

# Guideline for Management of Pediatric HIV/AIDS



**Ministry of Health  
Royal Government of Bhutan**

**HIV/ AIDS & STI control program  
Department of Public Health  
Thimphu : Bhutan**

## **ACKNOWLEDGEMENTS**

The guideline was formulated with the core technical team of the following officials:

1. Dr. K.P. Tshering, Head, Department of Pediatric, JDWNRH
2. Dr. Mimi Lhamo, Pediatrician, Mongar Regional Referral Hospital

The review of the guideline was conducted by the technical committee comprising doctors and the representatives from the Ministry of Health. We are deeply indebted to the Royal Thai Government for kindly facilitating the visit of our officials. The study visit of the team was supported by the UNICEF country office. We thank for all those who made it possible to bring out this important document.

**Program Manager**

<b>TABLE OF CONTENTS</b>	<b>PAGES</b>
Foreword .....	v-vi
Preface .....	vii
Abbreviations .....	viii
<b>Chapter 1:</b>	
Introduction .....	9-10
<b>Chapter 2:</b>	
Clinical manifestations.....	11 - 20
<b>Chapter 3:</b>	
Staging and classification.....	21 - 24
<b>Chapter 4:</b>	
Management of newborns born to HIV-infected mothers.....	25 - 27
<b>Chapter 5:</b>	
Management of HIV in children .....	28 - 35
<b>Chapter 6:</b>	
Diagnosis and treatment of OI in HIV infected children.....	36 - 54
<b>Chapter 7:</b>	
HAART in Pediatric HIV Infection.....	55 - 60
<b>Chapter 8:</b>	
Care and support for children living with HIV/AIDS.....	61 - 62
<b>Annexure 1</b>	
Pediatric ARV drugs.....	63 - 70
<b>Annexure 2</b>	
Pediatric forms .....	71 - 77
<b>Annexure 3</b>	
WHO classification of HIV infection .....	78 - 80
<b>Annexure 4</b>	
References.....	81



## FOREWORD

Patterns of transmissions of HIV vary widely between countries. They also change over time within a single country. The recent years have witnessed a steady increase in HIV infection among young children. The first pediatric HIV case in Bhutan was detected in 2002. By February 2008, the number of children infected through the maternal route rose to 13 accounting for 9% of the nations HIV infected population.

Infected children differ from infected adults in several ways. The disease progresses much more rapidly in children, recurrent bacterial infections are more common and children are more susceptible to opportunistic infections because of lack of prior immunity. In the absence of treatment infected children will have a shorter life expectancy than those with out infection.

An essential part of the Royal Governments response to the HIV/AIDS epidemic has been its policy of introducing Antiretroviral Treatment (ART) which can dramatically reduce morbidity and mortality. This window of hope modifies the subsequent risk of death for children who remain infected. The needs of these children are also being met through special care and support programmes.

However, we must not forget that the key to preventing HIV infection in children clearly lies in preventing their parents from acquiring the disease. Increased attention must also be focused on strategies to prevent mother to child transmission and the prevention of unwanted pregnancies in HIV-infected mothers. The availability and the use of family planning for mothers infected with HIV/AIDS will also reduce the number of infected children. HIV infected women should have access to information, follow up clinical care and support including family planning and nutritional support. Information and education efforts should be urgently directed to the public, affected communities and their families.

The HIV pandemic threatens to erode many of our hard earned gains made in reducing infant and child mortality. The concerted efforts of parents, care takers, health workers and policy makers will be crucial to reducing the number of new infections and preventing deaths among our children.

The Pediatric Guideline for management of HIV/AIDS is intended to serve as basic reference document for the treatment of HIV infected children in Bhutan. I urge all health professionals to be mindful of sensitivities while providing service to these young children.



Dasho (Dr) Gado Tshering  
secretary  
Ministry of Health

December 2008

## **PREFACE**

This “National guideline on Management of Pediatric HIV/AIDS” is prepared keeping in view specific needs in managing HIV infection in children in our country’s context. It covers important practical aspects of managing HIV/AIDS in children and can be used by Medical officers; pediatricians and all health professional. The content of this document are a synthesis of the lessons learnt from other countries and is formulated to suit the needs of Bhutan. The document broadly contains two topics:

The first component deals with the clinical management of pediatric group of HIV/AIDS in Bhutan. All the sections and the approaches to handling the pediatric HIV/infected child are clearly outlined.

The second component covers formula feeding techniques for the children born to HIV infected mothers. The National Policy for infant and young child feeding in Bhutan recommends formula feeding in Bhutan. Bhutan however, is an ardent believer of the benefits of the breast feeding and is actively promoted in the general population. The issue of whether breast feeding be recommended for infants born from HIV infected mothers has been discussed in depth at the highest HIV/AIDS policy body in the National for HIV/AIDS Commission.

The document is kept simple to make it more user-friendly. Once again, it is worthwhile mentioning that this document will remain receptive to change in future to adapt to changing concepts, practices and evidences in HIV/AIDS.

## **ABBREVIATIONS**

AIDS	Acquired Immune Deficiency System
ARV	Antiretroviral
ART	Antiretroviral Treatment
HAART	Highly Active Antiretroviral Treatment
ELISA	Enzyme Linked Immuno Sorbant Assay
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother to Child Transmission
OIs	Opportunistic Infections

# CHAPTER 1

## 1. INTRODUCTION

The HIV/AIDS epidemic is not merely a health issue, but a challenge on the social, economic, culture, political and legal aspects of society. Pediatric AIDS strikes the population devastated by multiple social stresses. The epidemic further aggravates the socio-economic vulnerabilities of the weakest in the society including women and children. Health care workers must help in clarifying misconceptions and creating awareness for prevention strategies of this disease.

Every day 8,500 children and young people around the world are infected with HIV. As of the end of 2004, some 2.2 million children under 15 years were living with HIV. Many children were born to mothers with HIV acquiring the virus around the time of birth or from breast feeding. In the absence of any interventions, about a third of children born to HIV infected mothers will be born with HIV or infected through breastfeeding.

Children born with HIV have very high mortality. They are over four times more likely to die by the age of two than children born without HIV. HIV has contributed to a rise or stagnation in under- five mortality in several countries in Africa, but is not the only factor behind these trends.

The clinical manifestations of HIV infection in children are different from those in adults. The immune system of young children, who are infected perinatally, is immature and hence dissemination throughout the various organs may occur very early. Organs such as the brain may be susceptible to the effects of the virus in a manner different from the

observed in adults. Even the pattern of opportunistic infections in children is different from those in adults. Children tend to suffer from primary infection while adults are more likely to suffer from reactivation of infection as their immunity wanes in response to advanced HIV-infection.

Bhutan has recorded increase of HIV infection among the children. So far 13 children are recorded with HIV infection from their mothers. Currently the mother to child transmission constitutes nearly 9% of the total 160 cases.

The advent of potent antiretroviral therapy (ART) in 1996 led to a revolution in the care patients with HIV/AIDS in developed world. Although the treatment are not a cure and presents new challenges of their own with respect to side effects and drug resistance. They definitely improve the quality of life and reduced morbidity and revitalized communities and transformed the perception of HIV/AIDS from a plague to a manageable chronic disease.

It is well known that a combination of VCT, ART during pregnancy and safe delivery practices without breastfeeding of infants can bring down the rate of transmission of HIV from mother to baby to less than 2%. The Royal Government has taken the initiative to provide all HIV exposed infants with free supply of commercial infant formula for the first twelve months of life. In addition medicines for the management of OI would be included in the essential drug list.

## CHAPTER 2

### CLINICAL MANIFESTATIONS OF HIV/AIDS IN CHILDREN

#### 2.1 DIFFERENCE IN PEDIATRIC AND ADULT HIV-INFECTION

- Overall progression of disease is more rapid in children.
- Immune system is more immature with higher CD4 counts
- Recurrent invasive bacterial infections are more common in children.
- Disseminated CMV, Candida, Herpes Simplex and Varicella zoster are more common.
- LIP occur almost exclusively in children.
- CNS infections are common.
- Peripheral neuropathy, Myopathy is rare in children.

#### 2.2 PATTERNS OF MANIFESTATIONS

Most infected infants do not have any abnormal findings on clinical examination at birth. The mean age of presentation is 17 months, though sometimes the symptoms may not be apparent even till the age of 7 years. On the basis of age of presentation, these children can be divided into three groups.

- a. The first group- **rapid progressors**- consists of infants who have manifestations of HIV-infection within first few months of life. Opportunistic infections and neurological manifestations are the usual clinical features that are noted in these children. These are seen in 20-30% of cases, and they undergo a rapid natural downhill progression.

- b. The second group consists of children who develop manifestations after the age of one year and they usually display failure to thrive, recurrent bacterial infections and lymphoid interstitial pneumonitis.
- c. The third groups, **slow progressors**- comprises of children who reveal minor manifestations later in childhood and in that respect, might be considered “adult equivalents”

### 2.3 CLINICAL MANIFESTATIONS

The manifestations of the infection vary widely among infants, young children and adolescents. Most infected children are asymptomatic and do not have any abnormal findings on clinical examination at birth. The initial manifestations of the disease are mild and non-specific, these include lymphadenopathy, chronic or recurrent diarrhea, failure to thrive, and wasting and oral thrush. In contrast, the presentation in adolescents is similar to that in adults.

### COMMON MANIFESTATIONS OF HIV-INFECTION IN CHILDREN

Manifestations MORE commonly seen	Manifestations LESS commonly seen
Lymphoid interstitial pneumonia (LIP) Chronic parotid swelling Opportunistic infections: <ul style="list-style-type: none"> <li>• Pneumocystic Carinii pneumonia</li> <li>• Serious recurrent bacterial infections</li> <li>HIV Encephalopathy</li> </ul>	Kaposi’s sarcoma malignancies: CNS lymphoma Opportunistic infections: <ul style="list-style-type: none"> <li>• Cryptococcosis</li> <li>• Histoplasmosis</li> <li>• Toxoplasmosis</li> <li>• Disseminated Mycobacterium avium Complex (MAC) infection</li> </ul>

Children who acquire the infection due to transfusion blood tend to have an incubation period ranging up to 4 years.

The manifestation of HIV-infection in these children are similar to those in perinatally infected children and include prolonged pyrexia, progressive weight loss, recurrent bacterial infections, lymphadenopathy, prolonged diarrhea, oropharyngeal candidiasis, bleeding manifestation due to thrombocytopenia and alopecia.

#### **A. FAILURE TO THRIVE**

- Failure to thrive is very common feature of pediatric HIV-infection.
- HIV-infection has adverse effect on the growth of the infected children.
- Can manifest as early as 4-6 months of age in perinatally infected children, which has been correlated with high viral load in mothers.
- The cause factors are low birth weight, decreased energy intake, diarrhea, malabsorption, and chronic disease of the heart, kidney and lungs, micronutrient deficiencies, neuroendocrine abnormalities and repeated episodes of infection.
- Length/height and weight, which are anthropometrical parameters that represent growth in children in children needs to be, monitored regularly for early detection and treatment.

#### **B. HEPATOMEGALY**

- Hepatomegaly is a common GI manifestation of pediatric HIV-infection.
- It is likely to be caused by the replication of the virus in the reticuloendothelial tissue of the liver.
- Development of hepatomegaly within 3 months of age (in perinatally acquired HIV-infection) has prognostic significance since it is known to be associated with rapid progression of the disease.

- Malnutrition, fatty liver, steatosis, drug administration, CMV infection and malignancy can be some of the other causes for hepatomegaly in HIV-infection children.
- Co-infection of hepatitis C with HIV is well known.

### **C. LYMPHADENOPATHY**

- HIV, after initial viremia, gets trapped in the lymph nodes and also multiples there.
- The replication of HIV in the nodes is the primary cause of lymphadenopathy.
- Other important conditions commonly associated with HIV-infection that can give rise to generalized lymphadenopathy in HIV -infected children include tuberculosis, disseminated infections with other mycobacterial species, viral infections with CMV, Epstein -Barr virus(EBV) and malignancies like lymphoma and lymphosarcoma.

### **D. CHRONIC DIARRHEA**

- Diarrhea is a very common clinical manifestation of HIV-infected infants and children in developing countries.
- The causes are infections, other inflammatory processes and malabsorption of carbohydrate and fats.
- It is believed that HIV replication in the gastrointestinal mucosa can lead to diarrhea itself leading to HIV enteropathy.
- Opportunistic enteric infections with common organisms like Candida, Cryptosporidium, Cytomegalovirus, Giardia, Isosporabelli and salmonella can cause chronic diarrhea.
- Persistent infection leads to prolonged diarrhea with malabsorption and malnutrition.

**E. PAROTITIS**

- Parotitis occurs as recurrent or chronic hypertrophic parotitis.
- The parotid swelling evolves gradually in patients with HIV disease. It may be due to the direct infection of parotid gland by HIV or due to lymphocytic infiltration of the gland.
- The swelling may be unilateral or bilateral but is classically painless and recurrent.

**F. SKIN MANIFESTATIONS**

- HIV -infection in children is associated with a number of skin manifestations. These can be due to infectious or non-infectious causes.
- Viral, bacterial and fungal infections have been frequently reported in HIV infected children, common skin diseases may present with unusual skin lesions such as Norwegian scabies, disseminated, confluent and large lesions of Molluscum contagiosum.

Infectious disorders and lesions	Non-infectious Disorders and lesions
<ul style="list-style-type: none"> <li>• Viral infections: Herpes simplex, Herpes Zoster, CMV, Molluscum contagiosum, warts</li> <li>• Fungal infections: Candida, Tinea, Onchomycosis</li> <li>• Bacterial: impetigo</li> <li>• Others: Scabies</li> </ul>	<ul style="list-style-type: none"> <li>• Seborrhic dermatitis, atopic dermatitis</li> <li>• Generalized dermatitis, Nutritional deficiency</li> <li>• Eczema, Psoriasis, Drug eruptions</li> <li>• Eczema, Psoriasis, Drug eruptions</li> <li>• Vasculitis</li> <li>• Alopecia, Papular pruritic eruptions</li> </ul>

**G. ORAL CANDIASIS**

- Oral candidiasis is the most common form of fungal

infection encountered with HIV-infected children.

- Esophagus is involved in 20% of cases and denotes significantly impaired T-cell function, presenting with symptoms as anorexia, dysphagia, vomiting and fever.
- Other oral manifestations included in differential diagnosis are gingivostomatitis, aphthous ulcer, herpes labialis, and oral hairy leukoplakia.

## 2.4 HEMATOLOGICAL MANIFESTATIONS

Pediatric HIV disease is associated with different hematological abnormalities presenting as pallor, Neutropenia, Lymphopenia, Thrombocytopenia and eosinophilia. Thrombocytopenia can be present with petechiae and ecchymosis and may be diagnosed as immune Thrombocytopenia. Alteration of hematological profile occurs due to the virus itself, opportunistic infections, drug side effects or antibody mediated cellular destruction.

### HEMATOLOGICAL ABNORMALITIES CLINICAL MANIFESTATIONS AND UNDERLYING MECHANISM

Hematological Abnormality	Mechanisms
Anemia	Auto-immune antibodies that cause destruction of erythrocytes, Suppression of the bone marrow by drugs used in treatment of HIV-infection (e.g. AZT) or of associated infections (i.e. ganciclovir, cotrimoxazole; nutritional deficiency (folic acid, vitamin B 12, micronutrients)
Thrombocytopenia	Immune-mediated destruction of platelets, Nutritional deficiency ( i.e.vitamin B 12 deficiency)
Neutropenia	Immune-mediated destruction of leukocytes
Lymphopenia	Bone marrow suppression due to altered cytokine production, CD4 + apoptosis induced by HIV replication
Eosinophilia	Shifting of immune response from Th 1 to Th2 cytokine profile.

## 2.5 CARDIAC MANIFESTATION

- HIV infection does not increase the risk of developing congenital cardiac malformations. However, cardiovascular diseases do seem to develop in HIV-infected children, and they are often clinically silent.
- The cardiac manifestations include cardiomegally, congestive cardiac failure, non-bacterial thrombotic endocarditis, cardiomyopathy, pericardial effusion, cardiac tamponade, conduction disturbances and sudden death.
- Cardiomyopathy is frequently present in patients with encephalopathy. The factors that have been implicated in the causes of cardiomyopathy include primary HIV disease, immune-mediated reactions, intercurrent infections and drug toxicity
- Cardiomyopathy decreases the survival rates and is one of the clinical indicators of starting ARV drugs.

## 2.6 NEUROLOGICAL MANIFESTATION

- Primary CNS infection by HIV is quite common as it is a neurotropic virus...
- Two forms of encephalopathy exist- **Progressive and static.**
- HIV leads to myriad of CNS problems of varied etiology that are both infectious and non-infectious.

According to the CDC revised system, the diagnosis of encephalopathy requires one of the following progressive findings to be present for at least 2 months in the absence of other identifiable causes.

- Failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychiatric tests.
- Impaired brain growth or microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by CT or MRI, with serial imaging required in children less than 2 years of age.

- Acquired symmetric motor deficit manifested by two or more of the following paresis, pathological reflexes, ataxia or gait disturbances.
- CT may show evidence of cortical atrophy, prominent sulci, and enlarged ventricles and decreased attenuation of white matter suggestive of progressive multifocal leucoencephalopathy.

## 2.7 NEPHROPATHY

- The proportion of HIV-infected children who have nephropathy is variable and is more in adolescent.
- The manifestations or renal disease associated with AIDS include proteinuria, hematuria hypertension, renal tubular acidosis, acute renal failure and progression to end-stage renal disease.
- In the initial stages, the patient could be asymptomatics, although laboratory evidence of nephropathy can be found on investigations.
- Histological changes in AIDS nephropathy reveal focal segmental glomerulosclerosis, minimal lesion glomerulonephritis, IgA nephropathy.
- Nephropathy may be due to direct infection of the virus, immune complex vasculitis, or as a result of various opportunistic infections or drugs.

## 2.8 RESPIRATORY MANIFESTATIONS

### ***Lymphoid Interstitial Pneumonitis (LIP) and pulmonary lymphoid hyperplasia :***

- They are the main presentations of the respiratory system involvement.
- The clinical presentation of these disorders is usually insidious. Cough and tachypnea are early clinical features, followed by Dyspnea at rest and development of clubbing.

- There are often no findings in the chest unless; recurrent bacterial infections have led to bronchiectasis. Hepatosplenomegaly, lymphadenopathy and parotid swelling are the common associated findings.
- The radiological findings of diffuse bilateral reticulonodular or interstitial infiltrates support the diagnosis of LIP. The nodules are usually 1-5 mm in diameter and hilar lymphadenopathy is frequently present.
- A presumptive diagnosis is made on the basis of clinical and radiological findings. However, one needs to exclude opportunistic bacterial infections that can present with similar clinical and radiological findings.
- Definitive diagnosis requires lung biopsy. Children with LIP have an increased incidence of pulmonary bacterial infections.

## TUBERCULOSIS

- It is the most important opportunistic infection encountered in children, occurring at a higher CD4 count when the immune-deficiency is comparatively less advanced.
- ***Mycobacterium avium intercellular (MAC)*** causes disseminated and usually non-pulmonary disease and is an important cause of morbidity in HIV-infected children. A CD4 count < 100 cells/mm<sup>3</sup> has been recognised as a primary risk factor for this infection.
- Respiratory viruses like respiratory syncytial virus, measles, parainfluenza, influenza, adenovirus, rhinovirus and corona virus, cause prolonged and severe disease.
- Fungal infections due to histoplasmosis, coccidioidomycosis and aspergillosis present similarly.

Pneumocystis carinii pneumonia (PCP) causes an acute life threatening pneumonitis.

## 2.9 MALIGNANCY

- The incidence of malignancy in HIV-infected children is higher than that in general population.
- However, the type of malignancies associated with children AIDS(non-hodgkin's lymphoma, leiomyoma and leiomyosarcomas and leukemia) is much different from that associated with adult HIV disease.
- The kaposi's sarcoma, a commonly encountered malignancy in adult HIV disease features is rare in children.

## 2.10 PROGNOSTIC INDICATORS

- In the underdeveloped countries the age at diagnosis and the type of clinical presentation are the only clinical factors related to prognosis.
- Infants who develop symptoms in the first year of life manifest the fastest progression of illness with worst outcome.
- Similarly, the occurrence of opportunistic infections, progressive encephalopathy or hypogammaglobunemia at any age often carries a poor prognosis.
- In contrast, generalized lymphadenopathy, hepatosplenomegaly, parotitis are associated with a more favorable outcome.
- **Viral load** is the most important prognostic marker of the risk of progression. But the availability and the cost are constraints. It is predicted that a favorable clinical outcome is most likely if virus replication is maximally suppressed before the immune system is irreversibly damaged.

## CHAPTER 3

### CLINICAL STAGING AND CLASSIFICATION

#### 3.1 WHO CLINICAL STAGING OF HIV/AIDS FOR INFANTS AND CHILDREN

The following WHO definitions are designed for use in developing countries. They are based on clear clinical markers and do not require any of the diagnostic technology which is likely to be lacking in countries where such resources are limited.

##### CLINICAL STAGE 1

- Asymptomatic.
- Persistent generalized lymphadenopathy.

##### CLINICAL STAGE 2

- Hepatomegaly.
- Papular pruritic eruptions.
- Seborrhoeic dermatitis.
- Fungal nail infection.
- Angular cheilitis.
- Lineal gingival erythema.
- Extensive molluscum contagiosum.
- Extensive human papilloma virus infection.
- Recurrent oral ulcers.
- Parotid enlargement.
- Herpes zoster.
- Recurrent RTI (otitis media, otorrhoe or sinusitis) twice or more in any six-month period.

##### CLINICAL STAGE 3

- Unexplained moderate malnutrition not adequately responding to standard treatment.

- Unexplained persistent diarrhea, (14 days or more)
- Unexplained prolonged fever (intermittent or constant), >one month.
- Oral candidiasis (thrush).
- Oral hairy leukoplakia.
- Pulmonary tuberculosis within the past year.
- Severe bacterial infections (i.e.pneumonia)
- Acute necrotizing ulcerative gingivitis or stomatitis, or acute necrotizing ulcerative periodontitis.
- LIP.
- Chronic HIV -associated lung disease( including bronchiectasis)
- Unexplained anemia (<8 g/dl), and or neutropenia (<500/mm<sup>3</sup>) and thrombocytopenia (< 5000/mm<sup>3</sup>) for more than one month.

#### CLINICAL STAGE 4

- Unexplained severe wasting, or severe malnutrition or stunting not responding to standard treatment.
- *Pneumocystis pneumonia*. (PCP)
- Recurrent severe presumed bacterial infections (two or more episodes in one year). e.g. meningitis, empyema. Pyomyositis, bone or joint infection, bacteremia)
- Chronic herpes simplex infection( orolabial or intraoral lesions of more than one month or visceral of any duration.
- Oesophageal candidiasis.
- Extrapulmonary TB.
- Kaposi's sarcoma.
- Toxoplasmosis of the brain.
- Cryptococcal meningitis.
- *HIV encephalopathy, as defined by the Centers for Disease Control and Prevention.*
- *CMV retinitis and CMV of an organ other than liver, spleen or lymph nodes.*

- *Progressive multifocal leukoencephalopathy.*
- *Any disseminated endemic mtcosis (i.e. histoplasmosis, coccidioidomycosis).*
- *Candidiasis of the trachea, bronchi or lungs.*
- *Atypical mycobacteriosis, disseminated.*
- *Non-typhoid Salmonella septiceamia.*
- *Crptocosporidiosis*
- *Isosporiasis*
- *Cerebral or B cell non-hodgkin lymphoma*
- *HIV -associated cardipathy and nephropathy*

Note: both definitive and presumptive diagnoses are acceptable.

HIV wasting syndrome : weight loss >10% of body weight, plus either unexplained chronic diarrhoea (>1 month ) or chronic weakness and unexplained prolonged fever (>1 month).

HIV encephalopathy: *clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.*

### **3.2 CLINICAL DIAGNOSIS OF HIV/AIDS IN CHILDREN**

**Two major and two minor signs are required in the absence of known causes of immunosuppression.**

#### **MAJOR SIGNS ARE DEFINED AS:**

- *Weight loss or abnormally slow growth.*
- *Diarrhoea lasting more than one month.*
- *Fever lasting more thn one month.*

#### **MINOR SINGS ARE DEFINED AS:**

- *Persistent generalised lymphadenopathy.*
- *Candida in the mouth or oesophagus.*
- *Cough lasting more than one month.*
- *Widespread itchy rash.*

- Repeated Common infection (otitis, sore throat etc).
- Confirmed maternal HIV infection.

### 3.3 IMMUNOLOGICAL STAGING OF PEDIATRIC HIV INFECTION

Immunological staging for children can be done on the basis of absolute CD4 counts or the percentage values in healthy infants. CD4% is recommended in children as CD4 count varies with different age groups. CD 4% can be measured using the following formula:

$$\text{CD4 count} = \text{CD4\%} \times \text{Absolute lymphocyte count.}$$

Thus whenever CD4 counts is being done for children always ask for the CBC from where you could calculate the ALC.

The ALC also significantly correlates with the risk of mortality in HIV infected children <18 months with a ALC < 1500 / mm<sup>3</sup>. also in places where CD4 counts cannot be assessed the ALC may be used as a substitute for an indication of treatment of infants and children with documented HIV infection in the presence of symptomatic disease - stage 2 and stage 1 of the WHO classification.

#### *PEDIATRIC HIV IMMUNE CATEGORY CLASSIFICATION SYSTEM*

	<b>&lt; 12 months</b>		<b>1 -5 years</b>		<b>6 - 12 years</b>	
<b>Immune category</b>	No/mm <sup>3</sup>	CD4%	No/mm <sup>3</sup>	CD4%	No/mm <sup>3</sup>	CD4%
	CD4		CD4		CD4	
<b>Category 1:</b>	>1500	>25%	>1000	>25%	>500	>25%
<b>No suppression</b>						
<b>Category 2:</b>	750-1499	15-24%	500-999	15-24%	200-499	15-24%
<b>Moderate</b>	(1000)	(20%)	(650)	(20%)	(275)	(20%)
<b>suppression</b>						
<b>Category 3:</b>	<750	<15%	<500	<15%	<200	<15%
<b>Severe</b>						
<b>suppression</b>						

## CHAPTER 4

### MANAGEMENT OF NEWBORN BABIES BORN TO HIV INFECTION MOTHER

Early identification of HIV infected women is crucial for the health of such women and for HIV exposed and infected children. HIV counseling and voluntary HIV testing can best accomplish this through the identification of HIV infected women before or during the pregnancy.

#### 4.1 IMMEDIATE NEWBORN CARE

Newborn care of an HIV exposed infant is the same as that of any other newborn baby except that in this case the health care worker needs to give bath to a baby immediately after birth normal soap and water. The first bath to the baby needs to be given wearing gloves. Thereafter gloves are not needed for normal handling of the baby.

- Maintain universal precautions of care and treatment.
- Wear gloves to handle the baby.
- Dispose off all needles properly.
- Clamp cord immediately after birth and do not milk the cord.
- Avoid mouth operated suction devices.
- Give immediate bath to clean the baby.

#### 4.2 ARV PROPHYLAXIS FOR THE NEWBORN BABY.

As a part of PMTCT, ART is given to the baby to reduce the risk of transmission of HIV from mother to baby in the following recommended doses.

- Single oral dose of NVP 2mg/kg within 12 hours or at least before 72 hours after delivery.
- AZT 2mg/kg orally every 6 hours for 7 days

**Note:** if the mother received less than 4 weeks of AZT during pregnancy, extend AZT to 4 weeks for the baby.

### **4.3 PROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE IN INFANTS**

- All children born to HIV infected mothers should receive PCP prophylaxis irrespective of clinical evidence of HIV disease.
- Age to start - 6 weeks of age.
- Give TMP -SMZ 6-8 mg/kg/day as a single dose daily. (PCP prophylaxis)
- Give till 12 months of age
- After one year of age prophylaxis should be given if CD4 % is less than 15 %
- Prophylaxis can be stopped at 4 months of age if HIV infection in the baby can be ruled out by DNA PCR on two separate occasions, one month apart (currently this facility is not available in Bhutan).

### **4.4 INFANT FEEDING**

Breastfeeding is associated with significant additional risk of HIV transmission from mother-to child. The risk of transmission is about 20 - 35% with breastfeeding up to six months. These risk further increases to 30 - 45 % if breastfeeding is continued to 24 months. The Royal Government of Bhutan has thus decided to counsel all HIV positive mothers not to breast feed and that the Government will supply infant formula for the first twelve months of life. All HIV infected mothers will be counseled for formula feeding and provided with formula milk support till one year of age. (Details given in chapter 6 of the PMTCT Guideline)

### **4.5 IMMUNIZATION**

Almost all the baby are asymptomatic at birth even if they have been infected with HIV from the mother. Hence the routine immunizations as per the national guidelines must be carried out.

### **4.6 REGULAR MONITORING**

- Infants born to HIV -infected mother should be followed up regularly and monitored to ensure early intervention if symptoms develop.

Follow up visits:

- At age 6, 10, and 14 weeks on the occasion of routine immunizations.
- At 6 weeks prophylaxis for PCP should be started.
- Thereafter once a month up to 1 year.
- Every 3 months from 1 year to 5 years.

## 4.7 HIV TESTING IN BABIES

As antibodies are transferred from the mother to baby in utero the baby may be falsely HIV positive. These antibodies persist in the baby for 12 to 18 months. Thus, HIV testing has to be done at 18 months to definitely say whether the baby is infected or not.

### HIV TESTING IN INFANTS AND INTERPRETATIONS

Age in months	Test	Result	Inference	Remarks/follow-up
12	Rapid tests	HIV-Negative	uninfected*	Graduate from PMTCT
≥18	Anti-body testing (ELISA)	HIV-Positive	?infected	Elisa at 18 month
		Negative	Uninfected*	No further testing-needed*
		Positive	Infection	Regular clinical follow-up

\*Unless breast-feeding is ongoing or was stopped in the last three months

However, when DNA - PCR facilities become available. We can definitely say whether the baby is infected or not by 4 months. We need to have two negative DNA - PCR test results done more than one month apart to declare that the baby is infected. However an antibody test is still done at 18 months to definitely say that the baby is uninfected.

## CHAPTER 5

### MANAGEMENT OF HIV INFECTED CHILDREN

#### 5.1 DIAGNOSIS OF HIV INFECTION

A child is suspected to have HIV infection if he has clinical features described earlier in chapter 2 and 3. It is then confirmed by a HIV antibody testing after 18 months of age.

#### 5.2 EVALUATION

**History taking and physical examination** are essential for:

- Classifying the patient as asymptomatic, and for detecting the onset of disease. It should be done every month till the infants are 12 months old and then every 3 months till their HIV status is confirmed. This can be done at the same time that the baby attends the MCH clinic for growth monitoring.
- Early diagnosis of common infections, which tend to be more severe and persistent and do not respond as well to treatment in HIV -infected children
- Early diagnosis of opportunistic infections and complications of HIV disease.

#### **History should include the following**

- When and where was the diagnosis of HIV made.
- What is the child's possible source of HIV infection.
- What are the current symptoms and concerns of the child.
- Past medical history of symptoms, known diagnosis and treatments given.
- Known allergies to drugs or other substances or materials.
- History of recurrent infections in the past.
- History of possible contact with TB.
- Current and prior opportunistic infection (OI) prophylaxis.
- Current and previous ART.
- Attitude to and readiness to commence ART.
- Ability of the care-giver to adhere to OI prophylaxis and other drugs (such as TB therapy) in the past.
- Ability to keep scheduled appointments in the past.
- Family history e.g. other immediate family members especially mother with known HIV infection and their state of health.
- Psychological and financial and family support.
- History of drug and alcohol use in older children.
- Enquire about toxicity and side effects of ART.

<b>Checklist for symptoms and signs</b>		
General	Symptoms Fever  Fatigue Temperature Appetite Failure to thrive	Signs and physical examination Body weight, height, head circumference (for infants <2 yrs.) Lymphadenopathy Pallor Parotitis
Cutaneous	Rash  manifestations	Skin rash, herpes zoster(current or past), pauplar pruritis Pruritis eruptions(PPE), diffuse skin dryness, etc
Oropharyngeal manifestations	Pain, odynophagia Dysphagia	Candidiasis  Oral hairy leucoplakia(OHL) Mouth sores
Gastrointestinal system	Nausea or vomiting Diarrhea Abdominal pain	Jaundice  Examination of abdomen particularly for liver and spleen enlargement
Respiratory system	Cough Difficulty in breathing Cheat pain	Tachpnea, respiratory distress Signs of consolidation Cyanosis Signs of pleural effusion
Cardiovascular system	Dyspnoea	Cardiomegaly Murmurs
Neurological and musculoskeletal system	Mental and motor Development abnormalities Headache, dizziness tingling, seizures Irritability	mental state, motor and sensory deficit Microcephaly Signs of raised intracranial pressure
Eye	Any visual changes	Examination of optic fundus, retinitis, papilloedema
Ear, nose, throat	Sore throat Recurrent URTID Discharge from ears	Otitis media Sinusitis Pharyngeal thrush
Functional Status	Able to go school Ambulatory Bedridden	

**THE PHYSICAL EXAMINATION SHOULD INCLUDE THE FOLLOWING:**

- General temperature, weight, height, body length and head circumference in infants.
- Skin-Herpes Zoster, herpes simplex, folliculitis, pruritis, candidiasis in the diaper area, seborrheic dermatitis, condyloma, molluscum
- Ear, Eyes, nose
- Throat and oral cavity-examine for thrush, ulcers on the tongue and buccal mucosa.
- Lymphnodes
- Abdomen -distention, hepatosplenomegaly  
Neurodevelopment- milestones, tone and reflexes, motor abnormalities
- Heart
- Respiratory system

**5.3 LABORATORY INVESTIGATIONS AND MONITORING**

**A) ESSENTIAL:**

- HIV serology ( confirmed by ELISA)
- CBC
- CD4 counts and percentage
- Blood chemistry: RFT/electrolyte, LFT, Blood sugar, lactate level, lipid profile
- Chest X-ray
- PPD

**B) SUPPLEMENTARY:**

- Urine microscopy
- Hepatitis markers
- Cultures: blood, urine, sputum and fungi
- Ultrasound and other imaging techniques as per the clinical pictures.

## 5.4 SUGGESTED FOLLOW-UP OF HIV INFECTED CHILDREN NOT ON HAART

As majority of pediatric cases of HIV are through maternal transmission the follow up is the same as mentioned in the previous chapter, i.e., every month in the first year of life and then every three months till the child is five years of age for early detection of any growth faltering and early institution of nutritional management. (This is the same that is followed for all children below five years of age at the MCH clinic)

Follow up at this rate also allows for early management of pediatric HIV disease which is based on timely institution of chemoprophylaxis, immunization, management of opportunistic infections, nutritional support and ARV therapy.

## 5.5 SUGGESTED FOLLOW UP OF HIV INFECTED BABIES ON HAART

Time		Reasons
1	2 weeks	To increase NVP dose and to look for side effects.
2	Every month	<ul style="list-style-type: none"> <li>• To collect monthly drugs.</li> <li>• To check for drug adherence</li> <li>• Early detection of growth faltering</li> <li>• Early detection of treatment failure</li> </ul>
3	Every three months	To monitor for side effects of drugs.
4	Every six months	Do CBC, LFT, RFT, Lipid profile, CD4 % or counts.
5	Every 12 months	If <350 cells or 20 - 25% repeat after three months.
		<ul style="list-style-type: none"> <li>• Ophthalmic and cardiac evaluation.</li> <li>CT/MRI if feasible.</li> </ul>

## 5.6 NUTRITIONAL MANAGEMENT

- Nutritional status of the child is an important factor that determines the morbidity and mortality in HIV infection. Malnutrition and its associated complications aggravate the HIV disease. It also increases susceptibility to opportunistic infections and reduces the tolerance to medication.
- Repeated Painful oral or esophageal candidiasis, herpetic lesions and anorexia are common causes of inadequate intake, leading to starvation and cachexia. The loss of weight and subsequent failure to thrive in cachexia is due to preferential catabolism of lean body mass over body fat. Therefore, the resting energy expenditure is increased.
- Nutritional assessment and its counselling should be done on every visit. This should include a detailed dietary history of feeding, bowel habits, and emesis. Supportive laboratory assessments of hematocrit, electrolytes, serum proteins, and liver functions should be done.
- The aim of the nutritional therapy in HIV-infected children is most specifically to preserve the body weight. Regardless of the stage of illness, nutritional therapy need to be individualized, giving priority to locally available foods.
- Dietary counselling for both the parents and care givers is important. Food hygiene and proper hand washing by food handlers should be stressed to prevent food-borne opportunistic infections, leading to diarrhea.

## 5.7 IMMUNIZATION

Immunization schedule recommended by Royal Government of Bhutan for all other children is to be followed for HIV exposed infants. The main stress is to immunize asymptomatic children as per schedule and to withhold the live vaccines (BCG and OPV) in symptomatic immunocompromised HIV children.

### *Recommendations for immunization of children with HIV-infection*

Vaccines	Known asymptomatic	Known symptomatic
BCG	Yes	No
OPV	Yes	No
DPT / DT	Yes	Yes
Measles/MMR	Yes	Yes
Hepatitis B	Yes	Yes

## 5.8 MANAGEMENT OF OIs AND PROPHYLACTIC THERAPY

Appropriate management of OIs is challenging but rewarding as they improve the quality of life of HIV-infected children. OI encompasses a wide variety of microorganisms that produce fulminant infection in immunocompromised children. As immune response is weakened by decrease in CD4 cells, the HIV-positive patients are at increased risk of relapse or recurrence of previously treated infections. Therefore, it is important to identify and treat the infection as soon as possible, thereafter consistently administering prophylactic therapies. OIs and their management are discussed in other chapter in detail however these are again summarized below to serve as a ready reference.

### A. PNEUMOCYSTIC CARINA INFECTION (PCP)

PCP prophylaxis is recommended by Trimethoprim - Sulfamethoxazole (TMP - SMX) 6 - 8 mg/kg/day 12 hourly. It can be given daily or on three

alternating days, per week.

Indications for prophylaxis are:

- All HIV infected and children with unconfirmed infection from 6 weeks to 12 months of life. Thereafter give as per CD4 counts, CD4 %.
- HIV infected children 0 - 5 years: CD4 count less than 500/UL, CD4 % <15%  
6-12 years CD4 count less than 200/UL, CD4 % < 15 %
- All HIV infected children previously treated for PCP

## **B. SERIOUS BACTERIAL INFECTIONS.**

- Daily Prophylaxis with TMP-SMX protects against serious bacterial infections.
- Administration of IVIG (Intravenous Immunoglobulin ) 400 mg/ kg/months is recommended in children with Hypogammaglobulinemia, and in child with a history of two or more invasive bacterial infections in one year especially for those who have failed or are intolerant to antibiotic prophylaxis.

## **C. MYCOBACTERIUM TUBERCULOSIS INFECTION.**

- Prophylaxis with INH (Isoniazid ) 5 mg/kg/day for 12 months is indicated in the following circumstances :
- All tuberculin positive children with Mantoux (PPD) >5 mm, who had previously not received treatment for tuberculosis, Note that in children not infected with HIV the cut off for a positive PPD / Mantoux test is 10 mm.
- Children with recent contact with an infectious tubercular patient regardless of the result of tuberculin skin test or previous history of treatment.

In all the above cases, active tuberculosis should be ruled out by detailed history, clinical examination, chest X ray and other tests.

#### **D. DISSEMINATED MYCOBACTERIUM AVIUM INTRACELLULAR INFECTION.**

Children with advanced immunosuppression should receive prophylaxis against MAC infection with Clarithromycin 15 mg/kg/day, BID or Azithromycin 20mg/kg once a week. Prophylaxis is indicated in the following cases:

- Children < 12 months - CD4 counts less than 750 cells/ UL
- Children 1 - 2 years - CD4 counts less than 500 cells/UL
- Children 2 - 6 years - CD4 counts less than 75 cells/ UL
- Children > 6 years - CD4 count less than 50 cell/ UI

#### **5.9 HAART AND CONTINUED CARE OF THE HIV/AIDS CHILDREN ARE DISCUSSED IN SEPARATE CHAPTERS.**

## CHAPTER 6

### MANAGEMENT OF OPPORTUNISTIC INFECTIONS (OI's)

The natural history of opportunistic infections among children might differ from that observed among HIV-infected adults. Many opportunistic infections in adults are secondary to reactivation of previously acquired opportunistic pathogens, which were often acquired before HIV infection at a time when host immunity was intact. However, opportunistic infections among HIV-infected children more often reflect primary infection with the pathogen. In addition, among children with perinatal HIV infection, the primary infection with the opportunistic pathogen is occurring after HIV infection is established when the child's immune system might already be compromised. This can lead to different manifestations of disease associated with the pathogen among children than among adults. For example, young children with TB are more likely to have extra pulmonary and disseminated infection than adults, even without concurrent HIV infection.

Multiple difficulties exist in making laboratory diagnosis of various infections in children. Diagnosis is often compounded by a child's inability to describe the symptoms of disease. For infections where the primary diagnostic modality is the presence of antibody (e.g., the hepatitis viruses and cytomegalovirus), the ability to make a diagnosis in young infants is complicated by transplacental transfer of maternal antibody that can persist in the infant for 12 - 15 months. Assays capable of directly detecting the pathogen are required to definitively diagnose such infections in infants. In addition, diagnosing the etiology of lung infections among children can be difficult because they do not generally produce sputum, and more invasive procedures might be needed.

Opportunistic infections are the hallmarks of immunodeficiency. OIs are related to the rising plasma viral load and decreasing CD4 counts. It is essential to diagnose OIs, since acute infections could be life threatening. Effective prophylactic regimens against several OIs will reduce the frequencies of OIs and also improve the survival rates. It is therefore

essential to be aware of the clinical features of several OIs.

An effective ARV therapy that successfully decreases the viral load and preserves or restores the immune function reduces the risk of development of OIs.

### **6.1 PNEUMOCYSTIS CARINII PNEUMONIA (PCP).**

- PCP is the most common OI associated with HIV in children
- It is an infection of early infancy and predominantly occurs at the age of 3-6 months.
- P carinii is a protozoa, closely related to fungi.
- It establishes infection within the alveoli, where it proliferates as an extra-cellular parasite. Interstitial edema, hyaline membranes and proliferating organisms fill the air spaces, resulting in progressive hypoxemia and respiratory failure.

#### **CLINICAL MANIFESTATIONS:**

- Presents with tetrad of tachypnea, dyspnea, cough and fever.
- Physical examination reveals tachycardie, respiratory distress, accelerating tachypnea and diffuse retractions
- Auscultation does not reveal any characteristic findings.

#### **RADIOLOGICAL FINDINGS:**

- Signs of hyperinflation with peribronchial thickening, progressing to bilateral alveolar or interstitial infiltrates, spreading outwards from the hila.
- Further progression results in bilateral air-space disease with air-bronchograms, cavities, pleural effusion and pneumothorax.
- Consider the diagnosis if PCP in a patient of HIV with spontaneous pneumothorax.

**DIAGNOSIS:**

- Can be confirmed by Wright-Giemsa staining of induced sputum or samples obtained by Broncho-alveolar lavage (BAL). trophozoites and intracystic sporozoites can be demonstrated in the stained specimen.

**TREATMENT:**

- It is a medical emergency and treatment should not be delayed.
- Drug therapy

**DRUGS USED IN TREATMENT OF PCP**

No	Drugs	Dosing	Remarks
1	Trimethoprismsulphamethoxazole (TMP-SMX)	20 mg of TMP/kg/day, I.V. and 100 mg of SMX in 4 divided doses for 21 days.	The drug of choice, resort to oral as soon as clinical improvement occurs.
2	Pentamidine	4mg/kg/day, single dose I.V. for 21 days	Reserved for children who cannot tolerate TMP-SMX or if there is no improvement after 5-7 days' of therapy.

• A short course of corticosteroids reduces the chances of development of respiratory failure and decrease mortality. Should be started at the onset of symptoms. **Prednisolone** 2-4 mg/kg/d in 4 divided doses for 7-10 days, followed by tapering regimen for the next 10-14 days.

Or

**Methylpredisolone** 2mg/kg/day divided into 2 or 4 doses for 5-7 days.

- Respiratory support, oxygen supplementation, ventilation and good pulmonary toilet should be provided.
- Atovaquone is an alternative for treatment of mild to moderately severe PCP in adults. Data are limited for children;
- Clindamycin/primaquine has been used for treatment of mild to moderate PCP among adults, data for children are not available
- Dapsone/trimethoprim is effective in treatment of mild-to-moderate PCP. Dapsone is given as a once daily dose of 2mg/kg/day with TMP 15 mg/kg in three divided doses for 21 days.

## COTRIMOXAZOLE PROPHYLAXIS IN HIV EXPOSED AND HIV INFECTED CHILDREN

- **Cotrimoxazole** remains important even with increasing access to HAART, as it can improve survival independently of specific HIV treatment.
- It should be used before children require ARVs because it may even postpone the time at which ART needs to be started.
- It is highly effective for the treatment and prevention of PCP.
- In HIV infected children it also offers protection against other infections.

### WHO SHOULD GET COTRIMOXAZOLE:

- **All HIV exposed children** (children born to HIV infected mothers) from 4-6 weeks of age
- **Any child identified as HIV-infected** with any clinical signs or symptoms suggestive of HIV, regardless of age or CD4 count.

### HOW LONG SHOULD COTRIMOXAZOLE BE GIVEN:

- HIV exposed children - until HIV infection has been definitely ruled out AND the mother is no longer breastfeeding
- HIV infected children- indefinitely where ARV treatment is not yet available.
- Where ARV treatment is being given-cotrimoxazole can be stopped only once clinical or immunological indicators confirm restoration of the immune system for 6 months or more.

### UNDER WHAT CIRCUMSTANCES SHOULD COTRIMOXAZOLE BE DISCONTINUED:

- Occurrence of severe cutaneous reactions such as Steven Johnson's syndrome, renal and/ or hepatic insufficiency or severe hematological toxicity.
- In an HIV exposed child ONLY once HIV infection has been excluded:
  - For a non-breastfeeding child < 18 months of age this is by negative DNA or RNA HIV testing
  - For a breastfed HIV exposed child < 18 months – negative virological testing is only reliable if conducted 6 weeks after cessation of breastfeeding.
  - For a breastfed HIV-exposed child > 18 months- negative HIV antibody testing 3 months after stopping breastfeeding.

### IN A HIV-INFECTED CHILD:

- If the child is on ARV therapy, cotrimoxazole can be stopped ONLY when evidence of immune restoration has occurred. This can be assumed where the child is over 18 months of age and CD4% > 15% at two measurements, at least 3-6 months apart. If a CD4 count is not available, cotrimoxazole should not be stopped before a full 6 months of successful adherence to ARV therapy, and then only when clinical evidence of immune restoration is present.

Continuing cotrimoxazole may continue to provide benefit even once child has clinically improved.

- If any therapy is not available it should not be discontinued

#### **DOSAGE OF COTRIMOXAZOLE:**

- Syrup is recommended in very young children up to 10-12 kg
- Dosage of 6-8 mg/kg once daily should be used
- Single strength adult tab( sulfamethoxazole 400mg and trimethoprim 80mg)  
Up to 10 kg =half of a standard adult tablet  
10-25 kg = one tablet  
>25kgs = two tablets
- Use weight for dosage rather than body surface
- If the child is allergic to cotrimoxazole, dapsons( 2mg/kg/d orally, max. dose 100mg/day) is the best alternative.

#### **FOLLOW –UP:**

- Assessment of tolerance and adherence: cotrimoxazole prophylaxis should be routine part of care of HIV infected children, and be assessed at all regular clinic visits or follow –up visits by health workers and/or other members of multidisciplinary care teams.
- Initial clinic follow-up in children is suggested monthly, and then every 3 months, if cotrimoxazole is well tolerated.

## **6.2 TUBERCULOSIS**

- One of the most common HIV –related OI is tuberculosis.
- HIV increases the susceptibility to both the primary infections as well as to reactivation of tuberculosis -infection due to depressed cell-mediated immunity.
- Primary infection due to contact with an infectious case is common in children with HIV-infection.

- Another problem associated with HIV is high incidence of drug – resistant tuberculosis.
- The progressive depletion and dysfunction of CD4 cells with defect in the function of macrophages and monocytes associated with HIV-infection is responsible for development of extensive tuberculosis.

### CLINICAL FEATURES

- Fever, cough, and weight loss, night sweats and malaise are common clinical findings
- Extrapulmonary disease may involve other tissues and organs as the central nervous system, lymph nodes and mastoid.
- The manifestations in extensive tuberculosis are related to the system involved. The features include miliary tuberculosis, hepatosplenomegaly, lymphadenopathy, tuberculosis meningitis, and genitor-urinary tuberculosis.

### DIAGNOSIS

- Clinical history and features
- PPD, Mantoux test- is considered positive if the induration is 5mm or more.
- Chest radiology: may show features of lobar or multi-lobar infiltrates or diffuse interstitial disease or hilar adenopathy.
- Sputum AFB/gastric aspirate.
- Tissue specimen where ever possible( Lymph node biopsy, pus and CSF)

### TREATMENT:

Because of high risk of dissemination in children < 4 years treatment with ATT should be started as soon as TB is suspected

***Give DOTS therapy at least for the first two months.***

- It should be treated with 4-drug regimen consisting of isoniazid(INH), Rifampicin, Pyrazinamide, and Ethambutol.
- Duration: pulmonary TB- 9 months; extra-pulmonary TB: minimum 12 months.
- Second line ATT should be used to treat multi-drug resistant tuberculosis (MDRTB).  
The regimen should include some of the first –line drugs such as INH, and pyrazinamide.  
Second –line drugs are ofloxacin, thionamide, cycloserine, capreomycin and PAS.  
The minimum duration of therapy is 12 - 15 months.
- Rifampicin should be always included in the regimen. Rifampicin should not be given along with Protease Inhibitors (PI) or non-nucleotide reverse transcriptase inhibitors(NNRTI) as it lowers the concentration of anti-retroviral drugs by inducing the action of hepatic cytochrome 450.
- HAART can be started after 2 months ATT or when the CD4 counts is >200/mm<sup>3</sup> to increase adherence and better differentiate side effects.
- In children already on HAART, then the regimen needs to be modified to accommodate rifampicin in the regime.

### PROPHYLAXIS:

- Children with positive PPD test but without any other manifestation of active disease should receive INH for 12 months.
- Children with recent contact with an infectious tubercular patient.
- Children with a history of prior untreated or inadequately treated past tubercular infection

### 6.3 MYCOBACTERIUM AVIUM COMPLEX (MAC)

- These are ubiquitous saprophytes found in soil, water and food.
- Defective cell mediated immunity as reflected by low CD4 counts ( <50 cells) is an important risk factor for the development of this infection.
- Disseminated MAC rarely occurs in the first year of life.
- Lungs, liver, spleen, GIT, bone marrow and lymph nodes are common sites of involvement.

#### CLINICAL FEATURES

- High grade fever, weight loss, abdominal pain and anemia are common.
- Night sweats, diarrhea, malaise, hepatomegaly, osteomyelitis, meningoencephalitis, soft tissue abscess

#### DIAGNOSIS

- Blood culture ( positive in > 90% )
- Bone marrow, liver and lymph node biopsy
- Anaemia and neutropenia with non specific CXR changes or diffuse and focal infiltrates, cavitatory lesions and hilar adenopathy.

#### TREATMENT

- Combination therapy with a minimum of 2 drugs is recommended
- Clarithromycin 15 mg/kg/day in two divided doses ( max. 500mg/day ) + Ethambutol single dose of 15 – 20 mg/kg.
- In severe infection either add Amikacin 15 – 30 mg/kg/day in two divided doses or one may add

Ciprofloxacin 20 – 30 mg/kg/day, IV or orally, once a day. (Max. 1500gm).

## 6.4 CRYPTOCOCCAL INFECTIONS

- Cause disseminated infection in HIV immunocompromised children
- Features of sub acute meningitis and meningoencephalitis are common
- Pneumonia is seen in 50 % of the cases
- Post infectious sequelae are hydrocephalous, seizures, ataxia and cranial nerve palsy

### DIAGNOSIS :

- India ink staining of CSF
- Cryptococcal antigen (CRAG) in CSF has a sensitivity and specificity of 95 – 100 %
- Positive CSF culture
- CT scan findings of Cryptococcal granulomas

### TREATMENT:

- Initial therapy with Amphotericin B 0.5-1mg/kg I.V. once a day with Flucytosine ( 50 – 150 mg/kg/day orally in four divided doses for 14 days or till clinical involvement Followed by Fluconazole 8- 12 mg/kg/day orally (maximum 400 mg/day) for eight to ten weeks.

### PROPHYLAXIS:

- Life long secondary prophylaxis with Fluconazole 3-6 mg/kg/day orally
- Alternative is Amphotericin IV, 0.5 – 0.7 mg/kg/day, one to three times per week.

## 6.5 CANDIDA INFECTIONS

### CLINICAL FEATURES

- Severe oral candidiasis may be the first indication of HIV infection

- Oral thrush is extensive and relatively difficult to treat
- Diaper dermatitis is common
- Older children present with decreased oral intake and dysphagia
- Esophageal candidiasis present with substernal or abdominal pain, dysphagia and weight loss.
- Disseminated infection may manifest as sepsis and shock

### DIAGNOSIS

- Pseudohyphae seen on a KOH stained preparation
- Candida can be isolated from blood culture
- Endoscopy and biopsy for esophageal candidiasis

### TREATMENT OF CANDIDAL INFECTION

Condition	Drug	Dosing Schedule
Oral candidiasis	Nystatin suspension/lozenges	1–5 lakh U, 4 times a day X 14 d
	Clotrimazole	10 mg oral 4 times a day X 14 d
	Amphotericin B oral suspension	1mg oral, 4 times a day, X 14 d
	Fluconazole	3- 6 gm/kg, OD(max 100mg ) for 14 d
	Ketoconazole	5- 10mg/kg in two div doses X 14 d
Esophageal candidiasis	Fluconazole	• 3-6mg/kg OD ( max 200mg ) X 14d
	Amphotericin B	• 0.5-1mg/kg IV X 14d
Disseminated candidiasis	Amphotericin B	0.5 – 1 mg/kg/day IV X 21 d

### PROPHYLAXIS :

- Children with recurrent infections should be given prophylaxis with oral fluconazole
- Fluconazole 3-6 mg/kg/day oral, daily

## 6.6 HERPES SIMPLEX VIRUSES 1 & 2 ( HSV ) INFECTIONS

### CLINICAL FEATURES

- HSV 1 & 2 manifest as recurrent self limited clusters of orolabial ulcers, genital and anorectal ulcers in patients with CD4 > 100 cells
- In patients with < 100 cd4 counts lesions are seen more extensively along with systemic involvement
- Causes esophageal ulcers, meningoencephalitis, hepatitis, pneumonitis, ventriculitis, shock and transverse myelitis.

### DIAGNOSIS:

- Typical clinical appearance
- Tzanck smear
- HSV 1 & 2 antigen by immunofluorescence

### TREATMENT :

- Neonates – Acyclovir 45 – 60 mg/kg IV in 3 div. doses for 2 – 3 weeks
- Older children with severe infections – Acyclovir 30mg/kg/d in 3 div doses for 14 – 21 days
- Genital /primary gingivostomatitis may receive oral acyclovir 80mg/kg/d in 3 div doses for 10 days

### PROPHYLAXIS :

- Oral Acyclovir 80mg/kg/d in 2-3 div doses for recurrent or severe relapses or if they have severe and slowly healing lesions.

## 6.7 VARICELLA ZOSTER VIRUS (VZU)

### Clinical features

- Classically presents with fever and a generalized pruritic vesicular rash
- Persistent lesions ( i.e., continued appearance of new lesion

for more than one month after onset ) are seen in HIV infected children

- In chronic infections the lesions turn verrucous and necrotic.
- Pneumonia, hepatitis, and encephalitis seen with severe immunosuppression

## DIAGNOSIS

- Typical rash
- VZV –IgM antibody, and virus culture
- PCR and Tzanck smear

## TREATMENT

- Acyclovir 30mg/kg/day in three div doses, IV for 7 – 10 days or till no new lesions appear, whichever is later.
- Foscarnet 120 – 180mg/kg/day in 3 div doses, if no response to Acyclovir

## 6.8 HERPES ZOSTER

### CLINICAL FEATURES

- Multidermatomal infection, disseminated Zoster with over 20 lesions outside the primary dermatome
- Bilateral involvement with rash and retinitis
- Rarely pneumonitis, consumptive coagulopathy, hepatitis, and encephalitis
- Post herpetic neuralgia is common

### DIAGNOSIS

Classical presentation of painful vesicular eruption with dermatomal involvement Viral antigen from the skin kesions

### TREATMENT

- Treat patients with neurologic complications, and disseminated infections
- Acylovir 30mg/kg/day in three div doses, IV for 7 – 10 days no new lesions appear, whichever is later.

## 6.9 CYTOMEGALOVIRUS (CMV)

### CLINICAL FEATURES

- CMV retinitis is seen in patients with CD4 counts less than 50 cell/mm<sup>3</sup>. Nonspecific symptoms of blurred vision, floaters and flashes begin in one eye and progress to involve the other eye. Yellowish white areas of retinal necrosis with perivascular exudates and hemorrhages are seen
- GIT manifestations in the form of esophagitis, substernal pain, dysphagia, colitis, and loss of appetite.
- Pneumonitis presents with dyspnoea, cough and hypoxemia
- Encephalitis manifests as sub acute dementia complex which is difficult to distinguish from HIV encephalopathy.

### DIAGNOSIS

- CMV retinitis is diagnosed by fundoscopy
- CMV esophagitis by endoscopic findings of small and confluent ulcers.
- Sigmoidoscopy for CMV colitis which reveals diffuse areas of erythematic, submucosal hemorrhage and mucosal ulcerations.
- Serologic tests have limitations. Does not differentiate between new and old infection.

### TREATMENT

- Ganciclovir, 10mg/kg/d in 2 div doses, IV over 1-2 hrs for 14 – 21 days or

### PROPHYLAXIS

- Life long prophylaxis after an episode of end organ disease
- Ganciclovir, 5mg/kg/d IV, 5 days a week or
- Foscarnet 90 – 120 mg/kg/d IV as a single daily dose or
- Oral ganciclovir 30 mg/kg, three times a day

## 6.10 TOXOPLASMOSIS

- Congenital infection is common
- Features of congenital infection include low birth weight, microcephaly, hydrocephalous, hepatosplenomegaly and chorioretinitis.

CNS toxoplasmosis can present as headache, fever, changes in mental status, seizures, psychosis, focal neurological deficits, and cranial nerve palsies.

### DIAGNOSIS

- Congenital toxoplasmosis can be diagnosed by detecting *Toxoplasma*-specific IgM, IgA, in neonatal serum within the first 6 months of life or persistence of specific IgG antibody beyond age 12 months.
- A presumptive diagnosis of CNS toxoplasmosis is based on clinical symptoms, serologic evidence of infection, and the presence of a ring enhancing granulomas on imaging studies of the brain.
- Definitive diagnosis of *Toxoplasma* encephalitis requires histologic or cytologic confirmation by brain biopsy

### TREATMENT

- Congenital infection should be treated with 12 months and CNS toxoplasmosis for 6 weeks after resolution of all signs and symptoms of active disease.
- Pyrimethamine, loading dose of 12 mg/kg body weight/day for 2 days, then 1 mg/kg/day for 2 —6 months, followed by 1 mg/kg administered three times a week for the rest of the year plus Sulfadiazine 100mg/kg followed by 85 – 120 mg/kg/day in 4 divided doses
- Folinic acid ( calcium leucovorin ) 5 – 10 mg/kg/day, three times a week to prevent megaloblastic anaemia secondary to pyrimethamine.

- Prednisolone 1mg/kg day in the presence of chorioretinitis and when CSF protein is more than 1000mg% at birth.

## PROPHYLAXIS

- Infants previously treated for congenital toxoplasmosis
- An episode of CNS toxoplasmosis should be followed by life long suppressive therapy.
- Sulfadiazine 85 – 120 mg/gk/day in 2 – 4 divided doses *plus* pyrimethamine 1mg/kg/day *plus* leucovorin 5mg/kg every three days.
- Alternative, Clindamycin 20 – 30 mg/kg in 4 divide doses *plus* Pyrimethamine 1mg/kg/day *plus* Leucovorin 5mg/kg/day, three times a week.

## 6.11 RECURRENT BACTERIAL INFECTIONS

- Peculiar feature of HIV infection in children
- Defined as two or more bacteriologically documented, systemic bacterial infections including bacteremia, meningitis, pneumonia, osteomyelitis, sinusitis that occurred within a two year period.
- Common organisms are *S. pneumonia*, *H. influenza*, *Salmonella*, *Ps. Aeruginosa*, *Staphylococci*, *Klebseilla* etc.
- TMP – SMX prophylaxis for PCP also acts as a prophylaxis for severe bacterial infections

## DIAGNOSIS

- Blood culture, CSF examination, CXR, culture from abscess, bone scan.

## TREATMENT

- Bacteremia – Vancomycin and a third generation cephalosporin
- Pneumonia – Cefotaxime, Ceftriaxone, ampicillin –sulbactam.

If severe infection add anti pseudomonal agent.

- Meningitis - Ceftriaxone

### PROPHYLAXIS AND PERSONAL HYGIENE

- Administer vaccines included in EPI programme.
- Immunize against Hib and pneumococcal at appropriate age.
- Counsel the importance of hand washing, avoiding raw or under cooked food.
- Avoid drinking or swimming in lakes and rivers
- Risk of playing with pets

### CHEMOPROPHYLAXIS

- Daily prophylaxis with TMP-SMX protects against serious bacterial infections.
- Administration of IVIG (Intravenous Immunoglobulin ) 400 mg/kg/month is recommended in children with Hypogamma globulinemia, and in children with a history of two or more invasive bacterial infections in one year especially for those who have failed or are intolerant to antibiotic prophylaxis.
- Another indication for IVIG is chronic bronchiectasis that is sub optimally responsive to antimicrobial and pulmonary therapy.

### 6.12 DIARRHEA

- Chronic diarrhea is common in children
- May become a life threatening event
- May be due to infections with bacteria, protozoa, viral and also as a side effect of drugs
- Large watery stools with abdominal pain
- Chronic diarrhea may cause malnutrition
- Fever dehydration with loss of appetite may be seen

### ENTAMOEBA HISTOLYTICA.

- Diagnosis :stool trophozoites or cysts
- Serological test ( positive with tissue invasion )
- Endoscopy and biopsy if stool test is negative
- Treatment for gut infection diloxanide furoate  
For invasive disease give metronidazole 30mg/kg/d in three div. doses plus chloroquine.  
Giardial lamblia
- Trophozoites and cysts seen in stool, duodenal aspirates.
- Treat with metronidazole 15mg/kg/d in 3 div doses for 5- 7 days or
- Furazolidine 6 mg/kg/d in 4 div doses for 10 days

### ROTAVIRUS

- Elisa in stool sample
- Supportive treatment only needed

### CAMPYLOBADCTER

- Stool culture or blood culture
- Serology for ELISA
- Treat with Erythromycin 30 – 50 mg/kg/d in 4 div doses for 7 days
- Azithromycin 10mg/kg on day 1 followed by 5mg/kg OD for 5 days
- Ciprofloxacin 20mg/kg/d twice a day for 5 days

### SHIGELLA

- Stool culture
- Endoscopic evidence of deep mucosal ulceration and or pseudomembranes.
- Treat with ceftriaxone 50 mg/kg/d OD, IV or IM for 5 days
- Nalidixic acid 55mg/kg/d in 4 div doses for 5 days

### **SALMONELLA**

- Stool culture
- Cefotaxime 150 – 200 mg/kg/d in 3- 4 div doses
- Ceftriaxone 100mg/kg/d in 1- 2 doses IV
- Ciprofloxacin 15 – 30 mg/kg/d Oral or IV
- Duration is for 10 to 14 days

### **CLOSTRIDIUM DIFFICILE**

- Isolation of organism in stool
- Detection of toxin in stool by ELISA
- Colonoscopy show pseudomembranes nodules and plaques
- Treat by stopping the current antibiotic
- Metronidazole 30mg/kg/d in 3 div doses plus vancomycin 25 – 50 mg/kg/d in 4 div doses
- Duration of therapy is for 7 – 10 days.

## CHAPTER 7

### HAART IN PEDIATRIC HIV INFECTION

#### 7.1 PRINCIPLES OF ARV THERAPY

General principles are same as in adults.

Infants and children in need of ARV treatment according to international and national guideline should initiate treatment as soon as possible.

Harmonization of the guidelines with the adult and PMTCT ARV guidelines is desirable.

#### 7.2 GOAL OF HAART:

- a) Clinical goals: Prolongation of life and improvement in quality of life
- b) Virological goal: reduction in viral load to undetectable levels (<50 copies/ ml) for as long as possible, to halt disease progression and prevent and reduce resistant variants.
- c) Immunological goals: Achievement of immune reconstruction, prevent opportunistic infections and malignancies.
- d) Therapeutic goals: Rational sequencing of drugs that achieve virological goals, while also maintaining therapeutic options. Drugs must have the least possible side effects so that their adherence is not a major problem.
- e) Epidemiological goals: Reduce HIV transmission

## CLASSES OF ANTIRETROVIRAL DRUGS

1. Nucleoside reverse Transcriptase Inhibitors(NRT): <b>Zidovudine(Zdv)</b> <b>Stavudine (d4T)</b>  <b>Didanosine(ddI)</b> <b>Zalcitabine(ddC)</b> <b>Abacavir(ABC)</b> <b>Emtricitabine (fTC)</b>	2.Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI): <b>Nevirapine(NVP)</b> <b>Delavirdine(DLV)</b> <b>Efavirenz(EFV)</b> <b>Lamivudine 3TC)</b>	3. protease Inhibitors (PI) <b>Saquinavir(SQV)</b>  <b>Ritonavir(RTV)</b> <b>Nelfinavir(NFV)</b> <b>Amprenavir(NFV)</b> <b>Indinavir(IDV)</b> <b>Lopinavir</b> <b>Atazanavir</b> <b>Fosamprenavir</b>
---	---	--

### 7.3 When to start ARV Therapy in Infants and children

#### A) CLINICAL CRITERIA: INFANTS AND CHILDREN WITH CONFIRMED HIV INFECTION

- WHO pediatric clinical stage IV Disease: treat all children irrespective of the laboratory parameters; or
- WHO pediatric clinical stage III disease: treat all children irrespective of CD4; in children aged over 18 months treatment guided by CD4 where available, especially in children with lymphocytic interstitial pneumonia, or hairy leucoplakia, or low platelet count; or
- WHO pediatric clinical stage II disease: CD4 guided or where CD4 is not available, guided by total lymphocyte count; or
- WHO pediatric clinical stage I disease: treat only guided by CD4; where CD4 is not available children should not be initiated on HAART.

#### B) CLINICAL CRITERIA: SYMPTOMATIC INFANTS AND CHILDREN WITH UNCONFIRMED HIV INFECTION

For infants and children aged under 18 months where virologically testing or p24 antigen is not available to confirm the HIV infection status,

WHO recommends the initiation of HAART if a presumptive diagnosis of pediatric clinical stage IV disease has been established. It should be made if:

- The child's HIV – exposed is confirmed by antibody testing.
- The child is symptomatic with two or more of the following;
  - oral thrush
  - Severe pneumonia requiring oxygen
  - Severe wasting/malnutrition
  - Severe sepsis requiring intravenous therapy
- CD4 percentage, where available, are below 25%;
- Other factors support the diagnosis of clinical stage IV HIV-seropositive such as
  - Recent HIV-related maternal death;
  - Advanced HIV disease in the mother.

Where treatment has been initiated based on presumptive diagnosis efforts should be made to confirm the HIV status as soon as possible but at least with HIV antibody testing at 18 months of age. Decision on further treatment should be made accordingly.

### C) LABORATORY PARAMETERS FOR GUIDANCE ON DECISION MAKING

immunological markers <sup>1</sup>	Age-specific recommendation to initiate ART	<18 months	18 months-5 years	>5 years
CD4% <sup>2</sup>		<25%	<15%	<15%
CD4 count <sup>2</sup>		<1500 cells/mm <sup>3</sup>	<500 Cells/mm <sup>3</sup>	<200cells/mm <sup>3</sup>
Total lymphocyte count (where CD4 assays are not available)		<3400 cell/mm <sup>3</sup>	<2300 cells/mm <sup>3</sup>	<1200 cells/mm <sup>3</sup>

1) immunological markers supplement clinical staging

2) CD4 cell percentage is preferred in children aged under 5 years; for all other children CD4 count should be used

## 7.4 WHICH ANTIRETROVIRAL REGIMENT TO USE.

Combination therapy is the best available treatment. It slows the progression of disease and improves quality of living. It results in greater and sustained virological and immune response and also delays the development of viral mutations.

### a. First line:

AZT + 3TC + NVP

or

AZT + 3TC + EFV

(If the child does not tolerate NVP then switch with EFV in children more than three years or more than 20 kgs)

### b. Second line:

d4T + 3TC + NVP/EFV

## 7.5 WHEN TO CHANGE ANTIRETROVIRAL THERAPY

- Failure of the current regimen with evidence of disease progression based on virological, immunological or clinical parameter, warrants a change in ARV therapy.
- Also indicated in cases of unacceptable toxicity, intolerance and non adherence
- Development of drug resistance
- Clinical failure is defined as the occurrence of HIV related events even after **three months** of HAART
- Virologic failure is the persistence of viral load, HIV – RNA > 400 copies/ml after 24 weeks or >50 copies/ml after 48 weeks in a naive patient.
- Immunological failure is defined as failure to increase CD4 counts by 25 – 50cells by the end of one year of therapy with HAART

*Failure to respond to a second line regimen is highly suggestive of development of drug resistance. in such cases provisions must be made for drug resistance testing to be done from a higher center.*

**TABLE I. CLINICAL AND CD-4 COUNT DEFINITIONS OF TREATMENT FAILURE IN INFANTS & CHILDREN**

<b>Clinical signs of Treatment Failure</b>	<b>CD Cell Criteria for Treatment Failure<sup>1</sup></b>
<ul style="list-style-type: none"> <li>• Lack of growth among children who show an initial response to treatment, decline in growth among children who show an initial growth response to therapy.</li>   <li>• Loss of neurodevelopmental milestones or development of encephalopathy.</li>   <li>• Occurrence of new opportunistic infection or malignancy clinical disease progression<sup>2</sup>.</li>   <li>• Resurgent of prior opportunistic infections, such as oral candidiasis that is refractory to treatment.</li> </ul>	<ul style="list-style-type: none"> <li>• Return in CD4 cells percentage ( or for children &gt; 6 years of age, absolute CD4 cell count) to pre-therapy baseline or below, in absence of other concurrent infection to explain transient CD4 decrease.</li>   <li>• ≥50% fall from peak level on therapy of CD4 cell percentage( or of children &gt; 6 years of age, absolute CD4 cell count), in absence of other concurrent infection to explain transient CD4 decrease.</li> </ul>

## **7.6 MONITORING DURING HAART**

During HAART the child should be monitored regularly for:

- Clinical improvement and careful assessment of growth at each visit.
- Monitoring for other symptoms of HIV and/or opportunistic disease
- Immunological reconstruction ( CD 4 count, CD4 percentage, Absolute lymphocyte counts)
- Adverse effects of the HAART.
- Adherence to HAART

The details of the follow-up are described in chapter 5. See annexure for clinical monitoring form.

## CHAPTER 8

### CARE AND SUPPORT FOR CHILDREN LIVING WITH HIV/AIDS

As increasing numbers of mothers and children become infected, the infant and childhood mortality will be seriously affected. 20 – 30 % of HIV infected children who survive the first year will die before 5 years of age. The moral and humanitarian obligations to provide appropriate care and support to children infected with HIV and their families lies with health care providers and the government. The main goal should be to provide a good quality of life.

- To contain the disease to its minimum manifestation
- To encourage the normal growth and development of the child
- To support the child to use his maximum potential and abilities
- To prevent physical and psychological consequences
- To create awareness for preventative behaviour in adolescents.

#### 8.1 PRINCIPLES OF HIV/AIDS CARE

- Continuous care and management
- Care should be family based and community based.
- Care must be comprehensive, multidisciplinary, coordinated and collaborative.
- Care must be culturally appropriate, sensitive and non judgemental.
- Care should be centered on the quality of life of child and family

#### 9.2 LEVELS OF CARE

- Home –based care
- BHU level

- District hospital level
- Referral centers

## **8.2 PSYCHOLOGICAL CARE**

The HIV/AIDS epidemic is not merely a health issue, but a challenge on the social, economic, culture, political and legal aspects of society. Health workers should help in clarifying misconceptions and creating awareness for prevention strategies of disease. In addition, on going counselling must address denial, guilt, and anger of the family members and must maintain hope for the family.

Children affected with HIV face a number of psychological problems. Basic AIDS educational programmes for all children and adolescents should be factual and explicit. The support of child psychologist is needed to overcome these feelings.

## **8.3 DISCLOSURE OF THE HEALTH STATUS OF THE CHILD**

A child's HIV status should be kept confidential by the child's health care providers because of consideration of stigmatization, but in consultation with the guardian they should consider informing those who need to be aware, in order to provide proper care for the child. These include people who administer medications to the child and those who are trained to recognize acute signs and symptoms that would signal need of further medical evaluation.

As the child is not psychologically and mentally mature enough to understand the significant of being HIV positive, the positive status of the child need not be revealed to the child.

HIV infected children should not be excluded from schools, day care centers; sports and other group activities as long as their medical condition permits their participation. Testing for HIV should not be a prerequisite for inclusion in these activities.

Parents should know how to take care of any life threatening infections with appropriate and timely action, and should ensure proper immunization and nutritional care.

## ANNEXURE -1. PEDIATRIC ARV DRUGS

Name of drug	Formulations	Daily dose and frequency	Major toxicities	Other comments
<b><i>Nucleoside Reverse Transcriptase Inhibitors-NRTIs</i></b>				
Zidovudine (AZT,ZDV, retrovir	Syrub 10 mg/ml Caps: 100mg; 250 mg Tab: 300mg	Noenatal dose: 2mg/kg 6 hourly IV: 120 mg/m <sup>2</sup> /6 hourly or 20 mg/ m <sup>2</sup> day Oral: 360 mg/m <sup>2</sup> / day	Neutropenia, anemia, nausea, headaches, myopathy	Large volume of syrub not well tolerated in older children. Can give with food. Double dose for HIV Encephalopathy. Reduce in hepatic dysfunction
Lamivudine (3TC) Eпивir	Syrub 10mg/ml Tab. 150mg	Neonate < 30 days: 2mg/kg/dose twice daily<60kg : 4mg/kg/dose maximum dose: >60kg: 150 mg twice daily	Headache, pain abdo, pancreatitis, peripheral neutropenia, abnormal LTF	Well tolerated can give with food some solution at room temp(use within one month of opening) Tablets can be crushed and contents mixed with small amount of water or food and immediately taken

Stavudine (d4T) Zerit	Oral solution 1mg/ml Capsule 15 mg, 20 mg, 30 mg, 40 mg	< 30 kg : 1mg/kg/ dose twice daily 30-60kg : 30mg dose twice daily Max. dose 40mg BD	Headache, GI up- set, rash, periph- eral neuropathy and pancreatitis ( uncommon)	Large volume of solution Capsules can be opened up and mixed with small amount of water or food(stable in so- lution for 24 hour if refrigerated) Keep solution re- frigerated; stable for 30 days; must shake well. Need to be stored on glass bottle
<b>Non- Nucleoside Reverse Transcriptase Inhibitors(NNRTIs)</b>				
Nevirapine (NVP)	Oral suspension 10mg/ml Tablets: 200mg	15-30day: 5mg/ kg/dose once daily x 2 weeks, then 120mg/m <sup>2</sup> dose twice daily then 200mg/m <sup>2</sup> /dose twice daily	Rash 5-10% can treat, if stevens- johnsin-STOP. Elevated liver enzymes	Avoid use with rifampicin Store suspension in room tempera- ture, must shake well Can give with food Tablets crushed and can be mixed with food and water and taken immediately MUST WARN PARENTS ABOUT RASH.
Efavirenz (EFV)	Syrub 39mg/ml Tablets 50, 100, 200, 600mg	10-15 kg- 200mg OD 15-20kg- 250mg; 20-25 kg- 300mg; >40kg-600mg;	CNS Toxicity- som- nolence, abnormal dreams,	Dose may be best given at night

**PRINCIPLES FOR USE OF ARV FORMULATIONS IN INFANTS AND CHILDREN WITH CURRENTLY AVAILABLE PRODUCTS IN RESOURCE POOR SETTINGS**

**YOUNGER, SMALLER INFANTS (<10KG)**

Syrubs, solution or dissolvable formulations of the following remain the best options

- zidovudine(AZT), abacavir (ABC), lamivudine(3TC)
- nevirapine(NVP)
- lopinavir/ritonavir (LPV/r)  
Not ideally recommended in the very young due to problems in dispensing, acceptability, difficulty of use or need for refrigeration
- Stavudine (d4T) liquid
- didanosine(ddi) sachets
- nelfinavir powders
- Switch to available solid formulations as soon as possible or tolerated

**INFANTS AND CHILDREN ABOVE 10-12 KG**

- Switch to available solid formulations as soon as possible or tolerated.
- Use solid formulations of the first and second line drugs used for adults.
- Tablets may be divided in half but not further for drug safety reasons.
- Depending on the age/weight of the child, adult FDCs may result in under-dosing of individual components and this should be checked.
- If adult FDCs are used( crushed or solid), dual FDC may reduce chances of under-dosing of NVP. Adult FDCs can be used in combination with regular formulations either to augment one of the under dosed components of a triple combination ( example additional NVP with a triple

- FDC based combination), or to complement a dual combination ( example:AZT/3TC equivalent + nevirapine)
- There must be a single formulation of NVP as a single agent in addition to dual or triple NRTI FDC.
  - Frequent dose changes are required as children’s growth, weight and development improve due to treatment

**Tables of simplified pediatric ARV dose ranges**

ARV doses need adjustment with change in body weight during follow up as the child responds to ART with catch-up in growth and weight. These tables provide suggested simplified dose schedules based upon the existing formulations available in most countries. They provide the closest dosing possible using the specified formulation, and indicate where it is not possible to get a reasonable dosing range with a formulation or where the drug is usually not recommended for use in this age.

Doses are provided in weight bands and have assumed the basic conversion of body mass to weight as outlined in the table.

<b>Age or weight of child the child</b>	<b>Drug dosage by surface area (m2) of</b>
Neonatal (< 1 month)	0.2–0.25 m2
Young infant (1–<3 months)	0.25–0.35 m2
Child 5–9 kg	0.3– 0.45 m2
Child 10–14 kg	0.45–0/6 m2
Child 15 –19 kg	0.6–0.8 m2
Child 20–24 kg	0.8–0.9 m2
Child 25–29 kg	0.9–1.1 m2
Child 30–39 kg	1.1–1.3 m2

Example: if the recommended dose is given as 400mg/m2 twice per day, then for a child in the weight range 15–19 kg the recommended dose will be: (0.6–0.8) x 400 = 244–316 mg twice per day

## SINGLE ARV DRUGS:

### FIRST LINE REGIMEN DRUGS

The closest easiest dosing possible using the special formulation is suggested, and accompanied by alternative in brackets. Not recommended (N/r) is stated where no dosing is possible with the commonly available formulations.

**TABLE 1: EFAVIRENZ (EFV)**  
(usual dosing in those over 10kg or 3 years is 15mg/kg once daily (od) usually at night)

Weight (kg)	Efavirenz dose Syrub (30mg/ml) od	50mg caps	100mg caps	200mg caps	600 tablets mg
5-6.9	N/r <sup>1</sup>				
7.9.9	N/r				
10-11.9	5.5	(3) <sup>2</sup>	(2)	1	
12-14.9	6.5	(4)	(2)	1	
15-19.9		(5)	(3)	1.5	1/2
20-29.9			3	(2)	1/2
30-34.9			4	(2)	

**TABLE 2: LAMIVUDINE (3TC)**  
(Usual dosing 4mg/kg given twice daily- BD)

Weight(kg)	Lamivudine Dose Syrup (10mg/ml)	150 mg	300 mg
5-6.9	<b>2.5</b>		
7.9.9	<b>3.5</b>		
10-11.9	<b>4.5</b>		
12-14.9	<b>5.5</b>		
15-19.9	<b>7.0</b>	<b>1/2</b>	
20-29.9	<b>10</b>	<b>1</b>	<b>(1/2)</b>
30-34.9	<b>N/r</b>	<b>1</b>	<b>(1/2)</b>

<sup>1</sup> This is not usually recommended for use in this age or formulation.

<sup>2</sup> This is the closest dosing possible using the specified formulation.

**TABLE 3: NEVIRAPINE (NVP)**

Usual dosing is 7 mg/kg twice daily (BD), but first two weeks are dosed with half the total dose only- either as one dose or divided in two ( often called 'lead-in' dosing or 'dose escalation').

Weight (kg)	Nevirapine syrup		Nevirapine tablets	
	Lead in dose syrup Weeks 1 & 2 (10mg/ml)	Full dose syrup (10gm/ml)	Lead in dose Weeks 1 and 2 200mg tab	Full dose 200mg tab
5-6.9	<b>2.2</b>	<b>4.5</b>		
7.9.9	<b>3.5</b>	<b>7.0</b>		
10-11.9	<b>4.0</b>	<b>8.0</b>		
12-14.9	<b>5.0</b>	<b>(10)</b>	<b>1/2 am only</b>	<b>1/2</b>
15-19.9	<b>7.0</b>	<b>(14)</b>	<b>Either 1 am or 1/2 am and pm</b>	<b>1 am &amp; 1/2 pm</b>
20-29.9			<b>1/2 am and pm</b>	<b>1</b>
30-34.9				<b>1</b>

**TABLE 4: STAVUDINE (D4T)**  
**(Usual dosing 1mg/kg given twice daily BD)**

<b>Weight (kg)</b> (required mg dose given in brackets)	<b>Zidovudine Dose Syrup (10mg/ml)</b>	<b>100mg</b>	<b>250mg</b>	<b>300mg</b>
5-6.9 (84)	<b>2.5 ml</b>			
7.9.9 (96)	<b>4.0</b>	<b>1</b>		
10-11.9 (108)	<b>5.0</b>	<b>1</b>		
12-14.9 (120)	<b>6.0</b>		<b>1/2</b>	
15-19.9(168)	<b>8.0</b>			<b>1/2</b>
20-29.9 (204-216)	<b>N/r</b>		<b>1</b>	
30-34.9 (288)	<b>N/r</b>			<b>1</b>

**TABLE 5: ZIDOVUDINE (ZDU OR AZT )  
(Usual dosing above 3 months 240mg/m<sup>2</sup> kg given twice daily BD)**

Weight (kg)	Zidovudine Syrub Dose (100mg/ml)	100mg	250mg	300mg
(Required mg dose given in brackets)				
5-6.9 (84)	<b>2.5 ml</b>			
7-9.9 (96)	<b>4.0</b>	<b>1</b>		
10-11.9 (108)	<b>5.0</b>	<b>1</b>		
12-14.9 (120)	<b>6.0</b>		<b>1/2</b>	
15-19.9 (204)	<b>8.0</b>			<b>1/2</b>
20-29.9 (168)	<b>N/r</b>		<b>1</b>	
30-34.9 (288)	<b>N/r</b>			<b>1</b>

## ANNEXURE -2 PEDIATRIC FORMS

### GENERAL INFORMATION

Serial Number:.....RN.....Date:...../...../.....  
Name:.....Age:.....years Sex:  M  F  
Address:.....  
.....  
Parents: Father:.....Mother.....  
Occupation:  
Father.....Mother.....  
Education:  
Father.....Mother.....  
Immunization: Complete  Incomplete  Not given  
Parents addiction (if any):  Alcohol  tobacco  smoking  
History of Blood / Product transfusion: Yes No Not known  
Mother affected by HIV:  Yes  No  Not known  
HAART for PMTCT:  
A. During Pregnancy  do not know  No  Yes, details.....  
B. During Labour  do not know  No  Yes, details.....  
C. For baby after delivery  do not know  No  Yes, details.....  
History of HAART:  not known  No  Yes, details.....

## HISTORY OF SIGNS / SYMPTOMS - I

Symptoms	Duration
Weight loss > 10% of body weight	
Failure to thrive/gain weight	
Diarrhea > one month	
Fever > one month	
Cough > one month	
URTI, difficulty in feeding	
PGL > one month	
Herpes Zoster	
Extra Genital Molluscum	
Non-Healing Tropical Ulcer	
Extensive Seb. Dermatitis	
Oral candidiasis	
Extensive Erosive Herpes	
Hairy Leucoplakia	
Norwegian Scabies	

## HISTORY OF SIGNS / SYMPTOMS - II

Symptoms	Duration
Extensive Dermatophyteosis	_____
Pulmonary TB	_____
Extra Pulmonary TB ( including disseminated)	_____
Pneumonia	_____
Meningitis (Cryptococcal)	_____
Meningitis (Tubercular)	_____
Meningitis (Bacterial)	_____
Encephalitis (TOXO)	_____
Encephalitis (viral)	_____
Neuritis	_____
Genital Ulcers	_____
Genital Discharge	_____
Genital growth	_____
Bubo	_____
Others (specify)	_____

## GENERAL EXAMINATION

Height:.....cms Weight .....Kgs. Head Circumference ( if < 4 yrs):.....cms Mid arm:.....cms

Pallor:  Yes  No      Icterus:  Yes  No

Hair (Spares/Brittle/Lusterless):  Yes  No

Nail changes (yellow/leuco):  Yes  No

Adenopathy:  Cervical  Supracl  avicular  Axillary

Epitrochlear  Inguinal  Nil

Nutritional deficiency:      Yes  No

If yes specify: .....

## SYSTEMATIC EXAMINATION

<b>Head/ENT/Eye:</b>	<b>Skin/mucous membrane:</b>
<b>Respiratory system:</b>	<b>Cardiovascular system:</b>
<b>GI system:</b>	<b>Central nervous system:</b>
<b>Genitor-urinary system:</b>	<b>Joints:</b>
<b>Development milestones</b>	
Motor:	<input type="checkbox"/> normal <input type="checkbox"/> delayed
Sensory	<input type="checkbox"/> normal <input type="checkbox"/> delayed
Social:	<input type="checkbox"/> normal <input type="checkbox"/> delayed

## LABORATORY INVESTIGATION

Hb:.....gm% WBC: ...../cmm  
 DLC: P.....% L .....% E .....% B .....% M.....%  
 Platelet Count : ...../cmm ESR: .....mm  
 LFT: SGOT: .....IU SGPT .....IU  
 Ser. Bil. \_\_\_\_\_mg% t.proteins \_\_\_\_\_gm%  
 Albumin \_\_\_\_\_mg% Globulin \_\_\_\_\_gm%

VDRL:  Positive  Negative  Not done  Not known  
 HIV test:  Antibody test (ELISA)  Rapid tests  PCR  
 CD4 count:.....CD4 %.....  
 Other.....  
 .....

## OTHER INVESTIGATIONS:

<b>X-RAY CHEST</b>	<b>PPD:</b>
<b>USG</b>	
<b>Stool</b>	<b>Urine</b>
<b>CSF</b>	<b>Cultures:</b>

Name: \_\_\_\_\_

RN: \_\_\_\_\_

<b>Clinical staging (WHO):</b> Stage I      Stage II      Stage III      Stage IV		
<b>Immunological staging:</b> Mild Suppression    Moderate    Suppression    Severe Suppression		
: _____		
<b>Treatment</b>	Yes/No	Number of doses
<b>Antibiotic</b>	_____	_____
<b>ATT</b>	_____	_____
<b>Anti-diarrheal</b>	_____	_____
<b>Antifungal</b>	_____	_____
<b>Anti Viral</b>	_____	_____
<b>Others;</b>	_____	_____
<b>Treatment point:</b>	<input type="checkbox"/> Out Patient	<input type="checkbox"/> In patient <input type="checkbox"/> Not known
<b>Discharge in weeks:</b>	_____	
<b>Outcome:</b>	<input type="checkbox"/> Alive	<input type="checkbox"/> Dead <input type="checkbox"/> Lost to follow <input type="checkbox"/> Not known

## CLINICAL MONITORING FORM

Name _____		RN _____				
No. Visit	D/M/Y	Lab result	New OI	Side effects of HAART	ARV Regimen	Patient status
1	..... Weight ..... Height .....	CD4..... Cells/ mm <sup>3</sup> CD4% .....	! Non ! yes [ ] PCP [ ] T [ ] Crypto- coccus [ ] candidi- asis [ ] penicil- losis [ ] others ..... .....	! Non ! yes [ ] severe rash [ ] hepatitis [ ] lip- odystrophy [ ] anemia [ ] others specify .....	! AZT ! 3TC ! Nvp ! d4T ! EFV ! LPV/r !..... !.....	! 1. No drug ! 2. Start ARV !3. Same reg. ! 4. Change reg. ! 5. Stop ARV [ ] Rx failure [ ] ARV S/E [ ] Poor adher- ence ! 6 loss to FU ! 7. Re- fer..... ! 8. Expired from AIDS..... ! 9. Expired from other cause Next appoint- ment Date..... .....

<p>2</p>	<p>..... Weight ..... Height .....</p>	<p>CD4..... cells/mm<sup>3</sup> CD4% .....</p>	<p>! Non ! yes [ ] PCP [ ] T [ ] Crypto- coccus [ ] candidi- asis [ ] penicil- losis [ ] others ..... .....</p>	<p>! Non ! yes [ ] severe rash [ ] hepatitis [ ] lip- odystrophy [ ] anemia [ ] others specify ..... .....</p>	<p>! AZT ! 3TC ! Nvp ! d4T ! EFV ! LPV/r !..... !.....</p>	<p>! 1. No drug ! 2. Start ARV ! 3. Same reg. ! 4. Change reg. ! 5. Stop ARV [ ] Rx failure [ ] ARV S/E [ ] Poor adher- ence ! 6 loss to FU ! 7. Re- fer..... ! 8. Expired from AIDS..... ! 9. Expired from other cause Next appoint- ment Date..... .....</p>
	<p>..... Weight ..... Height .....</p>	<p>CD4..... cells/mm<sup>3</sup> CD4% .....</p>	<p>! Non ! yes [ ] PCP [ ] T [ ] Crypto- coccus [ ] candidi- asis [ ] penicil- losis [ ] others ..... .....</p>	<p>! Non ! yes [ ] severe rash [ ] hepatitis [ ] lip- odystrophy [ ] anemia [ ] others specify ..... .....</p>	<p>! AZT ! 3TC ! Nvp ! d4T ! EFV ! LPV/r !..... !.....</p>	<p>! 1. No drug ! 2. Start ARV ! 3. Same reg. ! 4. Change reg. ! 5. Stop ARV [ ] Rx failure [ ] ARV S/E [ ] Poor adher- ence ! 6 loss to FU ! 7. Re- fer..... ! 8. Expired from AIDS..... ! 9. Expired from other cause Next appoint- ment Date..... .....</p>

## ANNEXURE.3

### WHO CLINICAL STAGING OF HIV/AIDS FOR INFANTS AND CHILDREN

<p>Clinical stage 1</p> <ul style="list-style-type: none"><li>• Asymptomatic</li><li>• Persistent generalized lymphadenopathy</li></ul>	<p>Clinical stage 2</p> <ul style="list-style-type: none"><li>• Hepatomegaly</li><li>• Papular pruritic eruptions</li><li>• Serborrhoeic dermatitis</li><li>• Fungal nial infection</li><li>• Angular cheilitis</li><li>• Lineal gingival erythema</li><li>• Extensive molluscum contagiosum</li><li>• Extensive human papilloma virus infection</li><li>• Recurrent oral ulcers</li><li>• Parotid enlargement</li><li>• Herpes Zoster</li><li>• Recurrent RTI( otitis media, otorrhoe or sinusitis ) twice or more in any six-month period</li></ul>
---	---

<p>Clinical stage 3</p> <ul style="list-style-type: none"> <li>• Unexperienced moderate malnutrition not adequately responding to standard treatment</li> <li>• Unexplained persistent diarrhea, (14 days or more)</li> <li>• Unexplained prolonged fever (intermittent or constant), &gt; one month.</li> <li>• Oral candidias (thrush).</li> <li>• Oral hairy leukoplakia.</li> <li>• Pulmonary tuberculosis within the past year.</li> <li>• Severe bacterial infections ( i.e. pneumonia,)</li> <li>• Acute necrotizing ulcerative periodontitis</li> <li>• LIP</li> <li>• Chronic HIV -associated lung disease( including bronchiectasis)</li> <li>• Unexplained anemia ( &lt;8 g/dl), and or neutropenia (&lt;500/mmc) and thrombocytopenia (&lt; 5000/ mmc) for more than one month</li> </ul>	<p>Clinical stage 4</p> <ul style="list-style-type: none"> <li>• Unexplained severe wasting, or severe malnutrition or stunting not responding to standard treatment.</li> <li>• <i>Pneumocystis</i> pneumonia. (PCP)</li> <li>• Recurrent severe presumed bacterial infections ( two or more episodes in one year).e.g. meningitis, empyema. Pyimyositis, bone or joint infection. bacteremia)</li> <li>• Chronic herpes simplex infection( orolabial or intraoral lesions of more than one month or visceral of any duration</li> <li>• Oesophageal candidiasis</li> <li>• Extrapulmonary TB</li> <li>• <i>Kaposi's sarcoma</i></li> <li>• Toxoplasmosis of the brain.</li> <li>• Cryptococcal meningitis</li> <li>• <i>HIV encephalopathy, as defined by the centers for Disease Control and Prevention.</i></li> <li>• <i>CMV retinitis and CMV of an organ other than liver, spleen or lymph nodes.</i></li> <li>• <i>Progressive multifocal leuko-encephalopathy.</i></li> </ul>
---	--

## PEDIATRIC HIV IMMUNE CLASSIFICATION SYSTEM

	<b>&lt; 12 months</b>	<b>1 – 5 years</b>	<b>6 – 12 years</b>	
<b>Immune category CD4</b>	No/mm3	CD4 % CD4	No/mm3 CD4	CD4 % Cd4
<b>Category 1 : No suppression</b>	>1500	>25%	>1000	>25%
<b>Category 2 : Moderate suppression</b>	750-1499 (1000)	15 – 24% (20%)	500– 999 (650)	15 – 24% 20 %
<b>Category 3 : Severe suppression</b>	<750	<15%	<500	<15%

## CLINICAL DIAGNOSIS OF AIDS IN CHILDREN

<p><b><i>Two major and two minor</i></b> signs are required in the absence of known causes of immunosuppression.</p>	
<p><b><i>Major signs are defined as:</i></b></p> <ul style="list-style-type: none"> <li>• <i>Weight loss or abnormally slow growth.</i></li> <li>• <i>Diarrhoea lasting more than one month.</i></li> <li>• <i>Fever lasting more than one month.</i></li> </ul>	<p><b><i>Minor signs are defined as:</i></b></p> <ul style="list-style-type: none"> <li>• <i>Persistent generalized lymphadenopathy.</i></li> <li>• <i>Candida in the mouth or oesophagus.</i></li> <li>• <i>Cough lasting more than one month.</i></li> <li>• <i>Widespread itchy rash.</i></li> <li>• <i>Repeated common infection (otitis, sore throat etc).</i></li> <li>• <i>Confirmed maternal HIV infection.</i></li> <li>• <i>Candida in the mouth or oesophagus.</i></li> <li>• <i>Cough lasting more than one month.</i></li> <li>• <i>Widespread itchy rash.</i></li> <li>• <i>Repeated common infection (otitis, sore throat etc).</i></li> </ul>

## **ANNEXURE 4.**

### **Reference:**

1. Manual for Management of HIV/AIDS in children. Jointly compiled by NACO, IAP, UNICEF and WHO>
2. Scaling of Antiretroviral therapy in resource limited setting: treatment guidelines for a public health approach, WHO. Dec 2003.
3. Final review meeting of the ART guideline, 23 June, 2005, Ministry of health, Bhutan.
4. Joint WHO/UNAIDS/UNICEF statement on use of cotrimoxazole as prophylaxis in HIV exposed and HIV infected children.
5. Antiretroviral drugs for the treatment of HIV infection in infants and children in resource-limited settings. Recommendation for a public Health Approach ( 2005 revision), Geneva, Switzerland 20-21<sup>st</sup> June 2005.