

Prevention of Parent-to-Child Transmission of HIV



Clinical Guidelines



National AIDS Control Programme
Ministry of Health
Government of Pakistan



Prevention of Parent-to-Child Transmission of HIV



Clinical Guidelines



National AIDS Control Programme
Ministry of Health
Government of Pakistan



TABLE OF CONTENTS

(i)	ABBREVIATIONS AND ACRONYMS.....	4
(ii)	PREFACE.....	5
(iii)	ACKNOWLEDGEMENTS.....	6
I.	INTRODUCTION.....	7-8
II.	OBJECTIVES AND SCOPE.....	9
III.	BACKGROUND INFORMATION ON HIV IN PREGNANCY AND ON MOTHER-TO-CHILD TRANSMISSION.....	10
IV.	OVERVIEW OF CORE INTERVENTIONS FOR PREVENTING MOTHER TO CHILD TRANSMISSION OF HIV.....	12
	1. Summary of findings from trials of ARV Prophylactic Regimens.....	12
V.	ANTI-RETROVIRAL AGENTS AND THEIR SAFETY IN PREGNANCY AND FOR PMTCT.....	14
	1. Safety of ARV drugs during pregnancy.....	14
	1.1 Nucleoside reverse transcriptase inhibitors (NRTIs).....	15
	1.2 Non-nucleoside reverse transcriptase inhibitors (NNRTIs).....	15
	1.3 Protease Inhibitors (PI).....	15
VI.	RECOMMENDATIONS FOR PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV IN PAKISTAN.....	17
	1. Identification of HIV positive women by risk-based VCT.....	17
	2. Comprehensive MCH services and antenatal care package for HIV-infected women.....	18
	2.1. Cotrimaxazole prophylaxis and recommendations.....	19
	2.2. Screening, prevention and treatment of tuberculosis infection.....	20
	2.3. Nutritional support for HIV positive pregnant and lactating women.....	20
	3. Optimal Obstetric practices.....	21
	4. Selection of ARV Prophylaxis and treatment regimens for the prevention of Mother-to Child transmission of HIV.....	22
VII.	ARV PROPHYLAXIS AND TREATMENT IN DIFFERENT CLINICAL SITUATIONS.....	23
	RECOMMENDATIONS	23
	▪ Clinical Situation A: HIV-infected women with indications for initiating antiretroviral treatment who may become pregnant.....	23
	▪ Clinical Situation B: HIV-infected women receiving antiretroviral treatment who become pregnant.....	24
	▪ Clinical Situation C: HIV-infected pregnant women with indications for antiretroviral treatment	24
	▪ Clinical Situation D: HIV-infected pregnant women without indications for antiretroviral treatment	24
	▪ Clinical Situation E: HIV-infected pregnant women with indications for starting antiretroviral treatment but treatment cannot be arranged.....	25

▪	Clinical Situation F: HIV-infected pregnant women with active tuberculosis.....	25
▪	Clinical Situation G: Pregnant women of unknown HIV status at the time of labor but in whom HIV is suspected, or known to be HIV-infected but have not received antiretroviral drugs before labor.....	26
▪	Clinical Situation H: Pregnant women with known or suspected HIV who are unable or unwilling to access care at designated PMTCT intervention centers.....	26
▪	Clinical Situation I: Infants born to HIV-infected women who have not received any antiretroviral drugs.....	26
VIII.	COUNSELLING AND SUPPORT FOR SAFE INFANT FEEDING.....	31
IX.	CARE AND SUPPORT FOR THE MOTHER IN THE POST-PARTUM PERIOD.....	32
▪	Recommendations.....	33
▪	Summary of comprehensive PMTCT MCH services for HIV positive pregnant women.....	33
X.	CARE FOR INFANTS BORN TO HIV-INFECTED MOTHERS.....	36
XI.	APPENDIX I: Antenatal Care checklist for PMTCT.....	38
XII.	APPENDIX II.....	40
▪	Drug dosages for PMTCT prophylactic regimens for women on HAART.....	40
▪	Drug dosages for PMTCT prophylactic regimens for women not on HAART.....	40
▪	Dosages for common HAART drugs in pregnant women.....	41
XIII.	Appendix III: Sources and further reading.....	42

ABBREVIATIONS AND ACRONYMS

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired immuno-deficiency syndrome
ANC	Antenatal care
ARV	Antiretroviral
ART	Antiretroviral therapy
Bid	Twice a day
CD4	CD4+ T Lymphocyte
CTX	Cotrimoxazole
d4T	Stavudine
ddl	Didanosine
DNA	Deoxyribonucleic acid
EFV	Efavirenz
HAART	Highly Active Anti-retroviral Therapy
Hb	Hemoglobin
HIV	Human immunodeficiency virus
IDU	Intravenous Drug Use
MCH	Maternal-Child Health
MTCT	Mother-to-child transmission of HIV
NACP	National AIDS Control Program
NFV	Nelfinavir
NRTI	Nucleoside reverse transcriptase inhibitor
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
OD	Once daily
OI	Opportunistic infection
PCP	Pneumocystis jiroveci pneumonia (previously pneumocystis carinii)
PCR	Polymerase chain reaction
PMTCT	Prevention of Mother-to-Child Transmission of HIV
PPTCT	Prevention of Parent-to-Child Transmission of HIV
RTV	Ritonavir
SQV	Saquinavir
STI	Sexually transmitted infection
TB	Tuberculosis
TLC	Total lymphocyte count
UNAIDS	United Nations Joint Co-sponsored Programme on AIDS
UNICEF	United Nations Children's Fund
VCT	Voluntary Counseling and Testing
WBC	White blood cell
WHO	World Health Organization
ZDV	Zidovudine

PREFACE

In the light of increasing risk of mother to child transmission of HIV from HIV infected mothers to their infants; it is time to move beyond a single or rigid model of PMTCT interventions and prevention scenarios. These PMTCT Clinical Guidelines for Pakistan were designed to help develop a system and algorithm for delivering optimal and effective ARV prophylaxis, safe obstetrical practices and infant feeding options to HIV positive pregnant mothers in order to minimize (and prevent) the risk of HIV infection in their infants.

This document was developed keeping in mind the health care system of Pakistan, its strengths and limitations, and offers clinical management guidance on HAART, PMTCT prophylaxis, voluntary counseling and testing, and dealing with opportunistic infections in mothers and their infants. These guidelines are designed to help health care providers in deciding which and when PMTCT prophylaxis should begin, how to deal with side effects, alternative regimens, risks of and strategies to mitigate HIV transmission through safe obstetrical and infant feeding practices, and overall management of HIV positive pregnant women towards a safe and healthy outcome for both the mother and baby.

Recommendations made in these guidelines are the current “evidence based best practices” for resource limited settings and should be strictly adhered to by PMTCT health care providers to maximize the benefits, reduce risk of resistance and failure of effective PMTCT interventions, and achieve high quality integrated PMTCT care in Pakistan. Finally, these guidelines are based on strong scientific evidence and will need to be regularly revised as new information from ongoing clinical trials becomes available.

ACKNOWLEDGEMENTS

This publication on Preventing Mother-to-Child Transmission of HIV: Clinical Guidelines for Pakistan was developed after reaching broad consensus on the core elements to be incorporated in the strategic framework for PPTCT in Pakistan in a national consultative workshop held in Islamabad in February 2006. The consultation included obstetricians, pediatricians, infectious disease experts, public health experts, policy planners, UN agencies, and PLWHA representatives.

The Pakistan National AIDS Control Program would like to thank Dr. Anita K.M. Zaidi from the Aga Khan University for developing and writing these guidelines.

The NACP is also grateful to the following individuals for their technical inputs in making sure that these guidelines are up-to-date, scientifically sound, and in keeping with the guiding principles of the NACP, UN agencies, and Maternal-Child Health Care Programs of Pakistan: Dr. Ayesha Khan (NACP), Dr. Myo Zin Nyunt (UNICEF-Regional Office of South Asia), Ms. Bettina Schunter (UNICEF Pakistan), Dr. Nabila Zaka (UNICEF Pakistan) and Dr. Samia Hashim (UNAIDS).

The NACP especially wishes to acknowledge the financial and technical support of UNICEF in producing this publication.

I. INTRODUCTION

According to United Nations Year 2005 estimates, there are 2.3 million children living with HIV and/or AIDS in the world today. The vast majority of these children are living in Asia and southern Africa. Mother to child transmission during pregnancy, child-birth, or through breast-feeding is the most important source of infection in children.

HIV/AIDS has not spared Pakistan, and an increasing number of women and children infected with HIV are being reported from around the country. Although the documented number of peri-natally acquired cases among children in Pakistan is only 39 (NACP 2005), several factors contribute to suggest that this number is a significant under-estimate. These include the lack of awareness about HIV/AIDS among the general population and among health care professionals, the stigma associated with HIV/AIDS, lack of diagnostic testing facilities, and the difficulties of making a diagnosis in children, especially in a country where malnutrition rates are as high as 30% among children under 5 years of age.

To date, the majority of HIV-infected children identified in Pakistan have been born to mothers whose husbands' acquired HIV while working abroad and were identified through routine screening for visa processing/renewals. As national screening programs for voluntary counseling and testing (VCT) for HIV develop in Pakistan, it is expected that more HIV-infected individuals, including women in reproductive ages will be identified. Additionally, recent epidemiologic evidence from the National AIDS Control Program (NACP) and the provincial programs suggests that Pakistan is facing a concentrated epidemic (>5% seroprevalence) among intravenous drug users (IDUs) in several urban locations throughout the country, with rates as high as 26% in IDUs in Karachi (NACP 2005).

Through the efforts of the national and provincial AIDS control programs and the international health agencies, services for HIV prevention, counseling, and testing among vulnerable groups, as well as treatment including antiretroviral therapy and patient support programs are being developed in Pakistan. Much scientific information has recently become available from studies done in Africa and Thailand on how to prevent HIV transmission to the infants of HIV positive mothers. In 2001, the United Nations General Assembly Special Session of HIV/AIDS (UNGASS) committed countries to reduce the proportion of infants infected with HIV by 50% by 2010. Over the past several years, considerable efforts have been made internationally to apply this knowledge to introduce and expand programs to prevent mother-to-child transmission (PMTCT) of HIV in many countries. The strategic framework for preventing parent to child transmission (PPTCT) of HIV in Pakistan has recently been developed by the NACP in consultation with multiple stakeholders including pediatricians, obstetricians, service delivery organizations working with vulnerable groups, UN agencies, and representatives of people living with HIV/AIDS (PLWHA) in Pakistan.

The PPTCT Strategic Framework for Pakistan emphasizes the comprehensive four-pronged strategy for prevention of PTCT of HIV in Pakistan (Table 1). Being a generally low-prevalence country, the major focus is on efforts targeted towards primary prevention of HIV infection in the general population as well as among high-risk groups such as intravenous drug users, migrant workers, and commercial sex workers through a variety of awareness raising, VCT, family planning, and harm reduction service delivery interventions

(e.g. needle exchange programs, condom provision, screening and appropriate management of sexually transmitted infections).

Table 1: Strategic framework for prevention of parent to child transmission of HIV

Four Pillars of Prevention of Parent to Child Transmission of HIV			
<i>Prong 1</i>	<i>Prong 2</i>	<i>Prong 3</i>	<i>Prong 4</i>
Increasing HIV prevention and general awareness in women and men	Preventing unwanted pregnancies in HIV positive women	Preventing HIV transmission from HIV infected mother to her infant (PMTCT)	Linking HIV positive women and their children into a continuum of care and support services

Routine HIV screening of all women presenting for antenatal or delivery care to health facilities in Pakistan is not recommended at present until additional information from well-done representative mapping surveys is available to determine the cost-effectiveness of such an approach. However, VCT for vulnerable women is recommended wherever they present for care.

The initial approach recommended for medical interventions to prevent HIV among the infants of HIV-infected mothers (Prong 3) in Pakistan is based upon 1) appropriate identification of HIV positive pregnant women, 2) development of suitable infrastructure and availability of supplies and HIV health care-related human resources at selected tertiary care hospitals in the country, and 3) development of referral links of these hospitals with obstetric care providers, VCT service providers, and other outreach programs and services.

II. OBJECTIVES AND SCOPE

These guidelines cover recommendations mainly related to the third prong of the PPTCT strategic framework for Pakistan - i.e. specific interventions for pregnant women known or suspected to be HIV-infected. The guidelines have been adapted from recent WHO recommendations for resource-constrained countries which utilize evidence-based information and expert consensus where evidence is lacking. They were developed in consultation with national experts and representatives from UNICEF, UNAIDS, UNFPA and WHO.

These guidelines are aimed at health care professionals involved in the care of women and families with HIV both in the public sector and the private sector in Pakistan.

The objectives of these guidelines are to

- Provide an overview of information related to maternal to child transmission of HIV and its prevention
- Provide recommendations on specific programmatic interventions for prevention of HIV infection in infants including obstetric interventions, anti-retroviral (ARV) therapy and prophylaxis, and infant feeding advice
- Discuss various anti-retroviral prophylactic regimens useful in different health care scenarios, including resistance issues
- Serve as a reference for health care professionals providing care and counseling to women with HIV and care to HIV exposed and infected infants and children.

It is recognized that antiretroviral prophylaxis for PMTCT is a rapidly evolving field with new insights constantly being gained from studies going in other parts of the world. Additionally, it is worth noting that while anti-retroviral strategies have the potential to markedly decrease the risk of MTCT, the major challenge in reducing MTCT in Pakistan remains the identification of women with HIV infection and their entry into care programs that provide them access to good maternal care and care for their infants. Of special interest to Pakistan is knowledge to be gained about improving prophylactic ARV regimen options for breast-feeding women. Promoting exclusive breast-feeding is a cornerstone of improving child survival in Pakistan, and delivering anti-breastfeeding messages even in the context of HIV prevention requires caution. As such, it is expected that these guidelines will need to be reviewed and updated as new and relevant scientific information becomes available as well as operational issues regarding identification of HIV-infected women in Pakistan become clearer and program performance improves.

III. BACKGROUND INFORMATION ON HIV IN PREGNANCY AND MOTHER-TO-CHILD TRANSMISSION

Since the beginning of the pandemic, an estimated 5.9 million children have been infected with HIV worldwide, over 200,000 of them in Asia. Approximately 0.7 million children were newly infected with HIV in 2005, the vast majority in sub-Saharan Africa. HIV among children causes serious illness and suffering and threatens to reverse progress in improving child survival in countries hardest hit by the pandemic. Most HIV-infected children acquire the infection from their mother, either during pregnancy, labor and delivery, or during breast-feeding (Table 2). In the absence of any intervention, the risk of MTCT of HIV is 15-30% in non-breast-feeding populations, and 30-45% among populations with prolonged breast-feeding (Table 2). Prolonged breast-feeding approximately doubles the risk of MTCT.

Table 2: Rates of MTCT transmission of HIV without any interventions

Scenario	Rate of Transmission
During pregnancy	5-10%
During labor and delivery	10-20%
During breast-feeding	5-20%
Overall, without breast-feeding	15-30%
Overall, with breast-feeding for 6 months	25-35%
Overall, with breast-feeding for 18-24 months	30-45%

Pregnancy does not have major harmful effects on the natural history of HIV infection in women in most studies, although the woman is at increased risk of malnutrition in resource-constrained environments because of the triple burden of HIV, food scarcity due to poverty, and the pregnancy itself. On the other hand, HIV infection in the mother has serious adverse effects on the fetus. HIV infected pregnant women have increased rates of spontaneous abortion, low birth weight babies, stillbirths, preterm labor, premature rupture of membranes, other sexually transmitted diseases, pneumonia, and urinary tract infections.

MTCT is usually the result of a chain of events that most often involves an HIV-infected man infecting his wife, who then infects her next baby, and even subsequent babies if the infection is not picked up in time. In Pakistan, the usual scenario that health professionals are encountering are migrant workers deported from the middle-east on account of a positive HIV test obtained on health screening for visas. These deportees who are usually illiterate then come home and infect their wives. The problem comes to light when the deportee develops symptoms related to development of advanced disease (AIDS).

Most transmission during pregnancy occurs in the third trimester. The placenta is thought to play a protective role, but transmission can occur if the placenta is infected or if the mother has a very high viral load associated with recent infection or advanced immunodeficiency.

Infants are at greatest acute risk of infection during labor and delivery. Infants may acquire HIV by aspirating or imbibing maternal blood or secretions that contain HIV, or through mixing of maternal and fetal blood as the placenta separates. Factors associated with an increased risk of MTCT during labor and delivery include: prolonged duration of membrane rupture, acute chorioamnionitis, and invasive delivery techniques (artificial rupture of membranes, fetal electrode sampling, use of forceps or suction apparatus etc.). Prolonged duration of rupture of membranes (beyond 4 hours) has been shown to be an important risk factor. In an American study, duration of rupture of membranes of over 4 hours nearly doubled the risk of infection, regardless of the eventual mode of delivery.

Although the risk of HIV transmission to the infant through breast milk persists for the duration of breast-feeding, it appears to be the highest during the first 6 months and also appears to be higher in infants of women who do not practice exclusive nursing. The exact mechanisms are not well-understood but may relate to increased gut permeability providing an entry point for the virus among infants fed other diets, or because non-exclusive breast feeding may reflect breast pathology such as mastitis or cracked and bleeding nipples.

HIV infected children tend to show quicker progression to florid AIDS compared to adults, with approximately 20% dying by 12 months of age. Often optimal child care is significantly hampered by the presence of sick and dying parents or the lack of parents to take care of a sick child. This makes optimizing PMTCT interventions all the more important.

IV. OVERVIEW OF CORE INTERVENTIONS FOR PREVENTING MOTHER TO CHILD TRANSMISSION OF HIV

The risk of MTCT among HIV-infected pregnant women in industrialized countries has been dramatically reduced to below 2% by utilizing a package of interventions that include highly active anti-retroviral therapy (HAART) during pregnancy, ARV prophylaxis during pregnancy and labor and to the infant in the first weeks of life, obstetrical interventions including elective caesarian delivery before the onset of labor and rupture of membranes, and strict avoidance of breast-feeding their infants (Table 3).

Table 3: Core PMTCT interventions in ideal circumstances

1. Comprehensive maternal and child health services
2. Universal voluntary counseling and testing for all pregnant women
3. ARV prophylaxis and access to HAART for women in whom it is indicated
4. Optimal obstetric practices
5. Provision of safe and acceptable substitute infant feeding
6. Care and support for HIV infected women and their families

1. SUMMARY OF FINDINGS FROM TRIALS OF ARV PROPHYLACTIC REGIMENS

In countries with limited resources, where antenatal coverage rates are abysmally low, and most deliveries are performed by unskilled birth attendants at home, elective caesarian delivery is rarely a feasible and safe option and breast-feeding substitutes often not safe, acceptable, or available. Interventions instead have focused on the efficacy of long and short-term ARV prophylactic regimens using ARVs such as zidovudine, lamivudine, and nevirapine given to HIV-infected mothers and babies.

To date there have been more than 20 trials evaluating the success of different ARV prophylactic regimens for PMTCT in HIV infected pregnant women and their infants in both developed and developing countries in breast-feeding and non-breast feeding populations. Several other trials are on-going. *The consensus from these trials is that it is possible to reduce the risk of peri-natal MTCT (proportion of infected infants at age 6-8 weeks) to below 5% by providing ARV prophylaxis using relatively simple ARV regimens during labor and delivery and in the immediate post-natal period for mothers and babies, and by providing access to HAART for those pregnant women in need of therapy for advanced disease.*

Although much research evidence is available from trial settings using different ARV prophylactic regimens, PMTCT programs have generally not been scaled up for wider implementation in developing countries. The most experience has been gained from using single dose nevirapine (a non-nucleoside reverse transcriptase inhibitor) given to the mother during labor and a single dose to the infant given within 72 hours of birth, with transmission rates of between 8.7 - 22% reported among breast-fed infants. However, development of rapid resistance to nevirapine in the maternal virus, as well as infants who get infected has emerged as a significant concern in this regimen, although its programmatic feasibility and

low cost make it a very attractive option for resource-limited countries. As mentioned, several studies have shown that addition of one or two nucleoside reverse transcriptase inhibitors (zidovudine or zidovudine/lamivudine) to single dose nevirapine in short course combination regimens given peripartum to the mother and baby can reduce transmission to less than 5% in babies with efficacy measured at 6-8 weeks of age.

However, even when combination peripartum ARV prophylactic regimens are used, infants remain at substantial risk for acquiring infection during breastfeeding. Several trials have shown that prolonged breast-feeding reduces the *efficacy* of the peripartum ARV prophylactic regimen to only 25-40% at 18-24 months of age, compared to the placebo arm, with the risk of transmission to the infant as high as 15-23% (Table 4).

Table 4: Long-term efficacy of ARV prophylactic regimens in infants who are breast-fed

Study	Drugs	Antenatal and Intrapartum	Postpartum	Vertical transmission rate and efficacy at weeks - 6 months	Vertical transmission rate & efficacy at 18-24 months
DITRAME trial, Ivory Coast and Burkina Faso	ZDV versus placebo	Short (from 3 weeks); intrapartum	One week; Mother only	18% in ZDV arm; 27.5% in placebo at 6 months Efficacy: 38%	22.5% in ZDV arm; 30.2% in placebo at 24 months Efficacy: 26%
Petra Trial, South Africa, Tanzania, and Uganda	ZDV plus 3TC versus placebo*	Short (from 3 weeks); intrapartum	One week ; Mother and infant	5.7% in ZDV+3TC; 15.3% in placebo at 6 weeks Efficacy: 63%	14.9% in ZDV+3TC; 22.2% for placebo at 18 months Efficacy: 34%
HIVNET 012 trial, Uganda	NVP versus ZDV**	No antenatal ARV; Single dose NVP versus oral ZDV	Single dose NVP versus ZDV for 1 week; infant only	13.1% in NVP arm; 25.1% in ZDV arm at 14-16 weeks Efficacy: 47% compared to ZDV	15.7% in NVP arm; 25.8% in ZDV arm at 18 months Efficacy: 41% compared to ZDV

*Showing only 2 arms of a 4 arm study

**Both arms were active. The placebo arm was stopped

The estimated additional risk of post-natal transmission acquired through breastfeeding between the ages of 4 weeks to 6 months is 4.2% (95% confidence interval 1.8-6.7%), if neither mother nor infant receive ARV drugs during breast-feeding and the infant breast-feeds for a full 6 months. Reducing MTCT acquired via breast-feeding remains a major challenge in resource-constrained settings. Several on-going and planned trials are assessing the impact of ARV drugs given to the mother and/or baby during the breast-feeding period, combined with early cessation of breast-feeding at 6 months.

V. ANTI-RETROVIRAL AGENTS AND THEIR SAFETY IN PREGNANCY AND FOR PMTCT

ARV drugs, including nucleoside analogue reverse transcriptase inhibitors (NRTIs) such as zidovudine (ZDV) and lamivudine (3TC) and the non-nucleoside reverse transcriptase inhibitor (NNRTI) nevirapine (NVP), either alone or in combinations of two or three drugs have been shown to be effective in reducing MTCT. These regimens reduce the risk of MTCT by decreasing viral replication and through prophylaxis of the fetus and infant during and after exposure to the virus.

Short-term efficacy, as determined by infant infection status at 6-8 weeks of life, has been demonstrated for long- and short-course prophylactic ARV regimens comprising:

- ZDV alone
- ZDV together with 3TC
- NVP alone (single dose for mother and infant)
- ZDV plus single-dose maternal and infant NVP
- ZDV and 3TC plus single-dose maternal and infant NVP
- Highly-active antiretroviral therapy (HAART) regimens

Almost all regimens evaluated to date include an intra-partum component and varying duration of antepartum and/or mother and infant post-partum prophylaxis. Some antepartum prophylactic regimens have been started as early as 28 weeks of pregnancy, whereas others at 34-36 weeks or as late as at the onset of labor. **Evidence from these trials suggest that regimens using combinations, such as ZDV and 3TC plus single dose maternal and infant NVP, may be more effective than single drug regimens alone, and that longer courses are more effective than shorter courses.** However, comparing trials done in different settings with varying population characteristics is difficult and a consensus approach utilizing best available evidence and programmatic feasibility has been used to develop PMTCT recommendations and guidelines for settings such as ours.

1. SAFETY OF ARV DRUGS DURING PREGNANCY

ARV drugs may be used during pregnancy:

- as potent combination treatment (HAART) for maternal HIV disease if the woman requires treatment (CD4 count less than 250-300) and/or for the improvement of her own health (i.e mother is symptomatic with OIs); or
- as single, dual, or triple drug shorter term prophylaxis given to prevent HIV infection in infants

All ARV drugs are known to be associated with some toxicity but multiple trials have shown that ARV agents used for short-term prophylaxis for PMTCT are safe and well-tolerated, when evaluated in the short-term. However, sufficient information is still not available on the effects of short courses of ARV drugs to prevent MTCT on the long-term health of the infected mother (and that of her infant) on future ARV treatment options. Research in this area is on-going. Emergence of rapid resistance to NVP when single dose regimens are used has been clearly demonstrated, but the clinical significance of this is unknown. NVP has a much longer half-life than nucleoside analogues such as ZDV and 3TC. Thus, if a triple drug regimen that includes NVP is given for PMTCT, continuing the dual nucleoside reverse transcriptase inhibitors could decrease the risk of developing NVP resistance. This is the basis for recommending combination regimens.

- 1.1 **Nucleoside reverse transcriptase inhibitors (NRTIs):** The nucleoside analogue drugs commonly used in PMTCT regimens include ZDV and 3TC. The most frequent side-effects of these drugs are nausea, headache, myalgias, and insomnia. Contraindications to ZDV or ZDV plus 3TC for PMTCT include known allergy to these drugs, hemoglobin <7g/dl, severe neutropenia (absolute neutrophil count <750), and severe liver or kidney dysfunction. Long-term use of these agents can rarely cause lactic acidosis, pancreatitis, hepatic steatosis, and other disorders associated with mitochondrial dysfunction. Other NRTIs sometimes used in ARV treatment regimens are stavudine (d4T) and didanosine (ddI). Stavudine is among the nucleoside analogues that may be used in first-line treatment regimens in Pakistan. The major toxicities associated with long-term use of d4T are pancreatitis, neuropathy, and lipodystrophy. Combined use of stavudine and ddI in pregnant women has been associated with severe lactic acidosis, with some cases of maternal and fetal deaths. **Combination of stavudine and ddI should not be used in pregnancy.**

The major short-term toxicity among infants exposed to prophylactic ZDV is mild anemia. This is mainly seen among infants of mothers given ZDV for longer courses, and is reversible after treatment is stopped. Clinical trials and observational studies have shown no evidence of teratogenicity with exposure to ZDV.

- 1.2 **Non-nucleoside reverse transcriptase inhibitors (NNRTIs):** WHO-recommended first line ARV treatment regimens used for individuals in need of therapy use triple drug combinations of an NNRTI drug, NVP or efavirenz combined with two nucleoside analogues such as ZDV and 3TC. NVP is the NNRTI agent most commonly used in PMTCT regimens. Contraindications to NVP use include known allergy to NVP or to benzodiazepine derivatives which can result in idiosyncratic allergic reactions.

Single dose NVP prophylaxis to the mother during labor and to the infant within 72 hours of birth does not result in any significant clinical or laboratory toxicity.

The most frequent adverse effects of long-term NVP treatment are hepatic toxicity and cutaneous rash. The risk is greatest in the first 6 weeks of treatment and is 3-7 times higher in women than men. The risk is reduced if NVP is dosed at half its regular dose in the first 2 weeks of treatment (i.e 200mg once daily). Pregnant women with CD4 counts of greater than 250 per 10⁶ cells/L have about a 10-fold higher risk of severe symptomatic hepatotoxicity than women with lower CD4 counts, if exposed to long-term NVP for treatment purposes. **NVP should be avoided for treatment of pregnant women with good CD4 counts.**

Efavirenz (EFV) has been associated with significant teratogenicity if used in the first trimester in pregnant monkeys. EFV should be avoided for therapy for pregnant women in the first trimester. **EFV is not recommended for use among women of childbearing potential unless effective contraception can be ensured and pregnancy has been excluded.**

- 1.3 **Protease Inhibitors (PI):** Protease inhibitors (e.g. ritonavir, saquinavir, nelfinavir, lopinavir) are potent antiretroviral agents when used in combination regimens and can significantly reduce maternal viral load. None of the prophylactic regimens recommended for PMTCT in developing countries use PI drugs as they do not cross the

placenta and therefore do not provide prophylaxis to the fetus, unlike ZDV, 3TC, and NVP.

PI agents are regarded as second line therapeutic agents because of higher pill counts and significant drug interactions, side-effects, dietary and water requirements, and higher expense. The major side-effects observed with long-term PI use are hyperglycemia, lipodystrophy, and lipid profile abnormalities. In industrialized countries they are often included in complex regimens among individuals who have failed first line regimens, and have been used in pregnant women. They are effective in PMTCT because of their effect on reducing maternal viral load. PI-based regimens have been associated with an increased risk of pre-term delivery in some studies.

VI. RECOMMENDATIONS FOR PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV IN PAKISTAN

Recommendations on PMTCT interventions in Pakistan are based on scientific evidence, international expert consensus and opinions as collated by WHO, as well as an assessment of local capacity to implement the package of PMTCT interventions.

ARV drugs are now available free of charge to those who need them at Government of Pakistan supported HIV treatment and care centers in each province, and pediatric formulations are also being imported. The major challenges, as discussed above are the identification of HIV positive women, and their entry into high quality and comprehensive maternal referral care with community based linkages for continued care and support. This infrastructure currently does not exist in the public sector and is in the very beginning stages of development. Additionally, there are significant lack of trained human resource needs as well as improvement in infection control in MCH facilities which must be addressed before PMTCT interventions can be introduced successfully.

Table 5: Summary of recommended interventions for PMTCT in Pakistan

1. Identification of HIV positive pregnant women by risk-based VCT at health facilities and through community outreach programs
2. Referral to high-quality, linked comprehensive MCH services
3. Optimal obstetric practices avoiding unnecessary invasive procedures
4. ARV prophylaxis using combination regimens
5. Counseling and support for safe infant feeding, including exclusive breastfeeding for 6 months when replacement feeding is not acceptable, feasible, affordable, sustainable and safe

1. IDENTIFICATION OF HIV POSITIVE WOMEN BY RISK-BASED VCT

A pregnant woman's HIV status must be determined if she is to benefit from PMTCT interventions. Voluntary counseling and testing services for HIV infection are being established at multiple points across the country. Health care providers should ensure that testing is confidential, and the woman (including her spouse) is counseled about the value of the test to her health and that of her baby (Table 6). **Currently, universal antenatal screening is not recommended in Pakistan until the cost-effectiveness of this approach can be shown.** Information on the feasibility and acceptability of VCT in antenatal care clinics and during labor and delivery in Pakistan, as well as the performance characteristics of any HIV risk assessment instruments is lacking and appropriate studies are planned.

The current recommendation is that VCT for HIV should be offered to pregnant women in all healthcare settings in Pakistan if in the healthcare provider's judgment the woman faces an

increased risk of HIV infection based on historical information (husband's profession and labor history as migrant worker, use of intravenous drugs, husband's current health status, woman's history of blood transfusions, multiple injection use, engagement in commercial sex activity) or findings on physical examination (wasting, presence of generalized adenopathy or opportunistic infections associated with HIV/AIDS, or sexually transmitted infections). Although sero-prevalence of HIV among women infected with Hepatitis B and/or Hepatitis C in Pakistan is not known, since the route of acquisition of these pathogens is similar to HIV, these women may be at increased risk of HIV and VCT for HIV is indicated in such women.

Table 6: Indications for VCT for HIV in pregnant women

- Presence of HIV-related risk factors in medical and/or social history
- Presence of physical findings suggestive of HIV/AIDS
- Presence of Hepatitis B and/or C infection

Since experience from other countries shows that many women never return to learn the results of their HIV test, the best approach is to use a rapid HIV test where results can be available in 1-2 hours. *All positive results by one rapid test need to be repeated by another rapid test from a different methodology or supplier, before identifying and informing a woman as being confirmed HIV positive.* This is essential because in a low-prevalence country, rapid screening tests may falsely identify a person as having HIV, but the chance that two different rapid tests will be falsely positive is minimal. All laboratories performing HIV testing must stock test kits from two different suppliers.

2. COMPREHENSIVE MCH SERVICES AND ANTENATAL CARE PACKAGE FOR HIV-INFECTED WOMEN

For HIV positive pregnant women to optimally use PMTCT interventions, they must have access to good quality MCH services for antenatal and obstetric care. Wherever feasible, HIV positive pregnant women should be referred to designated MCH centers also offering PMTCT package of interventions. Fostering strong communication linkages between these centers and outreach programs working with vulnerable groups as well as public and private sector MCH providers is critical to ensuring the success of PMTCT initiatives.

Components of an antenatal care package for HIV positive pregnant women should include routine recommended health screening for pregnant women, including for sexually transmitted diseases particularly syphilis, nutritional status assessment, anemia assessment, tuberculosis assessment, management of any conditions or diseases identified, maternal tetanus toxoid administration, iron and folate supplementation, nutritional and dietary counseling, information on PMTCT, infant feeding, and family planning, and provision of ARV prophylaxis and treatment if indicated (Table 7). Consultation with an infectious disease expert for assessment of HIV-related clinical and immunological disease status and need for anti-retroviral therapy (and management of any opportunistic infections, if present) for the woman's own health is strongly advised.

Table 7: Components of antenatal care package for HIV infected pregnant women

- Education on ante-natal care, appropriate health-care seeking, self care, hygiene
- Birth preparedness advice including skilled birth attendance, emergency preparedness
- History and physical examination
- Nutritional assessment (weight, height, mid-arm circumference)
- Screening for sexually transmitted diseases
- Screening for tuberculosis if suggested by history or physical examination (tuberculin skin test and chest X-ray)
- Hemoglobin measurement
- Hepatitis B and Hepatitis C screening
- Tetanus toxoid administration
- Iron and folate supplementation
- Nutrition counseling
- Information and advice on PMTCT interventions
- Information and support on infant feeding
- Information on family planning
- Psychosocial support assessment
- Infectious disease expert consultation for clinical and immunological assessment of HIV disease status
- Management of other infections
- Provision of antiretroviral agents for prophylaxis and for treatment if indicated
- Provision of cotrimoxazole prophylaxis if indicated
- Linkage with PMTCT MCH care team (obstetrician, pediatrician, nurse, HIV counselor, outreach worker)
- Referral links with outreach service providers to PLWHA for care and support

The care and support team for an HIV positive pregnant woman should include obstetricians, pediatricians, nurses, counselors, and outreach support providers who have appropriate PMTCT-related training and can provide quality ethical and compassionate care. For PMTCT interventions to be effective, it is essential that motivated PMTCT care teams be developed at tertiary MCH centers that will offer care to HIV-infected women.

An Antenatal Care Checklist for HIV positive pregnant women is shown in Appendix I. Also see flowchart (Figure 1) for a summary of services needed for effective PMTCT interventions.

2.1 Cotrimoxazole prophylaxis

Cotrimoxazole prophylaxis, when indicated, is a key component of the package of care for HIV-infected pregnant women. The benefits of cotrimoxazole prophylaxis in HIV-infected individuals include the prevention of bacterial infections (*Pneumococcus*, non-typhoidal *Salmonella*), diarrhoeal disease (*Isospora*, *Cyclospora*), *Plasmodium falciparum* malaria, toxoplasmosis and *Pneumocystis jiroveci* pneumonia (PCP). Cotrimoxazole prophylaxis given during pregnancy also reduces chorioamnionitis and risk of preterm delivery before 34

weeks of pregnancy, with a decrease in neonatal mortality in women with CD4 cell count below 200cells/mm³.

Recommendations

Cotrimoxazole prophylaxis is recommended for all HIV-infected adults with WHO clinical stage III and IV disease, irrespective of CD4 cell count. Where CD4 testing is available, cotrimoxazole prophylaxis is recommended for all patients with a CD4 cell count below 350cells/mm³. Cotrimoxazole prophylaxis is also recommended for women with clinical stage II disease where CD4 testing is not available.

The risk of life-threatening infections in a pregnant woman with a low CD4 cell count or with clinical features of immunosuppression outweighs the theoretical risk of birth defects. Therefore, women who become pregnant while receiving cotrimoxazole should continue prophylaxis throughout pregnancy. For a woman who requires cotrimoxazole prophylaxis during pregnancy, it should be started regardless of the stage of pregnancy. In the rare situation, where a woman needs to initiate cotrimoxazole in the first trimester, deferral of initiation may be considered. For women receiving cotrimoxazole prophylaxis, this should be continued during the breastfeeding period.

2.2 Screening, prevention and treatment of tuberculosis infection

All HIV-infected pregnant women should be routinely screened at each visit for active TB infection. History of exposure and symptoms should be obtained. INH prophylaxis has been proven to be effective and not teratogenic in pregnant women treated with standard dosages (maximum dose 300 mg/day) for 9 months. Because of a significant risk of hepatotoxicity, baseline liver function tests should be performed before initiation of prophylactic therapy. In addition careful clinical and laboratory monitoring should be conducted.

All HIV-infected pregnant women with confirmed active tuberculosis infection should be monitored and treated according to Pakistan's National TB Guidelines. For initiation of ART for their own health or ARV prophylaxis for MTCT prevention, refer to recommendations on HIV-infected pregnant women with tuberculosis infection (**Clinical Situation F**).

2.3 Nutritional Support for HIV positive pregnant and lactating women

Nutrition advice, counseling, care and support for HIV-infected pregnant and lactating women is especially important because the dual burden of HIV and pregnancy produces acute nutritional vulnerability in women, especially poor women. Energy requirements for HIV-infected asymptomatic pregnant women are 10% more than HIV-uninfected pregnant women, and are increased by 20-30% in symptomatic HIV positive pregnant women compared to pregnant women without HIV. Nutrition counseling should cover:

- *ways of achieving adequate weight gain during pregnancy*
- *the prevention of anemia*
- *the importance of an adequate diet to support lactation and prevent nutritional depletion associated with childbearing*

Currently available data do not support providing high-protein supplements to HIV positive pregnant women. Micronutrient supplementation is recommended. Daily iron-folate supplementation (400 ug folate and 60 mg iron) to prevent anemia and twice daily to treat severe anemia should be given, in line with current WHO guidelines for management of pregnant women in developing countries. However, extra supplementation of Vitamin A is not recommended because of lack of proven benefit and some indication of increased risk of MTCT by increasing viral shedding in the lower genital tract. Daily Vitamin A intake during pregnancy should not exceed the recommended daily allowance. In areas where Vitamin A deficiency is endemic (Pakistan is in this category), WHO recommends a single high dose of Vitamin A (200,000 IU) for women as soon as possible after delivery and not later than 6-8 weeks after delivery.

Table 8 summarizes current recommendations for nutritional counseling and support for HIV infected pregnant women. Women with wasting due to HIV or related opportunistic infections, or who continue to lose weight despite optimal nutritional interventions should be referred urgently for initiation of anti-retroviral therapy and management of infections. Some women may face severe food insecurity due to poverty and may require food assistance. Referrals to support organizations providing services for PLWHA for food assistance should be made.

Table 8: Nutritional support recommendations for HIV positive pregnant women

- Nutritional assessment
- Increase daily caloric intake by 250 kcal/day in asymptomatic pregnant women and by 400 kcal/day in symptomatic women
- Increase daily caloric intake by 600 kcal/day in asymptomatic lactating women and by 800 kcal/day in symptomatic women
- Iron and folate supplementation per existing WHO guidelines
- Micronutrient supplementation: At least 1 RDA or daily supplement
- Vitamin A supplementation: Not to exceed 1 RDA
- Management of wasting: Screen for causes and treat as needed; counsel on increased food consumption; refer for ARV treatment and family food assistance as needed

3. OPTIMAL OBSTETRIC PRACTICES

Only 20-25% of births in Pakistan are assisted by skilled birth attendants, the vast majority happening at home. An important goal of the PMTCT program is to strengthen maternal and obstetric care services in the provision of safe delivery to women in Pakistan. In the initial stages of the program, designated MCH centers where PMTCT package of interventions will be offered are to be upgraded. Special attention needs to be given to improving infection control practices to eliminate any risk of occupational exposure to healthcare attendants as well avoiding nosocomial spread of HIV among patients. This involves standard (universal) infection control procedures, and provision of appropriate decontamination and antiseptic solutions, autoclaving facility for sterilization of instruments, gloves, syringes, and other disposable supplies. Burning linen used on HIV-infected women is not necessary. Adequate waste management should be ensured.

Transmission of HIV from mother to infant during labor and delivery is believed to be due the infant's exposure to infected blood and other body fluids from the mother. Elective cesarean section performed before the onset of labor and before rupture of membranes has been shown to approximately halve the risk of MTCT in industrialized countries. However, controversy about the need for cesarean delivery in women on HAART with undetectable viral loads remains, and the practice of elective cesarean section in these situations is increasingly being questioned.

The overall goal of safe delivery in HIV positive women should be to minimize the infant's exposure to maternal blood or other body fluids. Thus, great care must be taken to avoid any practices that may facilitate this exposure, such as artificial rupture of membranes, episiotomy, multiple vaginal examinations, scalp electrode monitoring, suction delivery etc. Similarly, vigorous suctioning of the infant's mouth and pharynx right after delivery should be avoided unless medically indicated. Umbilical cord cutting and care should be done in a way that minimizes the infant's and health provider's exposure to maternal blood.

Obstetric interventions that increase the chance of blood transfusions should be avoided. Disinfection of the maternal birth canal with antiseptics such as chlorhexidine is currently not recommended because of lack of sufficient evidence to indicate clear-cut benefit in reducing MTCT.

In Pakistan routine elective cesarean delivery is not recommended for HIV positive women for the purpose of prevention of MTCT, because of potential operation-related complications in the mother, and programmatic feasibility in the face of lack of clear evidence of substantial benefit when ARV prophylaxis or treatment is used in breast-feeding populations. Instead, attention should be paid to optimal obstetric practices outlined above. Cesarean delivery is only indicated if necessary for obstetric reasons.

For women who have decided to deliver at home or to a health facility close to home, despite counseling to deliver at the designated MCH center closest to them, effort should be made to provide skilled birth attendance through outreach service delivery organizations.

4. SELECTION OF ARV PROPHYLAXIS AND TREATMENT REGIMENS FOR THE PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV

The selection of an ARV regimen for treatment or prophylaxis for PMTCT depends on many factors such as when in pregnancy a woman identified as HIV infected, whether she needs therapy for the benefit of her own health, whether she is already on antiretroviral therapy, the availability of efficacious drugs, the ability to deliver these drugs in the setting in which the woman will deliver, issues of drug safety and toxicity, and of development of viral resistance.

Selection of an optimal prophylactic or therapeutic ARV regimen for PMTCT is a rapidly evolving field with new information being gathered at a very rapid pace. Therefore, it is expected that these guidelines will need to be revised and updated at frequent intervals, as new information becomes available.

See Summary Tables 9 and 10 for treatment and prophylaxis recommendations in different clinical situations. Drug dosages are listed in Appendix II

VII. ARV PROPHYLAXIS AND TREATMENT IN DIFFERENT CLINICAL SITUATIONS: RECOMMENDATIONS

The following table (Table 9) summarizes the current recommendations and the preferred regimen to be used for PMTCT in Pakistan and is based on the most recent guidelines from WHO issued in 2006. Although the regimen is complex, it has the advantages of increased efficacy and low risk of development of resistance to nevirapine in the mother. In many situations, complex prophylactic ARV regimens may not be possible, and alternative, simpler regimens are listed in Table 10.

Table 9: Preferred Antiretroviral Regimens for Prevention of Mother to Child Transmission of HIV

	Maternal HAART Indicated ¹	Maternal HAART Not Indicated ⁴
Mother		
Antepartum	HAART ²	ZDV starting at 28 weeks gestation or as soon as feasible thereafter
Intrapartum	HAART	SD NVP ⁵ + ZDV/3TC
Postpartum	HAART	ZDV/3TC x 7 days
Infant	ZDV x 7 days ³	SD NVP + ZDV x 7 days ³

¹ Maternal Highly-Active Anti-retroviral Therapy (HAART) indicated: HAART is recommended for all women with WHO clinical stage IV disease regardless of CD4 cell count; all with WHO clinical stage III disease if no CD4 count available, or women with CD4 count <350 if CD4 count available; and women with WHO clinical stage I or II disease and CD4 count <250. HAART should be initiated as soon as required during pregnancy (including first trimester), should be continued during labor, and maintained postpartum.

² First line HAART for pregnant women is ZDV + 3TC + NVP or d4T+3TC+NVP (see National Adult ART guidelines and text).

³ If the mother receives less than 4 weeks of HAART or ZDV during pregnancy, 4 weeks, instead of 1 week, of infant ZDV is recommended

⁴ Alternative regimens for situations in which complex regimens cannot be administered are delineated in Table 10.

The following recommendations pertain to ARV selection for the most commonly encountered clinical situations (Table 10). Drug dosages are listed in Appendix II.

1. Clinical Situation A: HIV-infected women with indications for initiating antiretroviral treatment who may become pregnant: The WHO-recommended first-line ARV regimens for women who may become pregnant and who have indications for starting ARV treatment are ZDV+3TC+NVP or stavudine (another nucleoside analogue, also referred to as d4T) +3TC+NVP. These regimens are also first-line therapy in Pakistan's National ARV Guidelines.

Indications for starting anti-retroviral therapy are the same as those for other adults, and are based on clinical staging and immunological damage assessment by CD4 count measurement (see Antiretroviral Therapy: National Guidelines. National AIDS Control Program, and Tables 9 and 10). EFV exposure may result in teratogenic effects and EFV should be avoided in women in whom effective contraception cannot be ensured.

2. Clinical Situation B: HIV-infected women receiving antiretroviral treatment who become pregnant: Although potential toxicity of ARV drugs to the fetus does exist, stopping ARV therapy during the first trimester is not indicated if the drugs were started because of the mother's own health. *If a woman on EFV becomes pregnant, substitution with NVP should be strongly considered because of the potential for serious fetal effects.* However, substitution with NVP is problematic in women whose CD4 counts are $> 250 \times 10^6$ cells/L because such women are at significantly increased risk of NVP-induced hepatotoxicity compared with women who are more immuno-suppressed. In such situations a protease inhibitor such as nelfinavir or saquinavir are recommended. Nelfinavir is available through the Government supported programs.

Pregnancy induced nausea and vomiting may make adherence to ARV difficult in some women. In these situations, all drugs should be stopped simultaneously and re-started together when tolerance improves to avoid the development of drug resistance.

It is important to continue the full ARV treatment regimen during labor and after delivery for the benefit of the mother's own health as well as preventing transmission to babies through breast-feeding. Infants born to women receiving full ARV treatment should receive one week of ZDV syrup after birth (Tables 9 and 10). If the mother receives less than 4 weeks of HAART during pregnancy, infant ZDV should be continued for 4 weeks.

3. Clinical Situation C: HIV-infected pregnant women with indications for antiretroviral treatment: Women who need ARV treatment should receive it for the benefit of their own health, regardless of pregnancy. Recommended first-line regimens are ZDV+3TC+NVP or d4T+3TC+NVP. EFV is to be avoided because of potential teratogenicity in the first trimester and using NVP in women with CD4 count >250 increases the chances of hepatotoxicity. Initiation of ARV therapy can be delayed to the beginning of the second trimester for women with higher CD4 counts. Alternatively, NVP can be substituted for a protease inhibitor agent such as nelfinavir (NFV) or saquinavir, if the women's medical condition indicates the need for urgent therapy. D4T+3TC+NVP or NFV are preferred regimens for women with severe anemia because of association of ZDV with worsening of anemia.

Treatment should continue during labor and the post-partum period, indefinitely, for the mother's own health. Infants should receive one week of ZDV syrup after birth. Duration of ZDV syrup in babies born to mothers with less than 4 weeks of ante-partum HAART should be increased to 4 weeks (Tables 9 and 10).

4. Clinical Situation D: HIV-infected pregnant women without indications for antiretroviral treatment: This is a rapidly changing field, as several studies assessing optimal ARV prophylactic regimens are currently on-going. In Pakistan, at present the recommended prophylactic ARV regimen to be used solely for preventing transmission of HIV to infants (i.e. not for maternal treatment because it is not medically indicated) are the following:

4.1 First-line prophylactic regimen: ZDV should be started at 28 weeks of gestation or as soon as feasible thereafter, combination therapy with ZDV+3TC+single dose NVP should be initiated at the onset of labor, and ZDV and 3TC continued during labor, and for one week post-partum in the mother (Tables 9 and 10). A single dose of NVP is sufficient to give prophylaxis for one week, because of its long half-life. However, used in the absence of other anti-retroviral agents, exposure to a single dose of NVP can lead to the rapid emergence of NVP-resistant virus.

The baby should receive single dose NVP as soon as possible after birth, combined with one week of ZDV syrup. If the mother receives less than 4 weeks of ZDV, infant ZDV should be prolonged to 4 weeks (Tables 9 and 10).

Maternal prophylactic regimen should be discontinued one week post-partum. However, occasionally, post-partum prophylaxis may be prolonged after discussion about appropriate regimens with an infectious disease expert in those situations where the mother is interested in a brief period of breast-feeding for socio-cultural reasons but can safely provide replacement feeding later.

4.2 Second-line prophylactic regimen: In situations in which antenatal HAART or ZDV cannot be arranged or started, prophylactic regimens can still be given during labor and post-partum period, and have been shown to reduce perinatal transmission (*in utero* transmission cannot be reduced in this way). In such cases the following regimens can be used at the onset of labor: ZDV+3TC and single dose NVP to the mother, with ZDV and 3TC continued post-partum for 1 week. The baby receives single dose NVP as soon as possible after delivery and one week of ZDV syrup (Table 10). Trials have demonstrated that SD NVP plus 1-4 weeks of infant AZT is superior to SD NVP alone and reduces infant NVP resistance.

If possible, ZDV should be given to the baby for 4 weeks. Recommendation for the addition of 4 weeks of infant AZT to SD NVP is based on extrapolation from a Thai study [Lallemant] that demonstrated longer infant prophylaxis was more effective than shorter infant prophylaxis if mother receives less than 4 weeks antepartum therapy. As in this situation no maternal antepartum therapy is received, 4 weeks of infant AZT is recommended as preferred component of the regimen when possible.

4.3 Third line prophylactic regimen: The least preferable regimen indicated for women who are delivering at home for whom more complex regimens will logistically be difficult to provide is single dose NVP given to the mother at the onset of labor, and single dose NVP given to the baby as soon as possible after birth. If possible, 1-4 weeks of ZDV syrup for the baby should be added.

5. Clinical Situation E: HIV-infected pregnant women with indications for starting antiretroviral treatment but treatment cannot be arranged: These women should be managed in the same way as described in Clinical Situation D.

6. Clinical Situation F: HIV-infected pregnant women with active tuberculosis: All HIV infected women with a productive cough for more than two weeks should be screened for tuberculosis. Tuberculosis is a very common co-infected in individuals with HIV who live in highly TB endemic countries. If HIV infected women also have tuberculosis, adequate therapy of tuberculosis becomes the first priority. Tuberculosis should be treated according to the National TB Guidelines of Pakistan. Treatment with ARV drugs becomes especially

complicated in HIV infected women on anti-tuberculosis drugs because of significant interactions of ARV drugs with rifampicin as well as the risk of increased hepatotoxicity. The optimum time to start ARV treatment depends on several factors, including clinical status, CD4 count, duration of pregnancy and ability to tolerate anti-tuberculosis therapy. In our setting, if ARV treatment is to be started, the initial choice can be ZDV plus 3TC plus efavirenz, started after the first trimester (EFV is avoided in the first trimester because of potential nervous system teratogenicity).

For women who do not receive HAART, the same ARV prophylaxis regimens as described in Clinical Situation D can be used. Although there is significant interaction between NVP and rifampicin, this is not likely to substantially decrease the efficacy of single dose NVP among women receiving rifampicin.

7. Clinical Situation G: Pregnant women of unknown HIV status at the time of labor but in whom HIV is suspected, or known to be HIV-infected but have not received antiretroviral drugs before labor: If HIV infection is suspected on the basis of history or physical findings in a woman presenting with labor, if there is time, counseling and rapid HIV testing should be offered. If this is not possible, testing and counseling can be offered shortly after delivery. Rapid HIV tests should be used so that the results can inform about the need for PMTCT interventions in a timely manner.

If HIV infection is confirmed before delivery, or the woman is known to be HIV-infected but has not received any ARV drugs before the second-line regimen described in Clinical Situation D - i.e. single dose NVP and ZDV+3TC during labor and one week post-partum should be used and the baby should receive single dose NVP and ZDV syrup for 1-4 weeks. If combination regimens are not available, the third-line regimen of single dose NVP in mother and baby (with or without ZDV for 1-4 weeks) can be used.

If HIV infection cannot be confirmed before delivery, then counseling and testing should be offered as soon as possible post-partum and follow the recommendations described in Clinical Situation I.

8. Clinical Situation H: Pregnant women with known or suspected HIV who are unable or unwilling to access care at designated PMTCT intervention centers: This situation is likely to be faced occasionally when an HIV infected man is seeking ARV therapy for himself and is known to have a pregnant wife at home but doesn't want to bring her to a hospital. Extensive and compassionate counseling should be undertaken, explaining the benefits of PMTCT interventions for his wife and future offspring. If he is still unwilling to seek care for his wife at one of the designated hospitals for PMTCT interventions, and outreach workers are involved with whom a mutually trusting relationship has been developed, the option of home-based VCT for the pregnant woman, safe delivery at an MCH center near home, and ARV prophylaxis with single dose NVP to mother and single dose NVP plus one to four weeks of ZDV, or single dose NVP only, for the baby should be explored.

9. Clinical Situation I: Infants born to HIV-infected women who have not received any antiretroviral drugs: If HIV infection is confirmed after the baby is already born, the baby should receive single dose NVP as soon as possible after birth, and 1-4 weeks of ZDV. If the baby is more than 3 days old (longer than 72 hours since birth), any ARV prophylactic regimen is unlikely to be effective.

Table 10: Clinical Situations and Recommendations for the Use of Antiretroviral Drugs in Pregnant Women and Women of Childbearing Potential

Clinical Situation	Recommendations
<p>A: HIV-infected women with indications for initiating HAART¹ who may become pregnant</p>	<p>First-line regimens: ZDV + 3TC + NVP or d4T + 3TC + NVP</p> <p>EFV should be avoided in women of childbearing age, unless effective contraception can be ensured.</p> <p>Exclude pregnancy before starting treatment with EFV</p>
<p>B: HIV-infected women receiving HAART treatment who become pregnant</p>	<p>Women Continue HAART unless it contains EFV, in which case substitution with NVP or a PI should be considered if the woman is in the first trimester. Continue the same ARV regimen during labor and after delivery</p> <p>NVP should be avoided in women with CD4 count >250 because of increased risk of hepatotoxicity</p> <p>Infants Single dose NVP soon after birth and 1 week of ZDV</p> <p>4 weeks of ZDV in infants whose mothers received less than 4 weeks of HAART</p>
<p>C: HIV-infected pregnant women with indications for HAART¹</p>	<p>Women If the woman needs therapy for the benefit of her own health follow the same treatment guidelines as for non-pregnant adults except that EFV is contraindicated in the first trimester</p> <p>First-line regimens: ZDV + 3TC + NVP or d4T + 3TC + NVP</p> <p>Infants Single dose NVP soon after birth and 1 week of ZDV</p> <p>4 weeks of ZDV in infants whose mothers received less than 4 weeks of HAART</p>

<p>D: HIV-infected pregnant women without indications for HAART</p> <p>Antepartum ZDV "First Line" regimen possible</p>	<p style="text-align: center;"><i>First line</i></p> <p>Women</p> <p><u>Antepartum</u>: ZDV started at \geq 28 weeks or as soon as feasible thereafter <u>Intrapartum</u>: ZDV + 3TC + single dose NVP at the onset of labor <u>Postpartum</u>: ZDV + 3TC for 1 week postpartum</p> <p>Infants Single dose NVP soon after birth and 1 week of ZDV.</p> <p>4 weeks of ZDV for baby if less than 4 weeks of ZDV by mother</p>
<p>HIV-infected woman presenting in labor or HIV-infected women in whom antepartum ARV was not given</p>	<p style="text-align: center;"><i>Second line</i></p> <p>Women</p> <p><u>Intrapartum</u>: ZDV+3TC + single dose NVP at the onset of labor <u>Postpartum</u>: ZDV+3TC for 1 week postpartum.</p> <p>Infants Single dose NVP soon after birth and 4 weeks of ZDV.</p>
<p>HIV-infected pregnant women in whom complex regimens are not possible</p>	<p style="text-align: center;"><i>Third line</i></p> <p>Women</p> <p>Single-dose NVP at onset of labor</p> <p>Infants</p> <p>Single dose NVP soon after birth \pm 1-4 weeks of ZDV ^{2,3}</p>
<p>E: HIV-infected pregnant women who have indications for starting ARV treatment but treatment is not available</p>	<p>Follow the recommendations of Clinical Situation D</p>
<p>F: HIV-infected pregnant women with active tuberculosis</p>	<p>Treatment of tuberculosis is the first priority</p> <p>If ARV treatment is initiated in the second trimester or later, first-line regimen is ZDV + 3TC + EFV or</p>

	<p>D4T + 3TC + EFV</p> <p>If treatment needs to be initiated in the first trimester, EFV will need to be substituted with saquinavir-ritonavir (protease-inhibitor combination) because EFV has teratogenic potential and NVP had drug interaction and increased potential for liver toxicity if used with rifampicin</p> <p>If ARV treatment is not initiated, follow the same recommendations as in Clinical Situation D</p>
<p>G: Pregnant women of unknown but suspected HIV status at the time of labor or women known to be HIV-infected who have not received ARV drugs before labor</p>	<p>If there is time, offer HIV counseling and testing to women of unknown status and if positive, initiate ARV prophylaxis, following the recommendations of Clinical Situation D</p> <p>If there is insufficient time to delivery, offer VCT as soon as possible after delivery and follow the recommendations of Clinical Situation I</p>
<p>H: Pregnant women with known or suspected HIV who are unable or unwilling to access care at designated PMTCT intervention centers</p>	<p>Women Single-dose NVP at onset of labor</p> <p>Infants Single dose NVP soon after birth \pm 1-4 weeks of ZDV ^{2,3}</p>
<p>I: Infants born to HIV-infected mothers who have not received any ARV drugs in the peri-partum period</p>	<p>Infants Single dose NVP soon after birth \pm 1-4 weeks of ZDV ^{2,3}</p> <p>If the regimen is delayed for more than two days after birth, it is unlikely to be effective</p>

¹ WHO and Pakistan NACP recommendations for initiating ARV treatment in HIV-infected adults. If CD4 testing is available, ARV treatment should be offered to patients with: WHO Stage IV disease irrespective of CD4 cell count, WHO Stage III disease with consideration of using CD4 cell counts less than 350×10^6 cells/L to initiate therapy, and WHO Stage I or II disease in the presence of a CD4 count less than 200×10^6 cells/L.

If CD4 testing is not available, ARV treatment is recommended for individuals with WHO Clinical Stage III or IV disease regardless of total lymphocyte count, or Stage II disease with a total lymphocyte count $< 1200 \times 10^6$ cells/L.

² Recommendation for the addition of 4 weeks of infant ZDV to SD NVP is based on extrapolation from Thailand ZDV study that demonstrated longer infant prophylaxis was more effective than shorter infant prophylaxis if mother receives less than 4 weeks antepartum therapy; because in this situation no maternal antepartum therapy is received, 4 weeks of infant ZDV is recommended as preferred component of the regimen when possible.

³ Studies have demonstrated that single-dose NVP plus 1 week of infant ZDV is superior to single-dose NVP alone and reduce infant NVP resistance

VIII. COUNSELING AND SUPPORT FOR SAFE INFANT FEEDING

Breast-feeding exposes the infant of an HIV-infected mother to significant risks of MTCT. As discussed earlier, prolonged breast-feeding (> 18 months) approximately doubles the risk of HIV transmission to the infant, and this continued risk of transmission has reduced the overall effectiveness of efforts to prevent MTCT. On the other hand, multiple studies from developing countries have shown that not breast-feeding during the first few months of life increases the risk of mortality from infectious diseases several fold. Promotion of exclusive breast-feeding are one of the most effective strategies for improving child survival and nutritional status of children in developing countries. Recognizing the risk of HIV to the infant from breast-feeding, as well as the risks associated with not breast-feeding, and the variation in individual circumstances of HIV infected women regarding affordability and acceptance of replacement feeding, WHO guidelines state "*when replacement feeding is acceptable, feasible, affordable, sustainable, and safe, avoidance of all breast-feeding by HIV-infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life and then should be discontinued as soon as it is feasible*". In Pakistan, the PMTCT care team should make a careful assessment of the mother's ability to provide safe replacement feeding (ability to purchase powdered infant formula on a regular basis, ability to sterilize bottles, and access to clean water) in a sustainable manner and counsel the mother about the most appropriate choice for her situation.

For women in whom replacement feeding is not possible, or not desired by the mother, exclusive breastfeeding should be advised, as rates of MTCT are lower in babies given breast milk exclusively compared with mixed feedings. Breastfeeding should be discontinued at six months of age after which the baby should receive a nutritionally balanced diet of safe complementary foods.

The effect of prolonged use of ARV drugs by the mother for prophylaxis against MTCT due to breast-feeding is not yet known and multiple studies are underway to address this question. In situations where the mother is interested in a brief period of breast-feeding and can safely switch to replacement feeding after a few weeks, use of longer periods of ARV prophylaxis may be warranted after discussion of the options available with an infectious disease expert.

IX. CARE AND SUPPORT FOR THE MOTHER IN THE POST-PARTUM PERIOD

PMTCT interventions should be part of an integrated continuum of HIV prevention, care, treatment, and support services. Maternal survival is critically linked to child survival in impoverished environments, and the importance of establishing linkages with outreach service delivery organizations in ensuring that the mother receives adequate health, nutritional, and social support in the post-partum period cannot be overemphasized. The infant too will need growth monitoring and routine child health interventions such as immunizations and micro-nutrient supplementation as well as monitoring for HIV status determination (see section X). Availability of such services will increase the number of people seeking and accepting voluntary counseling and testing. The flowchart in Figure 1 presents all the components of services needed for effective PMTCT programs to function.

Family planning and adequate birth spacing provide many benefits for women and their children. Women should wait at least two to three years between pregnancies. Many women with HIV have an unmet need for contraception during the postpartum period. Although HIV infection is associated with a reduction in fertility, women with HIV may be at high risk for pregnancy in the postpartum if they choose not to breastfeed or stop breastfeeding early and, therefore, have a shorter duration of lactational amenorrhea. Women should be informed that ovulation may occur as soon as four weeks after delivery among women who do not breastfeed. Condom use could also decrease in the postpartum period if women perceive themselves at low risk for pregnancy.

A number of factors influence the choice of contraceptive methods among postpartum women, including the physiological processes of the puerperium; the return of ovulation and fertility; infant feeding practices and the women's resumption of sexual activity. Women may be unaware of the effects of these factors on fertility and thus require counselling and information on fertility choices and effective postpartum contraceptive methods, as well as condom promotion and provision.

Table 11: Components of Post-partum Care and Support

- Assessment of maternal healing after delivery
- Assessment of post-partum complications including sepsis which are much more common in HIV-infected women
- PMTCT care team linked with outreach service delivery organization
- Management of HIV infection and related complications, plus ARV treatment for women in whom it is indicated
- Nutritional support
- Infant feeding support
- Psychological support
- Information on family planning and provision of contraception if requested
- Routine child health interventions (immunizations, growth monitoring, micronutrient supplementation)
- Cotrimoxazole prophylaxis for the infant
- Laboratory tests for diagnosis of HIV in the infant
- Care and medical management of HIV-infected infant

1. Recommendations

1.1. Women, who have not initiated ART prior to delivery, require continued HIV-related medical care and support in the postpartum period which includes clinical and immunological assessment to determine when ART is needed for their own health. Women who initiated ART during pregnancy require continued clinical and laboratory monitoring and linkages with ART services as necessary, through referral or co-management mechanisms.

Women may require additional adherence support during the postpartum because of the need to care for the newborn, possible postpartum depression and loss of incentive of MTCT prevention.

1.2. All women, whether they opt for exclusive breastfeeding or replacement feeding, should be provided with continued infant feeding counseling and support to safely carry out their feeding choice. Follow-up counseling and support aim to improve feeding practices, preventing HIV postnatal transmission as well as malnutrition and reducing the risk of death in children. To achieve this, attention should be given to providing women with safer feeding skills and disclosure support, and encouraging the involvement of partners and family members. Postpartum counseling visits could be scheduled, beginning with a session after birth before the woman leaves the health center, a visit within seven days of birth to monitor progress and monthly visits thereafter.

Supportive management of breast engorgement should be provided to women who opt for replacement feeding.

1.3. All HIV-infected women, whether on ART or not, should be offered appropriate sexual and reproductive health counseling and services. This includes sexual and reproductive health counseling and support, family planning counseling and services, routine postpartum care, prevention and treatment of reproductive tract infections and management of other sexual and reproductive health problems.

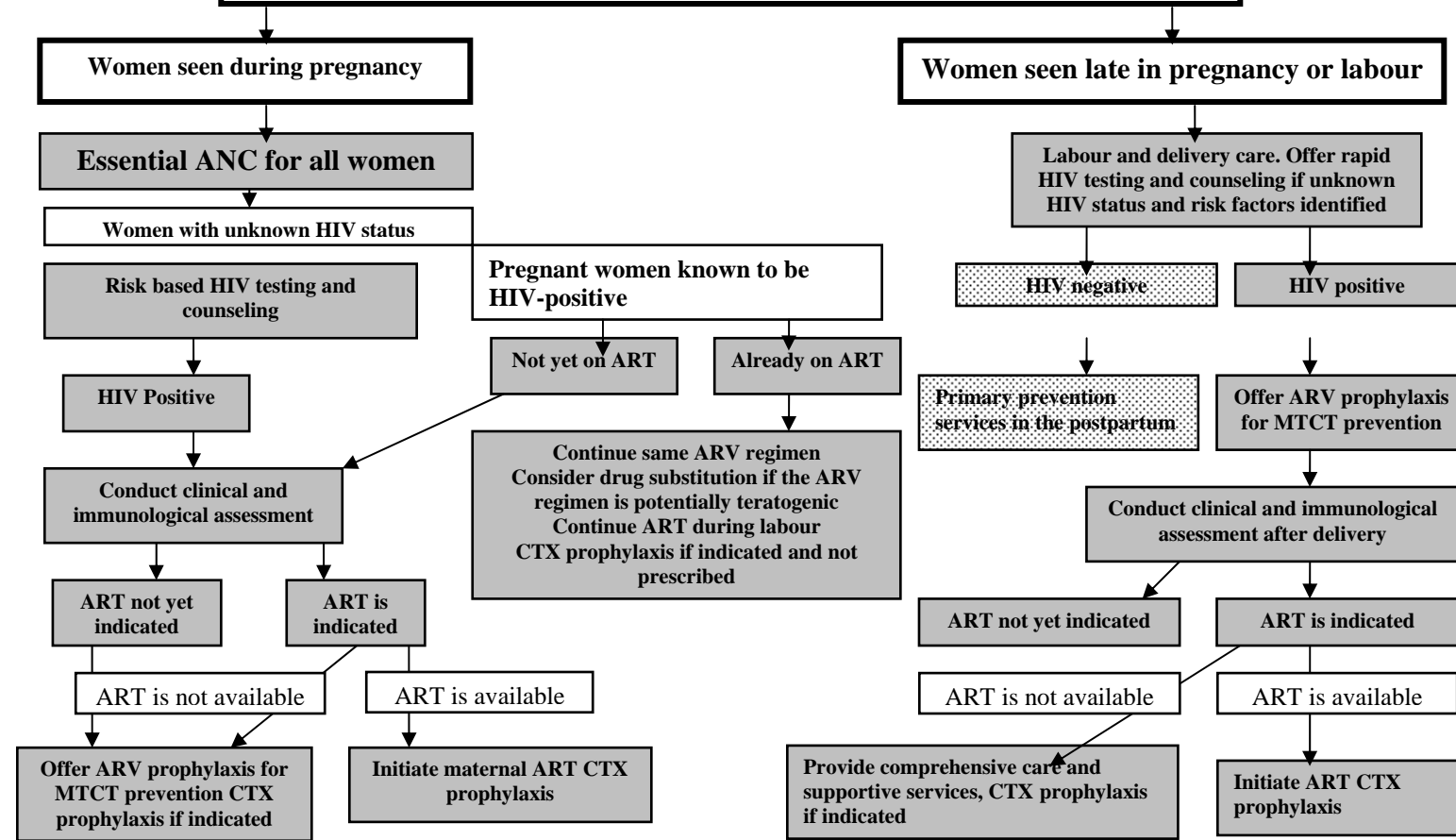
1.4. Counseling and support for effective contraception should be provided to women to reduce the likelihood of unintended pregnancy. This should start before hospital discharge. There is currently insufficient evidence to recommend that women on ART should not use hormonal contraceptives. If a woman on ART decides to initiate or continue hormonal contraceptive use, the consistent and correct use of condoms is recommended for preventing HIV transmission to a partner and to avoid re-infection. In addition, condoms may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive.

Oral hormonal contraceptive methods require daily administration which increases the pill burden that may include ARV drugs, and drugs for treatment or prophylaxis of opportunistic infections, symptoms management or treatment of concurrent illnesses. Therefore, when selecting a contraceptive method, health care providers and women need to consider the potential impact of pill burdens on adherence to contraceptive methods or HIV-related medication.

1. SUMMARY OF COMPREHENSIVE PMTCT MCH SERVICES FOR HIV POSITIVE PREGNANT WOMEN

PMTCT services can only be effective if all the components described above are in place and functioning optimally. The flowchart shown in Figure 1 summarizes the components of comprehensive PMTCT packages that need to be available for HIV positive pregnant women, if transmission of HIV to children is to be prevented.

Figure 1. Flowchart of Comprehensive PMTCT services



- ANC package of services**
1. Essential ANC services which include offer of HIV testing and counseling
 2. Clinical and immunological assessment of HIV-positive women
 3. Screening, prevention and treatment of TB
 4. Screening for and management of liver diseases
 5. Initiation of ART and ARV prophylaxis for MTCT prevention
 6. Cotrimoxazole and INH prophylaxis
 7. Nutritional counseling and support
 8. Infant feeding counseling and support

- For all HIV-positive women in the postpartum**
1. Offer infant feeding counseling and support
 2. Offer maternal and infant follow-up care
 - HIV-related care and ART when indicated
 - Cotrimoxazole prophylaxis for women and their infants
 - Sexual and reproductive health services
 - Nutritional counseling and support
 - Diagnosis of HIV infection in infants
 3. Adherence support for women receiving ART

X. CARE FOR INFANTS BORN TO HIV-INFECTED WOMEN

All HIV-infected women should be informed and counselled on the importance of follow-up care for their infants and children. Children born to HIV-infected women with HIV have specific follow up and care needs in addition to routine care and immunizations. Diagnosis of HIV infection in children, and care of HIV-exposed and infected children is covered in detail in the NACP Clinical Manual on Pediatric HIV infection in Pakistan. Recommendations are summarized below.

1. Specific Recommendations

- 1.1. Infants born to HIV-infected women should be washed before any blood sample is drawn or any injections or other invasive procedures are performed.
- 1.2. All HIV-exposed children (children born to HIV-infected women) should be assessed for their HIV-status. Confirming the diagnosis of HIV in young infants is problematic in Pakistan. PCR for early diagnosis of infection around six weeks as recommended in the WHO pediatric guidelines, but not available in Pakistan yet. Serological tests cannot be used in young infants (< 12 months) to confirm HIV infection because of trans-placental passage of maternal antibody. A negative serological test around 12-18 months of age excludes the diagnosis of HIV infection in infants. A positive test after age 18 months indicates HIV infection in the child.
- 1.3. PCP in HIV-infected infants can have an acute onset, often as the first indicator of HIV vertical transmission, and a high mortality rate. Unlike in HIV-infected adult patients, PCP in HIV-infected infants can occur at any CD4 cell count and before one year of age. Therefore, it is recommended that all infants born to HIV-infected women begin cotrimoxazole prophylaxis starting at six weeks of age and continuing until HIV infection is excluded. Prophylaxis in an HIV-infected infant should be continued until the age of 12 months, regardless of the CD4 cell count. After the age of 12 months, the need for prophylaxis is determined by the CD4 cell count according to current WHO recommendations on prophylaxis of OI among infants (see NACP pediatric guidelines).
- 1.4. All HIV-infected children should be offered ongoing care for appropriate growth monitoring, nutritional support and clinical and laboratory monitoring to assess their needs for HIV-related treatment including ART. This should be done through co-management and referral to HIV experts.

- 1.5 Although there are concerns about the safety of some live vaccines in potentially severely immunocompromised children, it is recommended that infants born to HIV-infected mothers follow the standard immunization schedule, until more information is available. WHO currently recommends giving bacille Calmette-Guerin (BCG) to all neonates, irrespective of HIV exposure, and to HIV-infected children who are asymptomatic in areas with a high prevalence of tuberculosis. Children with symptomatic HIV infection should not receive BCG vaccine.

Children with asymptomatic or symptomatic HIV infection also should receive routinely recommended childhood vaccines, including DTP, hepatitis B, and Hib conjugate vaccines, according to the recommended schedule. Oral polio drops are currently recommended until inactivated polio vaccine can be made available.

Because of the risk of severe measles in symptomatic HIV-infected children measles immunization is recommended for asymptomatic as well as symptomatic HIV-infected children.

APPENDIX I

ANTENATAL CARE CHECKLIST FOR PMTCT

Note: Mark the activities carried out as appropriate. Use the closest gestational age at the time of visit).

Name of the patient:-----Address and telephone No.-----

Clinic record No.-----

First Visit: <i>for all women at first contact with clinics, regardless of gestational age, if first visit later than recommended carry out all activities up to that time</i>	Visit			
	1 st 4 th <12 wks.	2 nd	3 rd	
Date: / /				
Clinical examination				
Clinical severe anemia? Hb test				
Ob. exam gestational age estimation, uterine height				
Gyn. Exam (can be postponed until second visit)				
Blood pressure taken				
Maternal weight/height/mid-arm circumference				
Screening for TB (chest X-ray, Tuberculin test) if clinically indicated				
Rapid syphilis test performed, screening for STIs done				
Urine test (dipstick) performed				
Blood type and Rh requested				
Hepatitis B and C screening done				
Tetanus toxoid given				
Fe/Folic acid supplementation provided				
Nutrition counseling provided				
Birth preparedness advice given				
Psychosocial support assessed				
Recommendation for emergencies/hotline for emergencies				
Information and advice on PMTCT interventions given				
Referral to infectious disease expert arranged				
Referral to outreach services arranged				
PMTCT team informed				
Complete antenatal card				
Second Visit and subsequent visit <i>approx.# of weeks</i>	<i>Gestational age -</i>			
	Date: / / <i>26wks</i>			
<i>32wks 38wks</i>				
Clinical examination for anemia				
OB.exam: gestational age estimation, uterine height, fetal heart rate				

Blood pressure taken				
Maternal weight/mid-arm circumference				
Clinical examination for STI screening				
Screening for TB if indicated				
Urine test for protein (only nulliparous women/ women with previous preeclampsia)				
Fe/Folic acid supplementation given				
Recommendation for emergencies/hotline for emergencies				
Consultation with infectious disease expert completed/HIV disease status known				
PMTCT plan in place				
HAART started if indicated				
Zidovudine given from 28 weeks onwards (if HAART not indicated)				
Other prophylaxis/therapy started if indicated (e.g. anti-tuberculous therapy, cotrimoxazole prophylaxis)				
Outreach services in place				
Nutrition counseling				
Psychosocial assessment				
Complete antenatal card				
Third visit: Add to second visit Date: / /				
Hemoglobin test requested				
Tetnus toxoid (second dose)				
Instructions for delivery/Plan for birth				
Mother taking HAART/ZDV				
Antiretrovirals available for intrapartum, post-partum, and infant use				
Advice and recommendations for safe infant feeding				
Advice and recommendations on family planning				
PMTCT team updated				
Fourth Visit: Add to second and third visits Date / /				
Detection of breech presentation/other possible obstetric issues and referral if needed				
PMTCT plan reviewed				
Complete ANC card, recommend that it be brought to hospital				

Staff responsible for antenatal care: Name-----

Signature_____

I. DRUG DOSAGES FOR PMTCT PROPHYLACTIC REGIMENS FOR WOMEN ON HAART

- HAART should be continued during labor, delivery, and post-partum period (see adult guidelines)
- Infants should receive 1 week of ZDV syrup 4 mg/kg twice a day
- If the mother receives less than 4 weeks of HAART during pregnancy, infant ZDV dosing should be extended to 4 weeks

II. DRUG DOSAGES FOR PMTCT PROPHYLACTIC REGIMENS FOR WOMEN NOT ON HAART

Regimen	Woman			Infant
	Antenatal	Intrapartum	Postpartum	
If complex prophylactic ARV regimens for PMTCT are possible				
ZDV plus SD NVP Plus ZDV/3TC tail	ZDV 300 mg twice a day starting at 28 weeks or as soon as possible thereafter ¹	ZDV 600 mg at onset of labour	ZDV 300 mg twice a day PLUS 3TC 150 mg twice a day for 7 days ²	SD NVP 2mg/kg oral suspension or 6mg immediately after birth PLUS ZDV 4 mg/kg twice a day for 7 days ³
		Plus SD NVP 200 mg at onset of labour		
		Plus 3TC 150 mg at onset of labour and every 12 hours until delivery ²		
If complex prophylactic ARV regimens for PMTCT are not possible				
Single-dose NVP		SD NVP 200 mg at onset of labour		SD NVP 2mg/kg oral suspension or 6mg immediately after birth ⁴
<p>¹If no antepartum prophylaxis has been given, the intrapartum and postpartum components of complex regimens can still be given. This is the preferred option in this situation, rather than SD NVP regimens. ZDV to infants should be given for 4 weeks.</p> <p>² If conditions to deliver the intervention exists, a seven-day tail of ZDV + 3TC given to the mother after delivery should be given to reduce the emergence of NVP resistance.</p> <p>³ If the mother receives less than 4 weeks of ZDV during pregnancy, infant ZDV dosing should be extended to 4 weeks</p> <p>⁴If possible, ZDV syrup should be added to the infant regimen for 4 weeks in the dosage of 4 mg/kg twice daily</p>				

II. DOSAGES FOR COMMON HAART DRUGS IN PREGNANT WOMEN

Drug	Formulation	Dose	Adverse events
Zidovudine (ZDV or AZT)	300 mg tablet	300 mg bid	Anemia, neutropenia, GI intolerance, headache, insomnia, myopathy, lactic acidosis (rare)
Lamivudine (3TC)	150 mg tablet	150 mg bid	Minimal toxicity Lactic acidosis with hepatic steatosis (rare)
Stavudine (d4T)	30 mg capsule	30 mg bid	Pancreatitis, peripheral neuropathy, lactic acidosis with hepatic steatosis (rare)
Nevirapine (NVP)	200 mg tablet	200 mg od for 14 days, then 200 mg bid	Rashes, Stevens-Johnson's Syndrome, hepatitis, life-threatening hepatotoxicity
Efavirenz (EFV)	200 mg capsule	600 mg od at bed-time	Dizziness, somnolence, insomnia, confusion, agitation, elevations in liver enzymes, skin rash

SOURCES AND FURTHER READING

- AIDS Epidemic Update. UNAIDS and WHO 2005.
- McIntyre J. Strategies to prevent mother-to-child transmission of HIV. *Current Opinion in Infectious Diseases*, 2006;19:33-38.
- National Guidelines for Anti-retroviral therapy. National AIDS Control Programme, Pakistan, 2005.
- Programme Recommendations for the Prevention of Mother-to-Child Transmission of HIV. UNICEF 2003.
- Prevention of Mother-to-Child Transmission of HIV in Asia - Practical Guidance for Programs. The Linkages Project, Academy for Educational Development, 2002. www.linkagesproject.org
- Strategic Framework for Prevention of Parent-to-Child Transmission of HIV in Pakistan. National AIDS Control Programme, Pakistan 2006.
- HIV in pregnancy: a review. UNAIDS and WHO. Occasional Paper 2.
- HIV and Infant Feeding - Framework for Action. WHO 2003.
- Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants - Guidelines on care, treatment and support for women living with HIV/AIDS and their children in resource-constrained settings. WHO 2004.
- Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. WHO May 2006 (Draft Document).
- Nutrition Counselling, Care and Support for HIV-infected women and their children in resource-constrained settings. WHO 2004.
- Management of HIV Infection in Children in Pakistan - National Guidelines. NACP, Pakistan, 2006.

