limitations in subsequent treatment options due to cross-resistance should it occur would also need to be taken into consideration.

- (f) Highly Active Antiretroviral Therapy (HAART) is indicated

When antiretroviral treatment is indicated, the highly active anti-retroviral therapy (HAART) should be prescribed. The recommended regimen includes 2 nucleoside reverse transcriptase inhibitors (NRTIs) and 1 protease inhibitor (PI). The rationale for the choice is to attain maximal suppression of virus replication. This approach has been successful in children with reduction of HIV RNA to undetectable levels. (19,20,21) While waiting for more clinical trials of antiretroviral drugs on children, some information regarding the efficacy of these drugs can be extrapolated from trials involving adults. The absence of clinical trials addressing paediatric-specific manifestations of HIV infection does not preclude the use of any approved antiretroviral drug in children. All antiretroviral drugs approved for treatment of HIV infection may be used for children when indicated — irrespective of labelling notations. The characteristics of antiretroviral drugs are listed in Table 5, 6 and 7.

For clinicians and patients who prefer to spare the use of protease inhibitors, an option is to initiate therapy with 2 NRTIs with a non-analogue nucleotide reverse transcriptase inhibitor (NNRTI), e.g., nevirapine.

Prophylaxis for PCP

22. The recommendations are covered earlier (paragraph 13).

Prevention of other opportunistic infections

23. Caregivers play a role in preventing opportunistic infections in the infants. Caregivers should be advised to avoid consumption of raw or undercooked meat, seafood or poultry, unpasteurised milk products as well as food prepared under doubtful hygiene conditions to decrease the risk of enteric infection. They should also be advised of the potential risks of infection from pets, e.g. cats that can transmit toxoplasma and bartonella, and turtles and reptiles that can transmit salmonella. Exposure to young farm animals should also be avoided to reduce the risk of cryptosporidiosis. On the other hand, HIV infected children should not drink or swim in lake or river water to reduce the risk of Cryptosporidium or Giardia infection. Practice of good handwashing and personal hygiene should be emphasised.

IMMUNISATION

Active immunisation

24. HIV-exposed and infected infants and children should receive standard paediatric immunisations with a few exceptions. Inactivated polio vaccine (IPV) should be given instead of the live oral polio vaccine (OPV). OPV-1 routinely given to all local newborns confers marginal benefit nowadays as compared to the situation in the sixties. Given its potential hazard to the HIV infected babies and their households, it is recommended that the first dose of OPV-1 routinely administered after birth prior discharge be omitted in babies born to HIV infected mothers (irrespective of whether the baby is infected). For infected children, IPV should continue to be used in the subsequent polio vaccination according to the schedule as for the normal children. If the child is ultimately found not to be infected, yet lives in a household with an immunocompromised person, polio vaccination should be continued with IPV.

25. Measles-mumps-rubella (MMR) vaccination is recommended for HIV-infected children who are not severely immunocompromised (CDC immune category 3)(22). This is due to the concern of possible dissemination of live attenuated vaccine viruses. Varicella vaccine should be considered in HIV-infected children with a CD4 T-lymphocyte percentage of $\geq 25\%$. Eligible children should receive 2 doses 3 months apart. (23). Influenza vaccine should be given seasonally and repeated annually for children who are at least 6 months of age and are infected (24,25,26) with HIV. Hepatitis A is prevalent in Hong Kong, with over 90% of adults above 40 years of age seropositive. There is no data to suggest that hepatitis A causes increased morbidity in HIV-infected individuals. Hepatitis A vaccination should therefore be considered on an individual basis (27).

26. HIV-infected children are at increased risk for infection by encapsulated organisms. Although a recent study found that less than a third of children with HIV had a detectable antibody response 6 weeks following vaccination, HIV-infected children should be immunised with the currently available 23-valent polysaccharide vaccine at 2 years of age with a booster dose 3-5 years after the first dose. When more information is available regarding the applicability of the currently licensed heptavalent conjugate pneumococcal vaccine in Hong Kong, immunisation with the conjugate pneumococcal vaccine should be considered. Conjugate Haemophilus influenzae type b vaccine should also be given according to schedule starting at 2 months of age.

27. Concern has been raised about the occurrence of disseminated BCG infection in HIV-infected infants immunised with BCG. However, in countries where the prevalence of tuberculosis is high, the World Health Organization recommends that BCG vaccination for infants at birth should be a standard practice and this applies to asymptomatic HIV infected infants on a risk-benefit basis (28). BCG is therefore recommended to all infants born to HIV-infected

mothers in Hong Kong. Summary of the recommended immunisation programme for the local children with HIV infection is shown in table 9.

Passive immunisation

Immune Globulin Intravenous (IGIV) Therapy

28. Double-blind, placebo-controlled trials have demonstrated that intravenous immune globulin reduces serious and minor bacterial infections and hospitalisations in HIV- infected children with early or advanced disease (29,30,31). IGIV at a dose of 400 mg/kg given every 4 weeks is recommended for HIV-infected children with the following:

- a) hypogammaglobulinaemia (IgG <250 mg/dL);
- b) recurrent, serious, bacterial infections (defined as 2 or more serious bacterial infections such as bacteraemia, meningitis, or pneumonia during a 1-year period), although IGIV may not provide additional benefit to children who are receiving daily trimethoprim-sulfamethoxazole (TMP-SMX); or
- c) failure to form antibodies to common antigens (eg., tetanus, measles, polio).

However, it should be noted that IGIV therapy inhibits response to MMR and pneumococcal vaccines.

29. Since HIV infected children do not have a reliable immune response to vaccination, therefore, for those children who are exposed to measles, varicella or zoster should receive IG prophylaxis and tetanus immune globulin should be administered to an HIV-infected child with a tetanus-prone wound regardless of immunisation status (27). However, children who have received IGIV or VZIG within 2 weeks of exposure do not require additional passive immunisation. The recommendations are summarised in table 10.

Nutrition

30. Breastfeeding by an HIV-infected mother carries a 16% excess risk of HIV infection for the infant and should be avoided. Wasting syndrome is a significant problem in HIV infected children, accounting for 17% of the reported AIDS-defining condition in the US in 1994. HIV-infected children require high-energy, high-protein, nutrient-dense diets. Depending on the child's ambulatory and clinical status, energy needs range from 75% to 150% of the recommended daily allowance (RDA) and protein needs should be between 100% and 150% of the RDA to support the immune system and avoid muscle wasting. (32) For early intervention, all infants and children diagnosed of HIV infection should receive a baseline nutritional assessment within 3 months of diagnosis with follow-up every 1 to 6 months depending on the child's status.

CARE OF ANTIRETROVIRAL EXPOSED, UNINFECTED CHILDREN

31. There are theoretical concerns of potential carcinogenicity of the nucleoside analogue antiretroviral drugs used in children postnatally and/or in utero exposure of ZDV or other antiretroviral agents. NRTIs may inhibit DNA polymerase gamma, a specific mitochondrial enzyme that controls mitochondrial DNA replication. In vitro, the NRTIs have demonstrated significant mitochondrial toxicity, with the eventual development of myopathy. ZDV use during pregnancy has also been associated with the development of mitochondrial toxicity among newborns. The concern for this and other yet unknown potential adverse effects have led clinicians to propose that children with antiretroviral exposure should be followed up into adulthood.(33) Long-term follow-up should include annual physical examination; and for older adolescent females, gynaecologic evaluation with pap smears has been proposed by some experts. A mechanism to evaluate antiretroviral exposed children in Hong Kong should be considered.

Appendix

Table 1. Recommendations for PCP Prophylaxis and CD4+ Lymphocyte Monitoring for HIV-Exposed Infants and HIV-infected Children by Age and HIV Infection Status

Adapted from: CDC. 1995 revised guidelines for prophylaxis against PCP for children infected with or perinatally exposed to HIV. *MMWR* 1995;44:RR-4

Age and HIV Infection Status	PCP Prophylaxis	CD4+ Monitoring
Birth to 4-6 wk, HIV-exposed	None	1 m of age
4-6 wk to 4m, HIV-exposed	Prophylaxis	3 m of age
4-12 m, HIV-infected or indeterminate	Prophylaxis	6,9 and 12 m of age
HIV infection reasonably excluded	None	None
1-2 y, HIV-infected	Prophylaxis if CD4+ count < 750 cells/ μ L in first 12m or <500 cells/ μ L at 12-24m, or CD4+ percentage < 15%	Every 3-4 m
2-5y, HIV-infected	Prophylaxis if CD4+ count < 500 cells/ μ L or CD4+ percentage < 15%	Every 3-4m
6-12y, HIV-infected	Prophylaxis if CD4+ count <200 cells/ μ L or CD4+ percentage < 15%	Every 3-4 m
Any age, HIV-infected, prior PCP	Prophylaxis till adulthood and lifelong prophylaxis should refer to latest recommendation for adults with HIV infection	Every 3-4 m

Table 2. Drug Regimens for PCP Prophylaxis for Children

Adapted from: CDC. 1995 revised guidelines for prophylaxis against PCP for children infected with or perinatally exposed to HIV. *MMWR* 1995;44:RR-4

Recommended regimen
TMP-SMX [♣] , 150 mg/m ² /d (or 5 mg/kg/d) of trimethoprim with 750 mg/m ² /d (or 25 mg/kg/d) of sulfamethoxazole, divided BD PO, 3×/week on consecutive days
Acceptable alternative TMP-SMX dosage schedules
150 mg/m ² /d of trimethoprim with 750 mg/m ² /d of sulfamethoxazole QD PO, 3×/week on consecutive days
150 mg/m ² /d of trimethoprim with 750 mg/m ² /d of sulfamethoxazole, divided BD PO 7 days/week
150 mg/m ² /d of trimethoprim with 750 mg/m ² /d of sulfamethoxazole, divided BD PO, 3x/week on alternate days
Alternative regimens when therapy with TMP-SMX is not tolerated*
Dapsone, 2mg/kg (not to exceed 100 mg), QD PO
Aerosolised pentamidine (for children ≥ 5y), 300 mg via Respigard II inhaler, once a month
If neither dapsone nor aerosolized pentamidine is tolerated, some clinicians administer 4 mg/kg of pentamidine intravenously every 2 or 4 weeks

♣ TMP-SMX indicates trimethoprim-sulfamethoxazole

* There is no official recommendation on children with G6PD deficiency

Table 3. Revised HIV Paediatric Classification System: Clinical Categories

Adapted and modified from:

- CDC. 1994 revised classification system for HIV in children less than 13 years of age. MMWR1994;43:RR-12
- Scientific Committee on AIDS. Guidelines on management of HIV infection in children. (revised edition) Hong Kong: Advisory Council on AIDS, 1995.
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Category N: Not Symptomatic
Children who have no signs or symptoms arising from HIV infection or who have only ONE of the conditions listed in Category A
Category A: Mildly Symptomatic
Children with ≥ 2 of the conditions listed below but none of the conditions listed in Categories B and C.
* Lymphadenopathy (>0.5 cm at > 2 site, bilateral =1 site)
* Hepatomegaly
* Splenomegaly
* Dermatitis
* Parotitis
* Recurrent or persistent upper respiratory tract infection, sinusitis or otitis media
Category B: Moderately Symptomatic
Children who have symptomatic conditions other than those listed for Category A or C that are attributed to HIV infection. Examples of conditions in clinical Category B include, but are not limited to:
* Anaemia (<8 g/dL), neutropaenia ($<1000/\text{mm}^3$), or thrombocytopaenia ($< 100,000/\text{mm}^3$) persisting for ≥ 30 days
* Bacterial meningitis, pneumonia, or sepsis (single episode)
* Candidiasis, oropharyngeal (thrush) persisting >2 months in children > 6 months of age
* Cardiomyopathy
* Cytomegalovirus infection, with onset before 1 month of age
* Diarrhoea, recurrent or chronic
* Hepatitis
* Herpes simplex virus (HSV) stomatitis, recurrent (>2 episodes within 1 year)
* HSV bronchitis, pneumonitis, or oesophagitis with onset before 1 month of age
* Herpes zoster (shingles) involving ≥ 2 distinct episodes or more than 1 dermatome
* Leiomyosarcoma
* Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
* Nephropathy
* Nocardiosis
* Persisting fever (lasting >1 month)
* Toxoplasmosis, onset before 1 month of age
* Varicella, disseminated

Category C: Severely Symptomatic

These are AIDS-defining conditions:

* Serious bacterial infections, multiple or recurrent (i.e., any combination of ≥ 2 culture-confirmed infections within a 2-year period) of the following types: septicaemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and in-dwelling catheter-related infections).

* Candidiasis, oesophageal or pulmonary (bronchi, trachea, lungs)

* Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)

* Cryptococcosis, extrapulmonary

* Cryptosporidiosis or isosporiasis with diarrhoea persisting > 1 month

* Cytomegalovirus disease with onset of symptoms at age > 1 month (at a site other than liver, spleen or lymph nodes)

* Encephalopathy (\geq one of the following progressive findings present for ≥ 2 months in the absence of a concurrent illness other than HIV that could explain the findings):

- a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard development scale or neuropsychological test;
- b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerised tomography or magnetic resonance imaging (serial imaging is required for children < 2 years of age);
- c) acquired symmetric motor deficit manifested by ≥ 2 of the following: paresis, pathologic reflexes, ataxia, or gait disturbance

* Infection with HSV causing a mucocutaneous ulcer that persists for > 1 month; or bronchitis, pneumonitis, or oesophagitis for any duration in a child > 1 month of age

* Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)

* Kaposi's sarcoma

* Lymphoma, primary, in brain

* Lymphoma, small, noncleaved cell (Burkitt) or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype

* *Mycobacterium tuberculosis*, disseminated or extrapulmonary; if pulmonary or cervical, patients need to be in immune category 3

* *Mycobacterium*, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph node)

* *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated (at site other or in addition to lungs or cervical or hilar lymph nodes)

* *Pneumocystis carinii* pneumonia

* Progressive multifocal leukoencephalopathy

* *Salmonella* (nontyphoid) septicaemia, recurrent

* Toxoplasmosis of the brain with onset at > 1 month of age

* Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings:

- a) persistent weight loss $> 10\%$ of baseline, **or**
- b) downward crossing of at least one of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child ≥ 1 year of age, **or**
- c) $< 5^{\text{th}}$ percentile on weight-for-age chart on 2 consecutive measurements, ≥ 30 days apart) **plus 1)** chronic diarrhea (at least 2 loose stools/day for ≥ 30 days) **or, 2)** documented fever (for ≥ 30 days, intermittent or constant)

* Penicilliosis, disseminated

Table 4. 1994 Revised Pediatric HIV Classification System: Immunologic Categories Based on Age-specific CD4+ Lymphocyte Count and Percentage

Adapted from:

- CDC. 1994 revised classification system for HIV in children less than 13 years of age. MMWR1994;43:RR-12
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Immune Category	Age of Child		
	≤ 12 months	1-5 years	6-12 years
	Cell/mm ³ (%)	Cell/mm ³ (%)	Cell/mm ³ (%)
Category 1: No suppression	≥ 1500 (≥ 25)	≥ 1000 (≥25)	≥ 500 (≥ 25)
Category 2: Moderate suppression	750-1499 (15-24)	500-999 (15-24)	200-499 (15-24)
Category 3: Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

Table 5. Characteristics of Nucleoside Analogue Reverse Transcriptase Inhibitors

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. www.hivatis.org
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Generic Name	Zidovudine (ZDV/AZT)	Didanosine (ddI)	Zalcitabine (ddC)	Stavudine (d4T)	Lamivudine (3TC)	Abacavir (ABC)
Trade name	Retrovir	Videx	Hivid	Zerit	Epivir	Ziagen
Preparation	100mg capsules 300 mg tablets 10 mg/ml IV solution 10 mg/ml oral solution	25, 50, 100, 150, 200 mg chewable tablets 100, 167, 250 mg sachets Delayed-release capsules: VIDEX EC-125, 250, 400 mg	0.375, 0.75 mg tablets	15,20,30,40 mg capsules 1mg/ml oral solution	150 mg tablets 10 mg/ml oral solution	300 mg tablets 20 mg/ml oral solution
Dose	<i>During labour and delivery:</i> Continuous IV infusion 2 mg/kg first hour, then 1 mg/kg until delivery <i>Neonatal:</i> 2 mg/kg Q6h <i>Paediatric:</i> 90-180 mg/m ² TDS or QID <i>Adult:</i> 200 mg TDS or 300 mg BD	<i>Neonatal (<90 days):</i> 50 mg/m ² q12h <i>Paediatric:</i> 90-150 mg/m ² q12h <i>Adolescent/Adult:</i> ≥60 kg, 200 mg BD; <60 kg 125 mg BD; VIDEX EC: ≥60 kg: 400 mg qd; <60 kg: 250 mg qd	<i>Neonatal:</i> unknown <i>Paediatric:</i> 0.005 to 0.01 mg/kg TDS <i>Adult:</i> 0.75 mg TDS	<i>Neonatal:</i> unknown <i>Paediatric:</i> 1 mg/kg BD <i>Adolescent/Adult:</i> < 60 kg, 30 mg BD; ≥60 mg, 40 mg BD	<i>Neonatal (<30 days):</i> (under study) 2 mg/kg BD <i>Paediatric:</i> 4 mg/kg BD <i>Adolescent/Adult:</i> < 50 kg, 2mg/kg BD; ≥ 50 kg, 150 mg BD	<i>Neonatal:</i> not approved for infants <3m. Infants 1-3m of age, 8 mg/kg BD under study <i>Paediatric/Adolescent:</i> 8 mg/kg BD, max 300 mg BD
Food Effect	No regard to meals	Take 1 h before or 1 h after meal	No regard to meals	No regard to meals	No regard to meals	No regard to meals
Toxic Effects	Anaemia, neutropaenia, headache. Less frequently: myopathy, myositis, hepatitis	Gastro-intestinal upset. Less frequently: peripheral neuropathy, electrolyte disturbances, hyperuricaemia. Rarely: pancreatitis hepatitis, retinal de-pigmentation	Headache, fatigue. Rarely peripheral neuropathy, pancreatitis hepatitis, skin rashes, oral and oesophageal ulcers, anaemia, neutropaenia	Headache, gastro-intestinal upset, skin rashes. Less frequently: peripheral neuropathy, pancreatitis, hepatitis, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported	Headache, fatigue, gastro-intestinal upset, skin rashes. Less frequently: peripheral neuropathy, pancreatitis, hepatitis, neutropaenia, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported	Nausea, vomiting, headache, fever, rash, anorexia, fatigue. Rarely potentially fatal hypersensitivity reaction, with fever, malaise, nausea, vomiting, diarrhoea and abdominal pain. Many have lymphadenopathy, mucous membrane ulceration or rash. lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

Table 6. Characteristics of Non-nucleoside Reverse Transcriptase Inhibitors:

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. www.hivatis.org
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Generic Name	Nevirapine	Delavirdine	Efavirenz
Trade Name	Viramune	Rescriptor	Stocrin
Preparation	200 mg tablets 10 mg/ml liquid	100 mg tablets 200 mg tablets	50mg, 100 mg, 200 mg capsules
Dose	<i>Neonatal through 2 months</i> (under ACTG P365): 5 mg/kg qd or 120 mg/m ² qd for 14 days, then 120 mg/m ² q12h for 14 days, then 200 mg/m ² q12h. <i>Paediatric:</i> 120-200 mg/m ² q12h Start at 120 mg/m ² (maximum 200 mg) qd for the first 2 weeks and increase to BD full dose <i>Adolescent/Adult:</i> 200 mg q12h (initiate at half dose for the first 14 d)	<i>Neonatal and Paediatric:</i> unknown <i>Adolescent/Adult:</i> 400 mg TDS or 600 mg BD (investigational)	<i>Neonatal:</i> unknown <i>Paediatric:</i> (no data on appropriate dosage under 3 yrs of age) 10- <15 kg: 200 mg qhs; 15- <20 mg: 250 mg qhs; 20- <25 kg: 300 mg qhs; 25- <32.5 kg: 350 mg qhs; 32.5- <40 kg: 400 mg qhs; ≥ 40 kg: 600 mg qhs <i>Adolescent:</i> 600 mg qhs
Food Effect	Can be given with food	Can be taken with food	Can be taken with or without food, avoid high fat meal with drug
Toxic Effects	Skin rash, (some severe, and life threatening), fever, headache, gastrointestinal. Rarely hepatitis, very rarely liver failure and granulocytopenia	Skin rash, headache, fatigue, gastro-intestinal disturbances	Rash, CNS involvement (somnolence, insomnia, abnormal dreams, confusion, impaired concentration, agitation, hallucinations), elevated aminotransferase

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

Table 7. Characteristics of Protease Inhibitors:

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. www.hivatis.org
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Generic Name	Nelfinavir	Indinavir	Ritonavir	Saquinavir	Amprenavir	Lopinavir/ Ritonavir
Trade Name	Viracept	Crixivan	Norvir	Invirase[hard gel], Fortovase [soft gel]	Agenerase	Kaletra
Preparation	50mg/scoop powder 250 mg tablets	200 mg, 400 mg capsules	80 mg/ml liquid 100 mg capsules	200 mg capsule Saquinavir hard gel capsule is not recommended except in combination with ritonavir	15 mg/ml liquid 50 mg, 150 mg capsules	80mg lopinavir and 20 mg ritonavir/ml capsules: 133.3 mg lopinavir/33.3 mg ritonavir
Dose	<i>Neonatal</i> (no data, under PACTG 353): 40 mg/kg BD <i>Paediatric</i> : 20-30 mg/kg TDS but many experts give a higher dose: 45 mg/kg/dose q8h to a maximum of 2 gm/dose (exceeding the adult dose of 1.25 gm BD) <i>Adolescent/Adult</i> : 750 mg TDS or 1.25 gm BD	<i>Neonatal</i> : dose unknown, should not be given to neonates (hyperbilirubinaemia) <i>Paediatric</i> (under study): 500mg/m ² q8h. Patients with small body surface areas may require lower doses (300-400mg/m ² q8h) <i>Adolescent/Adult</i> : 800 mg q8h	<i>Neonatal</i> : dose unknown <i>Paediatric</i> : 350-450 mg/m ² BD, start at 250 mg/m ² q 12h and increase stepwise over 5 days <i>Adolescent/Adult</i> : 600 mg BD, start at 300 mg BD and increase to full dose over 5 days	<i>Neonatal</i> : dose unknown <i>Paediatric</i> : under study: 50 mg/kg q8h as single PI; 33 mg/kg q8h as therapy with nelfinavir <i>Adolescent/Adult</i> : 1200 mg TDS or 1600 mg BD	<i>Paediatric</i> : <u>Liquid formulation</u> : 4-12 and 13-16 yrs (if <50 kg): 22.5 mg/kg Bid or 17 mg/kg TDS (maximum daily dose 1800 mg) <u>Capsules</u> : 4-12 and 13-16 yrs (if <50 kg): 20 mg/kg BD or 15 mg/kg TDS (maximum daily dose 2400 mg) <i>Adult</i> : 1200 mg BD	<i>Neonatal</i> : no data on children < 6 m <i>Paediatric</i> : <u>Not receiving nevirapine or efavirenz</u> : 7-<15 kg: 12 mg/kg lopinavir/3 mg/kg ritonavir BD with food 15-40 kg: 10 mg/kg lopinavir/2.5 mg/kg ritonavir BID with food >40 kg: 400 mg lopinavir/100 mg ritonavir (3 capsules or 5 ml) BD with food OR 230 mg/m ² /57.5 mg/m ² ritonavir BD with food up to maximum of 400 mg lopinavir/100 mg ritonavir <i>Adult/Adolescent</i> : 400 mg lopinavir/100mg ritonavir <u>On concomitant ritonavir or efavirenz or PI experienced</u> : 7-<15 kg: 13 mg/kg lopinavir/3.25 mg/kg ritonavir BD with food 15-50 kg: 11mg/kg lopinavir/2.75 mg/kg ritonavir BD with food >50 kg: 533 mg lopinavir/133 mg ritonavir (4 capsules

						or 6.5 ml) BD with food OR 300 mg/m ² lopinavir/75 mg/m ² ritonavir BD with food up to a maximum of 533 mg lopinavir/133 mg ritonavir <i>Adult/Adolescent:</i> 533 mg lopinavir/133 mg ritonavir BD with food
Food Effect	Administer with meal or light snack	Empty stomach 1 hr before or 2 hrs after a meal (or taken with a light meal)	Food increases absorption	Administer within 2 hours of a full meal to increase absorption. Grapefruit juice increases absorption	Can be given with or without food	Administer with food. High fat meal increases absorption, especially for liquid preparation
Toxic Effects	Diarrhoea, abdominal pain, fatigue, rash. Rarely: hyperglycaemia and diabetes	GI disturbances, headache, asymptomatic hyperbilirubinaemia. Less frequently: nephrolithiasis spontaneous bleeding episodes in haemophiliacs, hyperglycaemia, diabetes	GI disturbances, circumoral paraesthesia, hepatitis. Rarely: spontaneous bleeding episodes in haemophiliacs pancreatitis, increased triglycerides, cholesterol, hyperglycaemia, diabetes	GI disturbances. Rarely: spontaneous bleeding episodes in haemophiliacs, hyperglycaemia, diabetes	GI disturbances, rash, paraesthesia, Stevens-Johnson syndrome (1%), depression or mood disorder (15%), hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia	Diarrhoea, headache, asthenia, nausea and vomiting, increased in blood lipids, rash. Rarely: spontaneous bleeding episodes in haemophiliacs, pancreatitis, hyperglycaemia, ketoacidosis, diabetes, hepatitis

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

Table 8. Combinations of Antiretroviral drugs for Use in Paediatric Settings

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. www.hivatis.org
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. www.hivatis.org

Frequently used initial combination therapies in paediatrics:

Zidovudine + lamivudine + nelfinavir or ritonavir
 Stavudine + didanosine + nelfinavir or ritonavir
 Stavudine + lamivudine + nelfinavir or ritonavir
 Zidovudine + lamivudine + nevirapine
 Stavudine + lamivudine + nevirapine
 Stavudine + didanosine + nevirapine
 Efavirenz + 2NRTI
 Efavirenz + nelfinavir + 1 NRTI
 Nelfinavir + nevirapine + zidovudine + lamivudine
 Nelfinavir + efavirenz + zidovudine + lamivudine

Regimens to be avoided due to overlapping toxicity or antagonistic antiviral effect:

Zidovudine + stavudine
 Didanosine + zalcitabine
 Stavudine + zalcitabine
 Zalcitabine + lamivudine
 Monotherapy

Currently licensed antiretroviral preparations in the USA for treatment of HIV infection. (All except for Delavirdine, Amprenavir and Lopinavir/ritonavir are registered in Hong Kong and these three drugs can be obtained by special arrangement).

NRTI	NNRTI	PI
Zidovudine (ZDV or AZT)*	Nevirapine*	Ritonavir*
Didanosine (ddI)*	Delavirdine	Nelfinavir*
Zalcitabine (ddC)*	Efavirenz	Indinavir
Lamivudine (3TC)*		Saquinavir
Stavudine (d4T)*		Amprenavir*
Abacavir (ABC)*		Lopinavir/Ritonavir*

NRTIs: Nucleoside analogue reverse transcriptase inhibitors

NNRTIs: Non-nucleoside analogue reverse transcriptase inhibitors

PIs: protease inhibitors

* paediatric formulations commercially available

Table 9. Suggested programme of immunisation for HIV infected children (Hong Kong SAR) [programme for normal children for reference]

AGE	IMMUNISATION RECOMMENDED	
	Normal Children	HIV Infected Children
Newborn*	B.C.G. Vaccine	B.C.G. Vaccine
	Hepatitis B Vaccine - First Dose	Hepatitis B Vaccine - First Dose
	OPV-1	
1 month	Hepatitis B Vaccine - Second Dose	Hepatitis B Vaccine - Second Dose
2-4 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - First Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - First Dose
	Trivalent OPV- First Dose	IPV- First Dose Hib-first dose at 2 months and second dose at 4 months of age
3-5 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Second Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Second Dose
4-6 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Third Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Third Dose
	Trivalent OPV - Second Dose	IPV - Second Dose Hib-third dose at 6 months
		Influenza vaccine at 6 months and then annually
	Hepatitis B Vaccine - Third Dose at 6 months (updated on March 2002)	Hepatitis B Vaccine - Third Dose at 6 months (updated on March 2002)
1 year	MMR Vaccine (Measles, Mumps & Rubella) - First Dose	MMR Vaccine (Measles, Mumps & Rubella) - First Dose [see text]
1½ years	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Booster Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Booster Dose
	Trivalent OPV - Booster Dose	IPV - Booster Dose
2 years		Polysaccharide Pneumococcal vaccine-first dose
Primary 1	DT Vaccine (Diphtheria & Tetanus) - Booster Dose	DT Vaccine (Diphtheria & Tetanus) - Booster Dose
	Trivalent OPV - Booster Dose	IPV - Booster Dose
	MMR Vaccine (Measles, Mumps & Rubella) - booster Dose	MMR Vaccine (Measles, Mumps & Rubella) - booster Dose [see text]
		Polysaccharide Pneumococcal vaccine-booster dose
Primary 6	DT Vaccine (Diphtheria & Tetanus) - Booster Dose	DT Vaccine (Diphtheria & Tetanus) - Booster Dose
	Trivalent OPV- Booster Dose	IPV- Booster Dose

**NB. OPV-1 should be omitted for those children born from HIV infected mothers irrespective of whether those babies are truly infected or not. Hepatitis A and Varicella vaccine are not included but should be considered on individual basis (see text)*

Table 10. Passive Immunisation in HIV Infected Children Regardless of Immunisation Status

Possible Exposure	Passive Immunotherapy	Dosage
Measles	Immune globulin (IG)	0.5 ml/kg IM (maximum 15 ml) for HIV symptomatic child 0.25 ml/kg IM for HIV positive but asymptomatic child
Tetanus-prone wound	Human tetanus immune globulin (TIG)	250U IM
Varicella-zoster virus	Varicella-zoster immune globulin (VZIG)	VZIG 125U/10 kg IM (maximum 625U) Varitect 5-25IU/kg IV
Hepatitis B	Hepatitis B IG (HBIG)	0.5 ml IM (perinatal) 0.06 ml/kg IM (postexposure)

REFERENCES

1. Fowler MG, Simonds RJ, Roongpisuthipong A. HIV/AIDS in infants, children and adolescents. Update on perinatal HIV transmission. *Pediatr Clin N Am* 2000;47(1):21-38.
2. Rouzioux C. Estimated timing of mother-to-child human immunodeficiency virus type 1 (HIV-1) transmission by use of a Markov model. The HIV Infection in Newborn French Collaborative Study Group. *Am J Epidemiol* 1995;142(12):1330-1337.
3. American Academy of Pediatrics, Committee on Pediatric AIDS. Evaluation and Medical Treatment of the HIV-Exposed Infant. *Pediatrics* 1997;99(6):909-917.
4. Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001:1-70. www.hivatis.org
5. Laufer M and Scott GB. HIV/AIDS in infants, children and Adolescents. Medical management of HIV disease in children. *Pediatr Clin N Am* 2000;47(1):127-152.
6. American Academy of Pediatrics, Committee on Infectious Diseases. *Red Book: 2000 Report of the Committee on Infectious Diseases*. 25th ed. Library of Congress, American Academy of Pediatrics, 2000.
7. Kovacs A, Xu J, Rasheed S, et al. Comparison of a rapid nonisotopic polymerase chain reaction assay with four commonly used methods for the early diagnosis of human immunodeficiency virus type 1 infection in neonates and children. *Pediatr Infect Dis J* 1995;336:1343-1349.
8. Cunningham CK, Charbonneau TT, Song K et al. Comparison of human immunodeficiency virus I DNA polymerase chain reaction and qualitative and quantitative RNA polymerase chain reaction in human immunodeficiency virus 1-exposed infants. *Pediatr Infect Dis J* 1999;18:30-35.
9. Steketee RW, Abrams EJ, Thea DM et al. Early detection of perinatal human immunodeficiency virus (HIV) type I infection using HIV RNA amplification and detection. *J Infect Dis* 1997;175:707-711.
10. Nielsen K and Bryson YJ. Diagnosis of HIV infection in children. *Pediatr Clin N Am* 2000;47(1):39-63.
11. Centers for Disease Control and Prevention: Public Health Service task force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. <http://www.hivatis.org> updated 4 May 2001.
12. Advisory Council on AIDS. Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission. Hong Kong: Scientific Committee of the Advisory Council on AIDS, April 2001.

13. Centers for Disease Control and Prevention. 1995 revised guidelines for prophylaxis against *Pneumocystis carinii* pneumonia for children infected with or perinatally exposed to human immunodeficiency virus. *MMWR* 1995;44(RR-4):1-11.
14. Sherer WT, Quinn TC, La Russa P, et al. Viral load and disease progression in infants infected with human immunodeficiency virus type 1. *N Engl J Med* 1997;336:1337-1342.
15. Mofenson LM, Korelitz J, Meyer WA, et al. The relationship between serum human immunodeficiency virus type 1 RNA level, CD4 lymphocyte percent and long-term mortality risk in HIV-1 infected children. *J Infect Dis* 1997;175:1029-1038.
16. Lipshultz SE: Left ventricular structure and function in children infected with human immunodeficiency virus: the prospective P2C2 HIV Study. Pediatric Pulmonary and Cardiac Complication of Vertically Transmitted HIV Infection (P2C2 HIV) Study Group. *Circulation* 1998;97(13):1246-56.
17. Kuhn L, Abrams EJ, Weedon J et al. For the Perinatal AIDS collaborative Transmission Study (PACTS). Disease progression and early viral dynamics in human immunodeficiency virus-infected children to zidovudine during perinatal and perinatal periods. *J Infect Dis* 2000;182:104-111.
18. Centers for Disease Control and Prevention. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. *MMWR* 1994;43(RR-12):1-10.
19. Krogstad P, Wiznia A, Luzuriaga K, et al. Treatment of HIV-1 infected infants and children with the protease inhibitor nelfinavir mesylate. *Clin Infect Dis* 1999;28:1109-1118.
20. Mueller BU, Zuckerman J, Nelson JR, et al. Update on the pediatric phase I/II study of the protease inhibitor ritonavir (ABT-538). In: Proceedings from the Fourth Conference on Retroviruses and Opportunistic Infections; January 1997; Washington, DC. Abstract 722.
21. Yogev R, Stanley K, Nachman SA, Pelton S, McIntosh K, Wiznia A, for the PACTG 338 Protocol Team. Virologic efficacy of ZDV+3TC vs d4T+Ritonavir (RTV) vs ZDV+3TC+RTV in stable antiretroviral experienced HIV-infected children (Pediatric ACTC Trial 338). In: Proceedings of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); September 1997; Toronto, Ontario. Abstract LB-6.
22. American Academy of Pediatrics. Committee on Infectious Diseases and Committee on Pediatric AIDS. Measles Immunization in HIV-Infected Children. *Pediatrics* 1999;103(5):1057-1060
23. American Academy of Pediatrics, Committee on Infectious Disease. Varicella Vaccine Update. *Pediatrics* 2000;105(1):136-140.

24. Safrin S, Rush JD, Mills J. Influenza in patients with human immunodeficiency virus infection. *Chest* 1990;98:33-37.
25. Radwan H, Ellison R. Severe influenza pneumonia in HIV patients during 1997-1998 influenza season. Presented as a poster in Infectious Disease Society of American 36th Annual Meeting. Alexandria, VA: Infectious Disease Society of America, 1998.
26. CDC. Prevention and Control of Influenza. Recommendations of the Advisory Committee On Immunization Practices (ACIP). *MMWR* 2000;49 (RR-3):1
27. American Academy of Pediatrics. *2000 Red Book: Report of the Committee on Infectious Diseases*. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000:338-341
28. World Health Organization. Special programme on AIDS and expanded programme on immunization: joint statement—consultation on human immunodeficiency virus (HIV) and routine childhood immunization. *Wkly Epidemiol Rec* 1987;62:297-299.
29. The National Institute of Child Health and Human Developments Intravenous Immunoglobulin Study Group. Intravenous immune globulin for the prevention of bacterial infections in children with symptomatic human immunodeficiency virus infection. *N Engl J Med* 1991;325(2):73-80.
30. Mofenson LM, Moye J jr, Bethel J, Hirschhorn R, Jordan C, Nugent R. Prophylactic intravenous immunoglobulin in HIV-infected children with CD4+ counts of 0.20 x 10⁹/L or more: effect on viral, opportunistic, and bacterial infections. *JAMA* 1992; 268:483-488.
31. Spector SA, Gelber RD, McGrath N, et al. A controlled trial of intravenous immune globulin for the prevention of serious bacterial infections in children receiving zidovudine for advanced human immunodeficiency virus infections. *N Engl J Med* 1994;331:1181-1187.
32. Heller LS. Nutritional Support for Children with HIV/AIDS. *The AIDS Reader* 2000;10(2):109-114.
33. Connor EM, Sperling R, Shapiro D, et al. Long term effect of zidovudine exposure among uninfected infants born to HIV-infected mothers in Pediatric AIDS Clinical Trials Group 076. In: Proceedings of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); September 1995; San Francisco, Calif. Abstract 11.