

*"The only thing worse than losing a child to AIDS
is finding out you did not have to."*

HIV DISEASE
IN
PREGNANT WOMEN AND NEONATES

A Manual for PMTCT Programmes



एचआईवी



आईपासून बाळाला

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An effort to prevent HIV from reaching any infant

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Preface

PRAYAS is pleased to release this handbook to all the obstetric health care providers. The publication of this handbook has been possible through a grant released by the Elizabeth Glaser Paediatric AIDS Foundation, which has been supporting a private sector-NGOs joint effort to prevent mother-to-child transmission of HIV, by up-grading the existing reproductive and child health services.

For PRAYAS, this has also been an emotional journey. One of our very best friends, whose parents had died because of AIDS, we could not save from succumbing to this disease. We are pledged to help as many children as possible, which are infected, but also to have those who can be spared of the infection through effective interventions.

We dedicate this book to those, more than 4 million, children who have already died due to AIDS and also to those many more millions, who are going to be safe, if we can implement our programmes effectively.

We thank Dr. Subha Raghavan who has been very supportive throughout.

As always, publication of this handbook has been a team effort of all at PRAYAS.

We acknowledge the efforts of Mr. Dilip Chitre and Sandip Sonawane of Swaroop Mudran who designed and printed this handbook.

As would be evident from the following pages, PMTCT effort essentially involves voluntary counselling and testing of all pregnant women and then providing support to those identified HIV positive. You all are most welcome to contact PRAYAS, if you want to be a part of this initiative.

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1. Introduction

Natural history of HIV disease in men and women do not differ to great extent. However there are two very important aspects that need special focus. One is the complex nature of biological, social and cultural factors that lead to increased vulnerability of women to HIV. The second is the fact that more than 80% of the women infected with HIV are in their childbearing age. In some countries HIV infection has become the most common complication of pregnancy. Over 90% of HIV infections in children result from mother-to-child transmission (MTCT).

The majority of women and children infected with HIV are in the developing world. In some countries in sub-Saharan Africa HIV -1 related diseases may account for net 75% of annual deaths in adults. Life expectancy of adolescents is declining sharply in these countries, so is the rise in infant mortality. The issue of children who have lost their mothers or both parents to AIDS is another complex dimension of this epidemic.

India and other South Asian countries have many a lesson to learn from the African devastation. We must understand that we in India are at the shifting epicentre of the pandemic. Programmes for prevention of mother-to-child transmission of HIV (PMTCT) are crucial at this stage as they form an important link between the prevention and care components, both so very much important for a lasting impact on the epidemic.



2. Epidemiological Overview

The HIV pandemic continues to engulf the world even 21 years after the initial identification of this new infection. Unfortunately, it is seen that, it is affecting the world disproportionately. The brunt is being borne by the developing, poor countries while the developed rich world is largely able to contain it. The statistics show that by the end of 2001 approximately 40 million people were living with HIV all over the world of which 95% are in the developing countries. Approximately 14,000 new infections occur daily the world over, of which 90% are in resource-poor settings. In these settings women are being infected at an alarming rate. About 40-50% of the new infections are occurring in women.

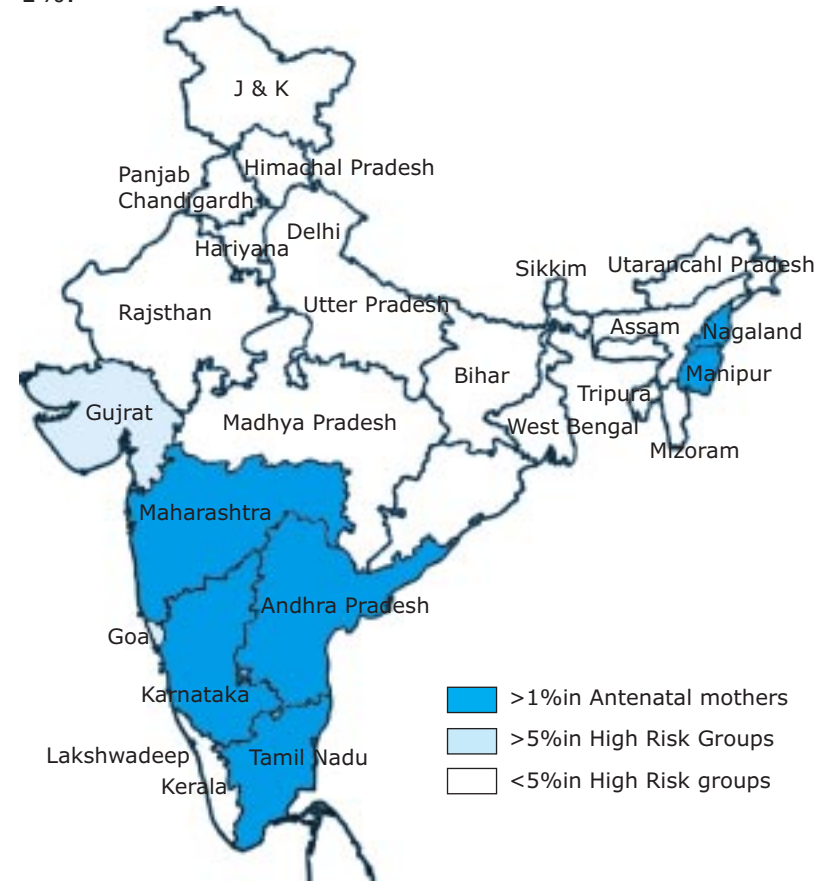
The African continent has long been recognized as the most affected zone, but Southeast Asia is fast emerging as the important hot spot. India seems to be the country with second largest population of HIV infected individuals in the world, only next to South Africa and estimated to be having around 4 million HIV infected individuals.

Global estimates for adults and children (End2001)

People living with HIV/AIDS	40 million
New HIV infections in 2001	5 million
Deaths due to HIV/AIDS in 2001	3 million

(UNAIDS data)

The analysis of the Indian epidemic also brings forth certain facts. NACO (National AIDS Control Organization) has declared six states (Maharashtra, Karnataka, Tamilnadu, Andhra Pradesh, Manipur and Nagaland) as high HIV prevalence states based on the HIV / AIDS surveillance data. This is because in these six states the HIV infection prevalence in so called 'low risk' population like pregnant women attending antenatal clinics has been observed to be more than 1%.



Dynamics of an Epidemic of Heterosexually Transmitted Disease

A disease like HIV, which is transmitted mainly through unsafe heterosexual contacts as seen in India, usually follows the following stages in the epidemiology.

As the disease is introduced in any new community, the first to be the victims are the women in prostitution. So the prevalence rates among this group start rising. This phase was observed in India in the latter half of the eighties.

In the second phase the disease starts affecting the male clients of women in prostitution. The proportion of men visiting the women in prostitution is huge and quite wide spread. It is not easy to identify and screen this difficult to reach population. An indication, however, of the prevalence among these men is possible through the screening of men attending the STD (sexually transmitted disease) clinics. Increasing rates among them were observed during the early nineties in India.

In the third phase the infection now starts spreading to the female spouses of these men. As these women (largely monogamous married women) are also very widely distributed and difficult to identify for screening. The only point to identify HIV infection in these young, newly married women early enough is while screening them in ante-natal clinics (ANCs). A prevalence of even more than 1% in this group informs us that the epidemic in these communities is no more restricted to the so called high risk groups but is wide spread in the general population.

The focus of people designing prevention programmes and strategies shifts from so called 'high risk groups' to 'high risk activities'. Unfortunately most people engaged in such high-risk activities are not aware of these risks. A very stark example is that, if we analyse the patterns of new HIV infections in women, we find that most

are apparently monogamous and married. They are getting infected because their husbands are infected. The husbands, due to lack of awareness and/or lack of symptoms, do not know about their own infection. For these young Indian women "marriage" (which is touted to give protection from HIV) is threatening to be the most important risk factor.

Emergence of paediatric HIV cases or identification of children with HIV as index cases in a family can be considered as the next phase of the disease.

As already discussed, at least 6 states in India have already reached this phase of the epidemic.

Magnitude of the Problem in India

- Approximately 27 million total pregnancies per year.
- At the average 0.3% there will be 1,00,000 HIV +ve pregnant women per year.
- At 30% transmission total 30,000 infants are likely to be born with HIV per year.
- With effective PMTCT programs 20000 can be spared of HIV infection per year. (If transmission rate is reduced to 10%)

Women and HIV- The Special Considerations

Before going into the details of the HIV in pregnancy it would be pertinent to just briefly review the reasons of women's susceptibility to HIV. It would then become apparent why women in developing countries are so vulnerable.

The reasons are both biological and socio-cultural.



Biological Factors:

The rate of transmission of HIV from male to female is two to three times higher than that from female to male. Anatomically, the vaginal mucosa provides a larger area for a longer duration of contact, with potentially infectious semen also it is more difficult to clean after sexual contact as compared to the penile skin. The Langerhan's cells population of the cervix may provide a portal of entry for HIV.

Vulval and vaginal inflammation due to other sexually transmitted infections increases the susceptibility further. Many of these infections are totally asymptomatic or minimally symptomatic. Ulcerative genital disease is an established co-factor for HIV infection and transmission.

Socio-cultural Factors:

In patriarchal societies where women have little control over their own bodies their vulnerability increases. They have little control over the expression of their sexual desires and have little negotiating capacity to ensure safety in sexual practices by modifying the sexual behaviour of their partners. Gender inequalities, poverty, unemployment, and lack of education force many women into commercial sex work as a need for survival. Issues of domestic violence, alcoholism and other substance use, stigmatization and discrimination, and the added burden of caring for sick members (partners and children) in the family add to their burden. Inability to choose the partner and lack of control over the sexual behaviour of the partner is putting even the apparently monogamous married women to risk and thus "marriage" is fast emerging as an important risk factor for young girls. Lack of women-controlled protective technologies leading to dependence on the male-controlled barrier method (condom) as the only technological solution is another important factor.

3. Importance of Prevention of Mother-to-Child Transmission Programmes (P.M.T.C.T.)

P.M.T.C.T. programmes form an important part of overall strategies for prevention of HIV epidemic.

In the initial phase of the epidemic usually the emphasis is on increasing public awareness and targeting the high-risk groups. When the epidemic expands, the programme starts looking at the so called "bridge populations". However epidemics of diseases like HIV, which are for most part of their natural course asymptomatic and also associated with social stigma, tend to remain underground and spread very rapidly, even at this stage.

Even the most aggressive of awareness campaigns thus fail to reach populations who do not consider themselves to be at risk.

Unfortunately, in all our campaigns so far, there has been a stress on avoiding promiscuity, avoiding pre- or extra-marital sexual relationships, etc. People-especially women-have thus been led to believe that if they are married they are safe. Add to this the overall reluctance to discuss sexuality related issues, let alone publicly, but even with one's spouse. This creates problems for women, in that they cannot negotiate 'safe-sex' even within a marriage. There are other issues of domestic violence, sexual abuse and substance use (mainly alcohol) but they are beyond the scope of discussion in this small booklet. PMTCT programmes, however, provide us a small but definite window of opportunity to discuss these matters with the women, their spouses and families and link prevention efforts with the care and support issue.

PMTCT programmes are possible because

1. Most women do seek help and support during pregnancy, so ANC clinics can be places where HIV awareness could be imparted;
2. Women are likely to be most receptive to the messages about the safety of the unborn child;
3. Their spouses/husbands are also likely to be ready to receive messages than at any other time;
4. All pregnant women can be offered counselling regarding the benefits and risks of screening for HIV. Screening based only on reported risk factors will fail to detect majority of HIV infected women;
5. We can offer all the options of prevention of transmission of HIV to the child depending upon the stage of pregnancy and other personal and social factors. Now that we have effective prophylaxis protocols available, majority of the transmission to the infants can be prevented;
6. Counselling will provide us the space to address issues of stigma, discrimination and support to HIV infected individuals and families;
7. Early detection of HIV infection in the mother, possibly also in the father, will provide them with all the options about better quality of life with HIV.

Potential Benefits to Women of Voluntary HIV Testing Prior to or During Pregnancy

1. Knowledge of infection can facilitate early counselling and treatment;
2. Diagnosis in the mother allows appropriate treatment and follow-up of her child;
3. Knowledge of her HIV status enables the women to take decisions on continuation of the pregnancy and

future fertility;

4. Testing allows an opportunity to implement strategies to attempt to prevent transmission to the child;
5. Knowledge of her HIV status enables the women to take precautions to help prevent transmission to her sexual partner;
6. Testing and diagnosis can lead to counselling and testing of partner;
7. If the test result is negative, women and their partners can be guided regarding appropriate HIV prevention measures and risk reduction behaviour;
8. Even if the overall prevalence of HIV in pregnant women in a community is as low as 1%, still counselling all pregnant women is going to provide the necessary scope for messages of primary prevention of HIV to penetrate deeper in the unsuspecting societies;
9. Early identification may prevent further pregnancies, further transmission of HIV and help control the epidemic.

In spite of all these advantages a word of caution. HIV testing in pregnancy, as in any other situation, does have possible risks of stigmatisation, discrimination and violence. So, good counselling facilities and some support infrastructure is absolutely essential before testing.

Testing for HIV in pregnancy should not be looked at as adding just another test to screening panel. It should be seen as part of the holistic and long term care of the woman.



4. HIV Testing in Pregnancy

- An HIV antibody test should be offered to all pregnant women.
- Since this is a voluntary test she may accept or refuse being tested.
- There could be two options for consent procedures.
Opt in consent: Every woman agreeing to get tested signs an informed consent form.
Opt out consent: Every woman not agreeing to get tested signs a consent form stating that she has been explained the importance of the screening but she is volunteering not to get tested.
- Counselling for HIV testing should be a part of overall comprehensive ANC counselling.
- The atmosphere should be such that the women feel comfortable to ask questions.
- Preferably the same health care provider who counselled her for getting tested should disclose the results.
- Confidentiality of the test results should be strictly maintained.
- Language of communication should be easy, simple and comfortable for the woman to understand.

- Importance of knowing more about one's pregnancy, risk of transmission from mother to child, risk of transmission from and to other members of the family, effects of HIV on pregnancy, utility of zidovudine and other prophylactic interventions, prognosis of a HIV infected child, need for further planning during and after pregnancy, should all be discussed.

Please, don't test without counselling!

- One has to remember that we are going to help the woman and her family to take an informed decision about the pregnancy. It is going to be HER/THEIR decision. We are not going to force our views on to them.
- We should always try to provide the woman with 'that' extra space in decision-making, which she would usually be denied in the patriarchal families. (Remember it is she who is going to go through the pregnancy, she is to undergo investigations, she has to take the medicines and face their side effects, if any, she has the primary responsibility of looking after the infant infected/not infected.) Let her take the decision; let the family respect her opinion.
- You may be asked not to disclose the results to the woman. It is definitely seen that disclosure coupled with proper counselling increases the chances of better participation of the woman in the programme and better overall outcome.

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Pre-test Counselling

- Make the woman comfortable.
- Assess the woman's awareness about HIV.
- Provide relevant information about HIV infection.
- Allow the woman to ask questions as well as express feelings and concerns related to the information provided.
- Explain advantages of early diagnosis (opportunity to prevent transmission to the child, need for specialized care, benefits as regards to her health, etc.)
- Explain that testing is voluntary.
- Explain the test.
- Reassure about absolute confidentiality.

- Explain that testing itself may be stressful and decisions regarding disclosure to others need to be taken very carefully to avoid getting stigmatised or suffering discrimination.
- Explain that positive results need to be confirmed, as there are chances of false positive results.
- Provide information about transmission of HIV and how it can be prevented. Also discuss use of condoms, prevention of sexually transmitted diseases and future pregnancies. (This is just to ensure that woman carries home at least some messages even if she refuses the test or doesn't turn up for any follow up visits.)

Post-test Counselling

The results of the test could be either positive or negative.

Negative Results:

- Inform significance of the negative test and depending upon the stage of her pregnancy suggest a repeat test at a later stage of pregnancy (at the end of 8th month if possible, if not possible then during labour.)
- Inform that the test should be repeated in subsequent pregnancies.
- Emphasize that a negative result doesn't mean immunity against HIV infection and encourage her to understand modes of transmission and discuss the same with her spouse/sexual partner.

Positive Results :

- Discuss the meaning of the positive result. Be considerate about stress she is bound to experience.
- Discuss the need for confirmation of the positive result.
- Inform that she will need specialized care for herself as well as for the protection of the infant.
- If you are not going to provide further care guide her to specialized facility.
- Discuss available options depending upon the stage of the disease. In countries like India where termination of pregnancy is legal upto a certain stage of pregnancy (20 weeks), this option also needs to be discussed

along with the other available protocols for prevention of mother to child transmission.

- Discuss the issues surrounding breastfeeding. If she is going to breastfeed ask her to give exclusive breastfeeding. If not, provide alternative (but ask not to give mixed breast and top feeds).
- Discuss the need to test the sexual partner. Offer counselling help for the partner.
- Educate on the use of condoms.
- Discuss and plan for future contraceptive options prior to delivery.

Sometimes the results of the test could be indeterminate. Seek help of an expert; suggest repeat testing after a month or suggest more specific tests.

Diagnosis of HIV Infection in Pregnant Women

Screening Test :

The most widely used serologic test for screening of HIV infection is the enzyme linked immunosorbent assay (ELISA). It is highly sensitive (>99.7%) but has lower specificity (>98.5%). Rapid test kits are widely available and are generally based on similar principle; however their specificity is still lower. This means that approximately 1% false positive results are expected. These occur in women who have received multiple transfusions, in multi-parous women, hepatic disease, haematological abnormalities and haematological neoplasias, renal transplant, collagen disease, chronic renal failure, acute infections with DNA viruses, pregnancy, etc.

Therefore all positive results need to be confirmed with another test.

False negative results can occur at the onset of the disease (in the window period). This window period is usually 4 to 12 weeks after infection. Other causes of false negative ELISA include bone marrow transplant, neoplasm, and B lymphocyte dysfunction.

Confirmatory Tests :

Western blot (WB): A very sensitive and specific test. Reaction (band formation) with at least two HIV proteins (some combination of p24, gp41, gp120, gp160) is taken as a positive result.

Indeterminate results need repeat testing.

Immuno-fluorescence reactions: Very sensitive and specific, also less expensive and easier to perform than WB, but are rarely available.

Positive predictive values of the tests vary with prevalence of the disease in the population concerned. Consider risk factors, symptoms and test results together to evaluate the test results.



Other methods of diagnosis include antigen detection (p24 assays), PCR (DNA/RNA) and viral culture. These are rarely used for diagnosis as they are very expensive, but are of value to confirm infection if regular serology is inadequate, or to clarify indeterminate western blot, to monitor drug trials or to plan and monitor antiretroviral treatment.

The CD4 cell count (number, percentage and CD4/CD8 ratio) is important in staging HIV disease, evaluating prognosis and planning treatment (both prophylaxis of opportunistic infections and antiretroviral treatment).

While it is generally true that we should not declare anyone as HIV infected individual unless the diagnosis is confirmed, in case of women presenting very late during pregnancy or during labour if single test is positive it would be better to provide antiretroviral prophylaxis to the mother and / or infant pending confirmation of the maternal disease.

A positive serology for antibodies with two different ELISA based tests using different sets of antigens is considered as confirmed diagnosis. In the absence of additional factors like risk behaviour, sexual partner's HIV-positive status, and symptoms suggestive of HIV, one may go in for more specific tests like Western Blot or HIV DNA - PCR, etc. But this is rarely required.



5. Strategies of HIV Testing in India

The National AIDS Control Organization (NACO) guidelines suggest the following:

Since the positive predictive value (PPV) of screening tests is low in populations with low HIV prevalence, WHO/GOI have evolved strategies to detect HIV infection in different population groups and to fulfil different objectives. The various strategies, so designated, involve the use of categories of tests in various permutations and combinations.

1. ELISA/ Rapid tests/ Simple (E/R/S) used in strategy I, II & III
2. Supplemental test like Western Blot and Line Immunoassay are used in problem cases e.g. in cases of indeterminate/discordant result of E/R/S.

Strategy I: Serum is subjected once to E/R/S for HIV. If negative, the serum is to be considered free of HIV and if positive, the sample is taken as HIV-infected for all practical purposes. Because of the enormous risk involved in transmission of HIV through blood, safety of blood and blood products is of paramount importance. This strategy is used for ensuring donation safety (blood/blood products, organ, tissues, sperms etc.) The unit of blood tested reactive (positive) is discarded. Donor is not informed. (If however counselling facilities are available and the donor has consented to follow up the results can be and should be discussed with the donor and the person encouraged going for additional tests for confirmation of the status.)

Strategy II: A serum sample is considered negative for HIV if the first ELISA report is so, but if reactive, it is subjected to a second ELISA, which utilizes a

system different from the first one. It is reported reactive only if the second ELISA confirms the report of the first. This strategy is used for surveillance and for diagnosis only if some AIDS indicator disease is present.

Strategy III: It is similar to strategy II, with the added confirmation of a third reactive ELISA test being required for a sample to be reported HIV positive. The test to be utilized for the first ELISA is one with the highest sensitivity and for the second and third ELISA tests with the highest specificity are to be used.

Strategy II & III are to be used for diagnosis of HIV infection. ELISA 2 and ELISA 3 ought to be tests with highest PPV possible to eliminate any chances of false positive results. Strategy III is used to diagnose HIV infection in asymptomatic individuals indulging in high-risk behaviour.

The positive sero-status of the spouse can be taken as a definite risk factor and decision about diagnosis taken accordingly.

UNAIDS and WHO recommendations for HIV testing strategies according to test objective and prevalence of Infection in the sample population

<i>Objective of testing</i>	<i>Prevalences of infection</i>	<i>Testing strategy</i>
Transfusion/transplant safety	All prevalences	I
Surveillance	>10%	I
	</=10%	II
Diagnosis: Clinical signs/ symptoms of HIV infection	>30%	I
	</=30%	II
Asymptomatic	>10%	II
	</=10%	III

Before going into the details of management of HIV infection in pregnant women let us recapitulate and reiterate certain facts:

- 1) It is becoming increasingly important that women know their HIV status. 'Marriage' threatening to be the most important risk factor for young girls pre-marital voluntary testing and if not before marriage, voluntary testing for HIV at least during pregnancy will help women know their HIV status early enough not only for prevention of transmission to the child but also for their own life prolonging and health sparing efforts;
- 2) Early identification of pregnancy and referral for prenatal care are important to ensure optimal outcome for both mother and baby;
- 3) Clinical intervention programs with antiretroviral medicines protocols will not succeed unless they are a part of comprehensive ANC programs that are available and accessible;
- 4) Identification of HIV infections in a pregnant women should also be taken as an opportunity for other interventions, e.g. counselling and testing of other family members of the index case (e.g. spouse and other children), testing of HIV exposed infants, prognostication of the disease in the woman as well as in other family members who are infected, providing PCP prophylaxis to HIV exposed infants, etc.

Counselling, HIV testing and antiretroviral therapy when needed must become the standard of care of pregnant women.



6. Care of HIV Positive Pregnant Women

We need to consider following issues.

1. Impact of pregnancy on the maternal HIV disease and treatment options;
2. Effect of HIV infection on pregnancy;
3. Mother to child transmission of HIV;
4. Medical management of HIV positive pregnant women;
5. Care and follow up of infants born to HIV positive pregnant women.

Impact of Pregnancy on the Maternal HIV Disease and Treatment Options

1. It is generally accepted that pregnancy does not accelerate progression of HIV disease;
2. Symptoms of pregnancy may mimic those of HIV disease;
3. Drugs for opportunistic infections and for treatment of HIV need to be carefully selected. Generally ART is well tolerated.

Effect of HIV Infection on Pregnancy

HIV has little effect on pregnancy outcome or complications, especially in the developed world. In the developing world, however, there have been multiple adverse effects reported, especially from Africa. However there are many variables and the results of studies are not very consistent.

Some of the effects reported are: higher rates of spontaneous abortion, higher rates of ectopic pregnancy, higher rates of bacterial pneumonia, urinary tract infection and other infections. Tuberculosis remains an important co-infection. Herpes zoster seems to occur more frequently in HIV infected pregnant women as compared to non-infected pregnant women. Pre-term labour seems to be more common in some studies, so are premature rupture of membranes and abruptio placentae. Low birth weights have been reported in some studies, the risk being higher in symptomatic HIV disease with pregnancy. Increased still birth rates have also been reported.

Infectious complications are also reported during the post-partum period. Caesarean sections being particularly associated with higher infectious morbidity.

Mother-to-Child Transmission of HIV (MTCT)

We now know that mother-to-child transmission of HIV-1 may occur in utero, during labour and delivery, or with breast-feeding; with most transmission occurring around the time of delivery.

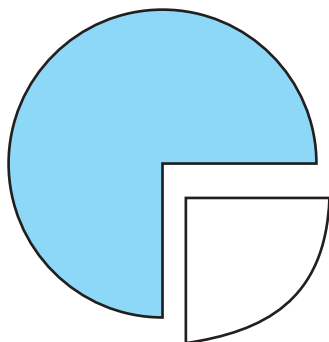
In women not receiving any antiretroviral therapy the risk of peri-natal transmission ranges from 9% to 55% in different studies. In the US and Europe the rates range from 10% to 25%. In contrast in Africa and Asia they are somewhat higher, 20% to 40%. This geographical difference mainly appears to be due to the differences in infant feeding practices, but may be due to malnutrition and the associated infections, etc. In India it is many times observed that pregnancy and infection are occurring almost simultaneously. High viral loads in early HIV disease may be contributing to increased transmission to the infant.

Mechanism of transmission :

As already discussed there are three ways of mother to child transmission.

- 1) **Antenatal:** Direct trans-placental in-utero transmission -which accounts for approximately 30% of total transmission;
- 2) **Perinatal:** During labour and delivery, through minor skin abrasions and subsequent direct exposure to infected blood or secretions, or by ingestion of maternal blood, etc. Almost 50% of mother-to-child transmission occurs during delivery;
- 3) **Postnatal:** Through breastfeeding. Breastfeeding is associated with a 5% to 22% increased risk of transmission.

For all practical purposes we can say that in the absence of any intervention the risk of mother-to-child transmission is approximately 25% to 30%.



Factors associated with an increased risk of transmission:

One must remember that there are no test or group of tests that can predict 0% risk of transmission.

The factors identified so far are:

HIV-related factors:

- 1) HIV-RNA levels or the viral load: Risk is extremely low in women with undetectable plasma viral loads. However transmission has been reported at all levels. Also, there is no established upper limit above which transmission always occurs;
- 2) Strain variations (genotype): Each individual's viral pool is comprised of a variety of HIV quasispecies and transmission seems to be selective for some of them;
- 3) Biologic growth characteristics (phenotype): blood mononuclear cells may be more susceptible to macrophage-tropic, non-syncytium-inducing HIV phenotypes;
- 4) Plasma vs. genital tract viral load: Though there is generally a correlation between the two, some discordance may exist, which also may explain transmission at undetectable plasma virus levels;
- 5) Genotypic resistance: Use of monotherapy regimens has led to a concern about transmission of resistant mutants;
- 6) CD4 cell counts: Lower CD4 counts, decreased CD4 to CD8 ratio have been consistently associated with increased risk of transmission;
- 7) Maternal immune response: No consistent results about risk of transmission associated with anti-gp120, anti-gp41, and autologous neutralizing antibody titres have been demonstrated.

Pregnancy in women with HIV-2 infection :

HIV-2 is endemic in West Africa and other areas of high prevalence including parts of India and Portugal. HIV-2 appears to be less pathogenic than HIV-1, with prolonged periods of asymptomatic infection and slower rates of disease progression reflecting a lower rate of viral replication. M.T.C.T. rates of HIV-2 are also low, 0-4% in breast-fed infants, in the absence of any intervention. Interventions to reduce M.T.C.T. of HIV-2 in pregnant women have not been clearly defined.

Because HIV-1 transmission, both due to its high prevalence and higher efficiency of transmission poses substantially higher risk of M.T.C.T., the whole discussion in this handbook refers to M.T.C.T. of HIV-1.

Maternal Factors:

- 1) Clinical stage of the disease: Advanced HIV disease is associated with increased risk;
- 2) Sexually Transmitted Diseases (STDs)/other co-infections: STDs lead to increased genital tract HIV shedding and increased plasma viraemia, both increase the risk of transmission;
- 3) Vitamin A deficiency: Though vitamin A deficiency was associated with increased risk of transmission recent data show no advantage of Vitamin A supplementation;
- 4) Substance abuse: It has been associated with increased transmission;
- 5) Cigarette smoking: It has been shown to be associated with increased transmission;
- 6) Use of antiretroviral agents: These drugs have been demonstrated to be effective in reducing the transmission;
- 7) Sexual behaviour: Unprotected sex with multiple

- partners increases the risk of transmission;
- 8) Gestational stage: Pre-term delivery increases the risk;
- 9) Duration of membrane rupture: The likelihood of transmission increases linearly with the duration of rupture of membranes, with a 2% increase in the risk for each hour increment;
- 10) Placental disruption-abruption, chorioamnionitis: This increases the risk of transmission;
- 11) Invasive foetal monitoring: This leads to increased exposure of the foetus to maternal blood and genital secretions;
- 12) Episiotomy, forceps: These have potential to increase the risk of transmission through trauma, but on the other hand their judicious use may shorten labour and may decrease likelihood of transmission;
- 13) Mode of delivery: Several studies indicate advantages of elective Caesarean section while others suggest that the decision for C-section should be entirely dependent on obstetric indications.

Foetal/Neonatal factors:

- 1) Immature immune system, especially in premature infants makes them more vulnerable;
- 2) Genetic susceptibility (HLA genotypes or CCR-5 receptor mutations) leads to variable potential of acquiring the infection;
- 3) Detectable immune responses (early-acquired cellular response) reduce the chances of infection;
- 4) Risk to first- born of the twins is higher than the second born.

Breastfeeding:

It is a factor that plays an important and significant role in transmission but the issues related to it remain unresolved.

Breast-feeding in the setting of established maternal infection has an increased additional risk of 14% transmission, while in acute maternal infection or recent seroconversion the risk is 29%.

Factors associated with breastfeeding :

- 1) Risk is highest in the earliest months of breast-feeding but increased duration increases the risk;
- 2) Breastfeeding patterns: Exclusive breastfeeding is shown to have less transmission potential as compared to mixed feeding. (A study from South Africa recently reported that the risk of MTCT was the lowest for children exclusively breastfed for 3 months (14.6%) as against those who were partially breastfed (24.1%) and never breastfed (18.8%). This was attributed to the protective immune factors such as secretory leukocyte protease inhibitors, lactoferrin, complement, glycosaminoglycan and growth factors useful in maintaining the integrity of the gut epithelium;
- 3) Avoidance of breastfeeding will eliminate risk of transmission through breastfeeding but would certainly increase risk of morbidity and mortality associated with substitute feeding;
- 4) Cracked nipples or breast abscesses, infant oral thrust may increase transmission.



7. Prevention of Mother-to-Child Transmission of HIV (PMTCT)

With increased knowledge about the different mechanisms of mother to child transmission of HIV we can now design different strategies to prevent or reduce the same. A number of strategies have been proposed.

The first and the foremost would be primary prevention through avoidance of HIV infection among the women of childbearing age and then, through proper contraception, avoidance of pregnancy in HIV positive women.

In case of HIV positive women with pregnancy following interventions have been considered.

1) Termination of Pregnancy

In a country like ours where medical termination is legal and the women is fulfilling other criteria of eligibility for MTP, this could be considered. (However we must remember that the decision to terminate should be taken by the woman as a well considered and informed decision and should not be thrust upon her. It can't be a public health intervention.)

2) Behavioural Interventions

- a) Reduce frequency of unprotected sex during pregnancy.
- b) Reduce number of sexual partners during pregnancy.
- c) Lifestyle changes, avoidance of drug use and smoking.

3) Therapeutic Interventions

- a) Antiretroviral therapy.
- b) Vitamin A and other micronutrients.
- c) Immunotherapy.
- d) Treatment of sexually transmitted infections.

4) Obstetric Interventions

- a) Avoidance of invasive tests.
- b) Birth canal cleansing.
- c) Caesarean section delivery.

5) Modifications in Infant Feeding Practices

- a) Avoidance of breastfeeding.
- b) Early cessation of breastfeeding.
- c) Heat treatment of expressed breast milk

In spite of several studies to evaluate the efficiency of different strategies listed above the only interventions proven to be effective in prevention of mother to child transmissions at present are:

1. Use of antiretroviral medicines;
2. Caesarean section; and
3. Modifications in infant feeding practices.

Application of these strategies in the field areas requires additional operational inputs and the results seen in clinical trial setting might differ from those in operational research studies.

Before contemplating to undertake any prevention of mother to child transmission program we must ensure that the following services are available:

- Access to appropriate antenatal, intra-partum and post-partum care.
- Adequate pre and post test counselling services.
- Reliable and affordable HIV testing.
- Appropriate laboratory facilities to monitor antiretroviral treatment.
- Materials to ensure universal precautions (disinfectants, gloves and clean needles).
- Acceptance of the service by HIV positive women.
- Use of logistically feasible regimens.



8. Antiretroviral Treatment in Pregnancy to Prevent MTCT

Several different regimens have been tried and evaluated in various studies. The most original one was the ACTG (AIDS Clinical Trial Group) or PACTG (Paediatric ACTG) 076 protocol, which successfully demonstrated that the MTCT could be reduced by almost 67%. In this trial zidovudine (ZDV/AZT) was used antenatal (oral), intra-partum (intravenous), and post-partum to the infant for 6 weeks (oral); in a non breast-feeding population.

The effect of this protocol appears to be partly through the reduction in maternal viral load and also through post-exposure prophylaxis effect in the infant. Use of this protocol has become standard of care in USA and Europe as also in Brazil and Thailand.

High cost of this intervention made it difficult to implement it in developing countries (where the majority of MTCT occurs). There were additional logistical problems of lack of monitoring blood parameters, drug reactions, nonavailability of IV infusion of zidovudine and treatment to the newborn for 6 weeks. It was also seen that in most of the developing countries women rarely attended antenatal clinics early enough to start the protocol. According to WHO, 43% deliveries take place without any attendant. There are no voluntary counselling and testing facilities. The infant feeding practices also are vastly different.

In view of these shortcomings alternative regimens were tried. Studies indicated that even if a mother (in labour) and a neonate (within 48 hours) receive ZDV prophylaxis, a significant proportion of MTCT could be reduced. A trial of short regimen zidovudine treatment in Thailand showed a significant effect in preventing

transmission. Zidovudine was used orally from 36 weeks of gestation until labour with stepped up doses during labour till delivery. The women did not breastfeed the babies and no zidovudine was given to the infants. The results showed 50% reduction in transmission risk. However, its applicability for countries where mothers cannot afford artificial feeds and those who are unable to maintain good hygiene became suspect.

Short-term ZDV studies were conducted in Burkina Faso and Cote d'Ivoire. In these trials more than 85% infants were breastfed for more than 3 months. Efficiency of prevention of transmission was estimated at 38%.

These and some other studies demonstrated that short-term use of zidovudine was safe and effective. There were some trials using combination of drugs, e.g. PETRA trial (zidovudine + 3TC (lamivudine)), French study (standard ACTG 076 + 3TC from 32 weeks).

Use of non-nucleoside reverse transcriptase inhibitors (NNRTI) has added another dimension to PMTCT programmes. Nevirapine, which achieves high circulating levels, which are long lasting, has been used as a single dose treatment in labour. The transmission rates were reduced by almost 50% in a study using single dose Nevirapine to the mother in labour and single dose to the infant between 48 to 72 hours (HIVNET 012 trial).

In many developed countries (where the problem of MCTCT has largely been controlled) women are taking full HAART (triple drug regimens) including a protease inhibitor.

Tables that follow give the summary of various trials of antiretroviral drugs to prevent mother to child transmission of HIV. There have been reports of development of resistant strains of HIV after any of these regimens, however the benefits seem to far outweigh this risk.

Important Practical Implications

At the present juncture we can say that we can have a following approach.

a) HIV infected pregnant women who have not received prior antiretroviral therapy:

These women should receive standard clinical, immunologic and virologic evaluation. Recommendations for initiation and choice of antiretroviral therapy should be based on same parameters used for persons who are not pregnant.

Initiation of therapy should be delayed until the first trimester is over. The protocols should be started at 14 weeks of gestation.

Regardless of CD4 count, viral load, or prior antiretroviral therapy, as a minimum, the ACTG 076 regimen or some modification thereof is recommended for all HIV-infected pregnant woman when possible.

Use of Zidovudine (ZDV)

Before delivery (Anytime after 14 weeks of gestation up to 34 weeks): Zidovudine 300mg twice a day (oral) or 200mg three times or 100mg five times a day until onset of labour.

During labour: (As IV zidovudine is not available) ZDV 300mg (oral) at the beginning of labour and then give 300mg oral every 3 hours until delivery.

Infant: ZDV syrup 2mg/kg (oral) every 6 hours for 6 weeks beginning 8 to 12 hours after birth.

Laboratory criteria for recommending ZDV in pregnant women:

Haemoglobin > 8mg/dl, platelets > 1lac/ml, normal liver and renal function.

Laboratory monitoring of pregnant women on ZDV: Complete blood counts, platelet counts and transaminases 15 days after starting medication, then once a month.

Laboratory monitoring of infants on ZDV: Complete blood counts and platelet counts at birth, then at 2 and 6 weeks.

Laboratory criteria to interrupt ZDV in pregnant women and infants :

Haemoglobin < 8mg/dl, platelets < 50000/ml, raised transaminases levels.

The ZDV regimens can be started any time after 14 weeks up to 34 weeks. Use of ZDV for less than 4 weeks duration has no advantage over single dose Nevirapine protocol. Original Thai/CDC study did not give ZDV postpartum to the infant. If resources permit one may add this component.

Mode of Delivery

Efficacy of Caesarean section done with ZDV has been reported in a number of studies; however most feel it is premature to recommend elective Caesarean section to all HIV infected women; mainly due to the problems regarding the feasibility. Maternal mortality is increased five-fold with Caesarean section and post operative complications have been reported in 31% of HIV infected women, three times more than HIV negative controls.

Elective Caesarean section may be recommended to women with very high viral loads as an exception and not the rule.

b) HIV infected women in labour who have had no prior antiretroviral therapy

Single dose Nevirapine 200 mg at the onset of labour followed by a single dose of Nevirapine 2 mg/kg to the newborn at 48 hours.

If the mother received Nevirapine less than 1 hour prior to delivery, Nevirapine 2mg/kg was given to the baby as soon as possible at birth and again at 48-72 hours.

Other approaches like oral ZDV + 3TC during labour followed by one week oral ZDV/3TC for the newborn or intra-partum IV ZDV followed by 6 weeks ZDV for the newborn do not offer any added significant advantage, are more difficult to manage in the field and are impossible in situations where IV ZDV is not available.

c) Infants born to mothers who have received no antiretroviral therapy during labour

Six weeks neonatal ZDV initiated as soon as possible after delivery - preferably within 6-12 hours.

In situations where HIV prevalence is very high, there is little possibility of testing and if there is very strong suspicion (oral candidiasis, herpes zoster scar, etc.) in the mother, it may be worthwhile giving the two-dose Nevirapine regimen to the infant even without a test.

d) HIV- infected woman receiving antiretroviral therapy during the current pregnancy

If pregnancy is identified after first trimester then continue therapy. ZDV should be a component of the therapy whenever possible, although may not always be

feasible.

If pregnancy is recognized during first trimester, then counsel regarding potential risks and benefits of continuing therapy. If therapy is discontinued, stop all drugs and reintroduce all, simultaneously at the end of the first trimester.

Regardless of what the mother is on, administer ZDV during intra-partum period and the newborn.

e) HIV positive pregnant woman not on antiretroviral treatment before but requiring treatment due to their own disease status:

Based on the results of CD4 counts and /or viral load and also taking into consideration the presence of symptoms and/or AIDS defining opportunistic infections or other conditions; one must consider initiating antiretroviral treatment. Follow the same guidelines given above.

Other Interventions

There have been several studies and recommendations e.g. use of passive immunization with hyper-immune HIV immunoglobulin (HIVG) and active immunization with HIV vaccines, nutritional interventions (Vitamin A, Zinc, Selenium), vaginal cleansing with antiseptics or antiviral agents, etc. These have not been shown to offer any advantage as far as PMTCT is concerned.

Modification of Infant Feeding Practices

Increased risk of HIV transmission through breastfeeding is well documented. Potential modifications of infant feeding practice include:

- a) Complete avoidance of breast-feeding.
- b) Early cessation,
- c) Pasteurisation of breast milk,
- d) Avoiding breast feeding in the presence of breast abscess or cracked nipples, and

As has been recently shown in some of the studies

e) Exclusive breastfeeding.

At the present juncture we can say that mother should be given the information on the advantages and disadvantages of breast feeding and replacement feeding with regard to HIV transmission and encouraged to make a fully informed decision. They should be supported in their decision.

ARV Regimens of Proven Efficiency

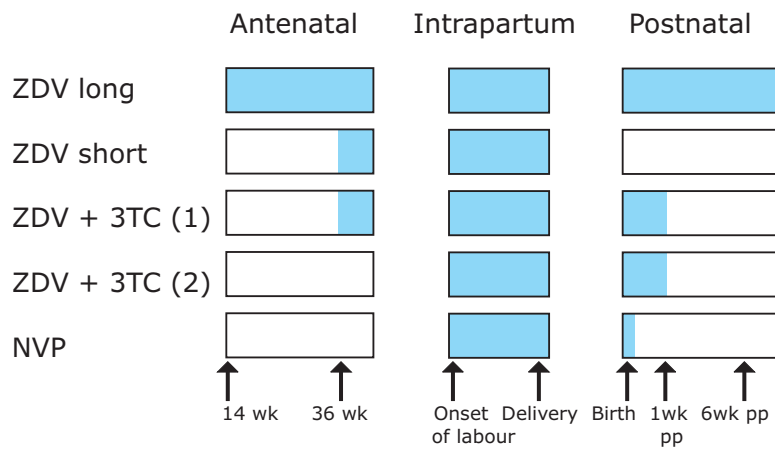


Table - Evidence of the efficacy of antiretroviral therapy to reduce the risk of mother-to-child transmission of HIV infection. Studies of antiretroviral therapy to prevent mother-to-child transmission in non-breast-feeding populations.

Study name	Countries	Study size	Treatment components			Age HIV assessed	Transmission rates (%)	% Reduction (p)
			Pre-partum (Initial gestation week)	Intra-partum (IV-Oral)	Post-partum (weeks)			
ACTG 076/ANRS 024 (10)	France USA	402	ZDV 100 mg 5 x daily 14-34	ZDV IV	ZDV 6	18 months (antibody)	22.6 placebo 7.6 ZDV	66.3% (0.00006)
Bangkok Trial(52)	Thailand	392	ZDV 300mg bd 36	Oral ZDV	Nil	6 months DNA PCR	18.9 placebo 9.4 ZDV	50% (0.006)
PHPT (51) Long/Long arm Short/Long arm Long/Short arm Short/Short arm	Thailand	1437	ZDV 300mg bd 28	ZDV Oral	ZDV 6	180 days DNA PCR	6.7	57.6% cf Short/ Short interi (0.004)*
			35	Oral	6		5.7	
			28	Oral	3 days		8.4	
			35	Oral	3days		10.6	
AL455-094 (66)	Soweto	197	ZDV 300mg bd d4T 40 mg bd ddl200mg bd d4T Et ddl 34-36	ZDV Oral d4T ddl d4T Et ddl	ZDV d4T ddl d4T Et ddl 6 weeks	6 weeks DNA PCR	6.3 4.2 1.9 2.0	On-going study

*Discontinued early because of higher rate of transmission (Short/Short arm).

Studies of antiretroviral therapy to prevent mother-to-child transmission in breast-feeding populations.									
Treatment components				Transmission rates (%)					
Study name	Countries	Study size	Pre-partum (Initial gestation week)	Intra-partum (IV-Oral)	Post-partum (weeks)	Age HIV assessed	DNA PCR	Place vs. ZDV	% Reduction (P)
Retro(57)	Cote d'Ivoire	230	ZDV 300mg bd 36	Oral	Nil	3 months 6 months 12 months 18 months 24 months	3 months 6 months 12 months 18 months 24 months	26.1 vs. 16.5 26.1 vs. 16.9 28.5 vs. 18.5 30.1 vs. 21.6 30.1 vs. 22.1	37% (0.07) 35% 35% 28% 27% (< 0.5)
DITRAME 58	Burkina Faso, Cote d'Ivoire	421	ZDV 300mg bd 36	Oral	1 week maternal	6 months 15 months	6 months 15 months	27.5 vs. 18 30.6 vs. 21.5	35% 30%
PETRA (74)	Republic of South Africa, Tanzania Uganda	1042	ZDV 300mg bd + 3TC 150mg bd Nil Nil 36	Oral Oral Oral Oral	Yes Yes Nil	6 months 6 months 6 months 6 months 18 months	6 months 6 months 6 months 6 months 18 months	19.5 vs. 9.2 26.6 vs. 20.7 19.2 vs. 12.6 26.6 vs. 24.4 19.2 vs. 18.4 26.6 vs. 25.7	50% (0.001) 22%(0.07) 37% (0.02) 8% (0.5) -3%(0.8) 3% (0.8)
HIVNET 0.12(68)	Uganda	618	Nil	ZDA 300mg stat + 3 hly vs. NVP 200 mg stat	ZDV 1 week vs NVP start 48<72h	6-8 weeks 12 months	6-8 weeks 12 months	ZDV vs. NVP 20.0 vs. 11.8 24.1 vs. 15.7	41%(0.006) 35%
SAINT (72)	Republic of South Africa,	1306	Nil	Oral ZDV + 3TC vs. NVP	1 week	8 weeks	8 weeks	ZDV + 3TC vs. NVP 9.5 vs. 12.7	Equivalence (>0.10)

IV - intravenous; ZDV = Zidovudine; NVP = Nevirapine; 3TC = Lamivudine.

FDA (USA) Classifications of Antiretroviral Drugs for Use in Pregnancy

DRUG	FDA CATEGORY
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS	
Zidovudine (ZDV, AZT)	C
Zalcitabine (ddC)	C
Didanosine (ddI)	B
Stavudine (d4T)	C
Lamivudine (3TC)	C
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS	
Nevirapine	C
Delavirdine	C
PROTEASE INHIBITORS	
Indinavir	C
Ritonavir	B
Saquinavir	B
Nelfinavir	B

Classification of the categories :

- A: Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the foetus during the first trimester of pregnancy (and there is no evidence of risk during later trimesters)
- B: Animal reproduction studies fail to demonstrate a risk to the foetus but well controlled studies of pregnant women have not been conducted.
- C: Safety in human pregnancy has not been determined, animal studies are either positive for foetal risk or have been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the foetus.
- D: Positive evidence of human foetal risk based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of drug in pregnant women may be acceptable despite its risks.
- X: Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.

Pregnant woman with no prior ART	Pregnant woman in labour with no prior ART
<p>Antepartum</p> <p>ZDV 300mg BD Initiate AZT prophylaxis starting at 14 weeks to 34 weeks (minimum 4 weeks before labour), continue throughout pregnancy.</p> <p>Intrapartum</p> <p>ZDV 300mg every 3 hourly during labour until delivery.</p> <p>Postpartum to newborn</p> <p>ZDV 2mg/kg 6 hourly for 6 weeks beginning at 8-12 hours after birth.</p>	<p>Single dose NVP 200mg to mother during labour</p> <p>Single dose NVP 2mg/kg to newborn at age 48-72 hours. If mother has received NVP less than 1 hour before delivery give 2 doses of 2mg/kg NVP to newborn, first as soon as possible after birth and second at 48-72 hours.</p>

Mother with no ART in labour	Pregnant woman receiving ART during current pregnancy	Symptomatic pregnant woman not on ART
<p>ZDV (2mg/kg 6 hourly) to newborn as soon as possible, within 6-12 hours after birth for 6 weeks.</p>	<p>Discontinue all the treatment simultaneously for first trimester Continue or modify therapy as per the need Counsel the patient regarding benefits and potential risk of ART during first trimester.</p> <p>ZDV is recommended during intrapartum period.</p> <p>ZDV prophylaxis is recommended to the newborn.</p>	<p>For pregnant woman who needs treatment for her own health consider the option of starting ART based on CD4 counts and viral load.</p>



9. Management of HIV-Positive Women During Pregnancy

The management of HIV positive women during pregnancy is multifaceted and requires team approach. It combines medical and obstetrical management with counselling and social support. This should be a part of the continuum of care for the mother and the child, (as also care of the father). Prevention of mother-to-child transmission programmes should therefore be stepping-stones to step-up all care and support programmes for people living with HIV.

Antenatal Care

Most HIV positive women will be asymptomatic and have no major obstetrical problems during their pregnancies. They should receive similar obstetric antenatal care to that given to HIV-negative women, unless indicated by the need to provide specific HIV related treatment. There is no need to increase the number of antenatal visits, but an additional counselling time will be required.

Following guidelines will be useful:

1) HIV History:

Date of diagnosis, history of HIV related symptoms or opportunistic infections or malignancies, CD4 counts, treatment received, etc.

2) Obstetric History:

Previous pregnancies and outcomes,

complications, mode of delivery, use of antiviral prophylaxis, HIV status of other children, etc.

3) Signs and symptoms of HIV/AIDS:

Look for generalized lymphadenopathy, oral thrush, tuberculosis, constitutional symptoms like fever, diarrhoea, cough, herpes zoster, peripheral neuropathy wasting, dysphagia, dyspnoea, persistent or recurrent herpetic ulcerations, etc.

4) Signs and symptoms of pregnancy related complications:

Elevated blood pressure, significant oedema, severe headache, vaginal bleeding or leakage of fluid, intractable nausea and vomiting, dysuria, vaginal discharge, persistent abdominal or back pain, decrease in foetal movements, etc.

5) Relevant family history

6) Ultrasound:

Indications for obstetric ultrasound are many, including pregnancy dating, evaluation of foetal growth, evaluation of vaginal bleeding during pregnancy, determination of foetal presentation, suspected multiple gestation, significant date/size discrepancy, pelvic mass, suspected ectopic pregnancy, foetal viability, state of liquor amnii, foetal abnormalities, etc. It is recommended that one ultrasound examination be done in each trimester.

In conditions with limited resources at least one ultrasound in early second trimester must be recommended.

7) Other Investigations:

A haemoglobin examination is mandatory and complete blood count may be performed.

Syphilis testing should be undertaken.

Testing for HIV serology if negative during the first visit should be advised at 34 weeks of gestation so that the window of opportunities for administering short duration ZDV regimens still remains available. All those who were tested negative at an early date and presenting during labour should again be screened with a rapid test (so that we may offer at least Nevirapine).

Hepatitis serology, especially for hepatitis B, has now become a part of standard panel of investigations.

Routine urine examination is an essential and simple investigation.

Blood sugar estimates for diabetes screening are recommended routinely. Blood group determination will help in two ways: planning for blood transfusions if required and for being aware of Rh incompatibilities.

All invasive investigative interventions (amniocentesis, chorionic villous sampling, percutaneous umbilical blood sampling, etc.) should be avoided.

8) Monitoring for HIV disease:

CD4 counts and viral loads may be done if resources permit. This will help in starting antiretroviral treatment to the mother or at least in providing appropriate opportunistic infection prophylaxis.

Intra-partum Care

Intra-partum care for HIV positive women should follow routine practice in most respects.

As already discussed, based on the available data, all HIV positive pregnant women should be counselled about possible benefits versus risks of scheduled C-section and the limitations of current studies.

Women should be informed that there is no therapy or combination of therapies, which can guarantee an uninfected infant.

Prolonged rupture of membranes should be avoided. Artificial rupture of membranes should not be undertaken if progress of labour is adequate.

Episiotomies should not be performed routinely, but reserved for those cases with an obstetrical indication.

If an assisted delivery is required, forceps may be preferable to vacuum extraction. Scalp electrodes or scalp blood sampling should be avoided unless absolutely necessary.

Prophylactic antibiotics should be given for both elective and emergency Caesarean sections.

Obstetric care of HIV infected pregnant women during labour

- 1) Universal precautions: Universal precautions (to be discussed later) should be applied in managing all women in labour irrespective of their HIV status;
- 2) Avoid invasive procedures;
- 3) Avoid artificial rupture of foetal membranes and consider shortening of labour;
- 4) Avoid episiotomy;
- 5) Clamp umbilical cord immediately after birth;
- 6) Cleanse the baby immediately after birth (use soap and water).

Specific measures for delivery

- 1) **Wear protective equipments, including gloves, gown, mask, cap, and eye protection to avoid exposure to blood and amniotic fluid;**
- 2) **Exercise special care in handling the placenta and umbilical cord;**
- 3) **Use plastic syringes preferentially;**
- 4) **Use scissors, rather than a scalpel blade for episiotomy and manipulation of the umbilical cord, etc;**
- 5) **Choose sutures with attached needles;**
- 6) **Avoid straight suture needles;**
- 7) **Avoid simultaneous suturing by two surgeons in the same surgical field.**

Post-partum Care

The post-partum care of HIV positive women should be similar to that for uninfected patients. They do not require separate nursing facilities. Women may however require private facilities to lessen the social stigma associated with not breast-feeding.

HIV positive women are more prone to post-partum infectious complications including urinary tract, chest, episiotomy and Caesarean section wound infections. Health workers should observe for signs of these and also inform the women to be aware of these, especially where the post-partum hospital stay is short. All women should be informed about perineal care and the safe handling of lochia and blood stained sanitary pads or materials.

Mothers should be provided information about care of babies without risk of exposure to infection.

The choices of infant feeding should be fully discussed, and adequate information regarding risks and benefits of the different choices should be provided. If she chooses not to breastfeed adequate information about replacement feeding up to two years, guidance on breast care until lactation stops should be provided.

Those who prefer to breastfeed should be informed about risks involved with cracked nipples, mastitis, and breast abscess or of oral lesion in the child.

Reducing the duration and early cessation of breast-feeding may be encouraged where this can be achieved safely.

For those who choose to breast-feed, importance of avoidance of mixed feeds and strict adherence to exclusive breast-feeding be emphasized.

Mothers should be counselled on the need for follow up care for themselves and their children, also regarding the available options for testing of the children.

Contraceptive advice is provided with encouragement to start with appropriate method.

Care of Neonates

Babies of HIV positive mothers should be handled with gloves until maternal blood and secretions are washed off. In fact this should be a part of universal precautions for managing all neonates.

Anaemia is the most common complication seen in neonates with the long course treatment of six weeks ZDV to the child. Haemoglobin should be checked at baseline and after six weeks and 12 weeks if this regimen is used.

Mothers should decide on infant feeding and be supported in their choice.

Children should be referred for long-term follow-up and for repeat testing for diagnosis of HIV infection, either by early PCR, if available, or by ELISA at 15 to 18 months.



10. Care of the HIV Exposed Infant

Diagnosis of HIV in a Neonate

The diagnosis of HIV infection in a neonate is difficult. ELISA tests, as also the rapid tests that detect antibodies may give false positive results till 15 to 18 months due to the presence of passively transferred maternal antibodies.

On the other hand an infant (especially the one being breastfed by a HIV positive mother) carries the risk of acquiring HIV infection for a much-prolonged period. The window period will extend up to 4 to 6 months after cessation of breast-feeding.

If there are no passively transferred maternal antibodies the tests could be negative in spite of the child being infected.

Positive antibody serology tests do not tell us whether the child is infected nor do negative serology tests rule out absence of infection.

The standard for diagnosis of HIV infection in exposed infants is use of viral assays HIV DNA PCR (preferred), HIV -RNA-PCR or viral culture obtained within 48 hours of birth, at 1-2 months and 3-6 months.

HIV can be excluded with two or more negative tests, one or two of which are performed at age ≥ 1 month and one performed at age ≥ 4 months.

Antibody based test with two negative results in a non-breastfed infant at ≥ 6 months and at least 1 month apart will also exclude infection.

P24 antigen testing is less sensitive and has high frequency of false positive results in infants < 1 month of age, and therefore should not be a preferred test.

HIV-DNA PCR has 93% sensitivity by age of 14 days. Using this approximately 40% of infected infants can be identified by the age 48 hours and are considered to have early or intrauterine infection. Infants with initial negative but subsequent positive tests are considered to have intra-partum/post-partum infection. Almost all infants can now be diagnosed by the age of 6 months.

ZDV monotherapy for peri-natal prophylaxis has not been shown to delay detection of HIV or decrease sensitivity of these tests.

Antiretroviral Treatment

All HIV exposed infants should receive prophylaxis according to the regimens used for the mother and as already discussed.

Once infection is documented, more intensive combination antiretroviral therapy is recommended to all neonates, if resources permit. It has been observed that almost 20% of HIV infected infants tend to be fast progressors with possibility of early and permanent tissue damage. There is no way to identify these fast progressors.

If resources do not permit then infants with clinical symptoms of HIV infection or evidence of immunosuppression (immune category 2 or 3, see table that follows) regardless of age or viral load should be offered anti-retroviral treatment.

A neonatologist or a paediatrician should be involved in care at the point of confirmation of diagnosis.

PCP Prophylaxis

All HIV exposed infants should receive PCP prophylaxis with trimethoprim/sulfamethoxazole (150-170 mg/m²/day of TMP and SMX 750/m²/day). This can be given in 2 divided doses daily or 2 divided doses daily on 3 consecutive days each week, or same dose once daily on

3 consecutive days a week, or twice a day given 3 alternate days a week. If TMP- SMX is not tolerated then dapsone (2mg/kg/day), monthly aerosolized pentamidine (in those older than 4 years) or IV pentamidine are other options.

PCP prophylaxis should be continued till HIV infection is conclusively ruled out.

Immunization

Infants born to HIV infected mothers should follow the routine immunization schedule. Those infants with symptomatic disease or with evidence of severe immunodeficiency should not be given live vaccines like BCG or oral polio vaccine. However the risk of live oral polio vaccination has not proved significant, so it is not necessary to substitute killed injectable polio vaccine. Hepatitis status of the HIV infected mother should be ascertained, so that Hepatitis B vaccination can be carried out if necessary.

1994 Revised Human Immunodeficiency Virus Paediatric Classification System: Immune Categories Based on Age-Specific CD4 + T- Lymphocyte count and percentage						
Immune Category	< 12 months		1-5 years		6-12 years	
	No./ml	(%)	No. /ml	(%)	No. / ml	(%)
Category 1: No suppression	> 1,500	(> 25%)	> 1000	(>25%)	> 500	(> 25%)
Category 2: moderate suppression	750-1499	(15%-24%)	500-999	(15%-24%)	200-499	(15%-24%)
Category 3 : severe suppression	< 750	(<15%)	<500	(<15%)	<200	(<15%)



11. Infection Control Measures

Exposure to blood and body fluids is common in obstetric practice. One also must remember that HIV-1 and HIV-2 are not the only infections that can be transmitted through such occupational exposures. Hepatitis B and C virus, human T- lymphotropic viruses 1 and 2 (HTLV-1 & HTLV-2) and other agents can be transmitted in the same way. Persons acquiring such infection may remain asymptomatic for prolonged periods and may not be aware of it.

Risk factors for occupational transmission are:

- 1) **Viral pathogen:** After a single percutaneous injury, the risk of transmission is estimated at 9% to 40% for hepatitis B virus, 1% to 10% for hepatitis C virus and 0.2% to 0.5% for HIV.
- 2) **Stage of illness / infection:** During stages of severe viremia the chances of transmission are higher. In case of HIV the viral loads are high during acute and advanced stages of infection and much lower during the asymptomatic phase.
- 3) **Route of exposure:** Intact skin is at virtually no risk for transmission. Breaks in skin and intact mucosal surfaces are associated with small but definite risk. Percutaneous injuries via contaminated sharp objects pose the highest risk. Hollow injection needles are the most dangerous among such sharps. Estimated risk of transmission of HIV from deep needle stick injury from HIV positive patient is 0.4% while from transcutaneous exposure it is 0.05%.

4) Barrier precautions: Gloves will protect against direct contact with the fluids but not against percutaneous injuries. However gloves do reduce the amount of exposure by 10 fold to 100 fold.

Contact with other body fluid, (Vaginal secretions, CSF, amniotic fluid, exudates, breast milk, etc.) is much less dangerous than contact with blood. Contact with saliva, urine, sweat, tears and faeces poses little risk unless these are contaminated with blood.

Periodic training of health care workers is the most cost effective universal precaution.

Universal Precautions

The best protection against occupational exposure to pathogens is the use of universal (or standard) precautions **in all cases.**

Important Precautions in Obstetrics

1. Reducing needle stick injuries by handling used needles as little as possible, using a needle holder, avoiding recapping disposable needles and taking great care in recapping blood sampling barrel system needles or non disposable syringes, placing needles and other sharps in the appropriate containers;
2. Washing hands with soap and water before and immediately after contact with blood or body fluids, and after removing gloves;
3. Wearing suitable gloves when expecting exposure to blood or body fluids;
4. Covering broken skin or open wounds with watertight dressings;
5. Wearing an impermeable plastic apron for delivery;
6. Wearing eye shield for operating or assisting at

- Caesarean Section, and for suturing episiotomies;
7. Wearing double gloves, if possible, for all operations, which considerably reduce the amount of blood carried through if a glove is punctured;
 8. Using an appropriate sized needle (21 gauge, 4 cm, curved) for the repair of episiotomy, together with a technique using a needle holder;
 9. Passing all sharp instruments onto a receiver, rather than hand-to-hand at Caesarean section and modifying surgical practice to use needle holders and to avoid using fingers in needle placement;
 10. Using long-cuffed gloves for manual removal of a placenta;
 11. Wherever possible, avoiding the need for suction of newborns and using wall suction or a suction machine when suction is required. Suction pressure should be less than 140 mm of Hg. to avoid damage to the neonate. If no other suction is available, ensuring that the trap in the mouth operated De Lee suction apparatus is functional;
 12. Disposing of solid waste, such as blood soaked dressings or placentas safely;
 13. Soiled linens should be folded (soiled parts facing in) and placed in plastic bags, then removed and washed with hot water and detergent;
 14. Spills should be cleaned by an individual wearing protective clothing and gloves as follows:
 - a) Wipe with disposable towels,
 - b) Cleanse areas with hot water and detergent,
 - c) Disinfect with dilute household bleach (1:10 for porous surfaces and 1:100 for smooth surfaces).

Use of protective barrier :

Protective barriers reduce the risk of exposure of the health care worker's skin or mucus membrane to potentially infective material.

Protective barriers include gloves, gowns, masks and protective eyewear.

Management of Needle Stick Injuries and Other Accidental Blood Exposure

There is evidence that the risk of infection is reduced by the use of post exposure prophylaxis with anti-retroviral drugs, by as much as 79%. The management of needle stick injuries should be according to local guidelines and antiretroviral drugs should be used for significant injury, if available in the country. Recent guidelines have set out recommendations for the use of anti-retroviral medicines in these cases.

First Aid Treatment

First aid measures should be undertaken as soon as possible after injury. These should include:

Decontamination of the exposure site as soon as possible;

Allowing a needle stick injury or cut to bleed, and not squeezing the wound;

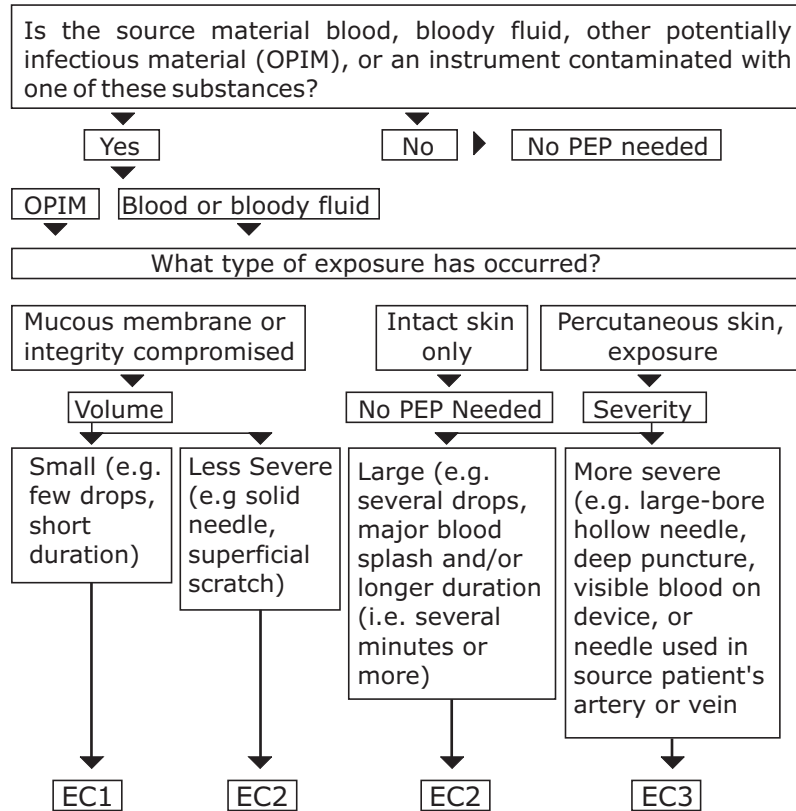
Washing the area with chlorhexidine or other antiseptics and decontaminating exposed mucosae or conjunctivae by vigorous flushing with water.

Types of Occupational Exposures to HIV for which Post Exposure Prophylaxis (PEP) is Recommended

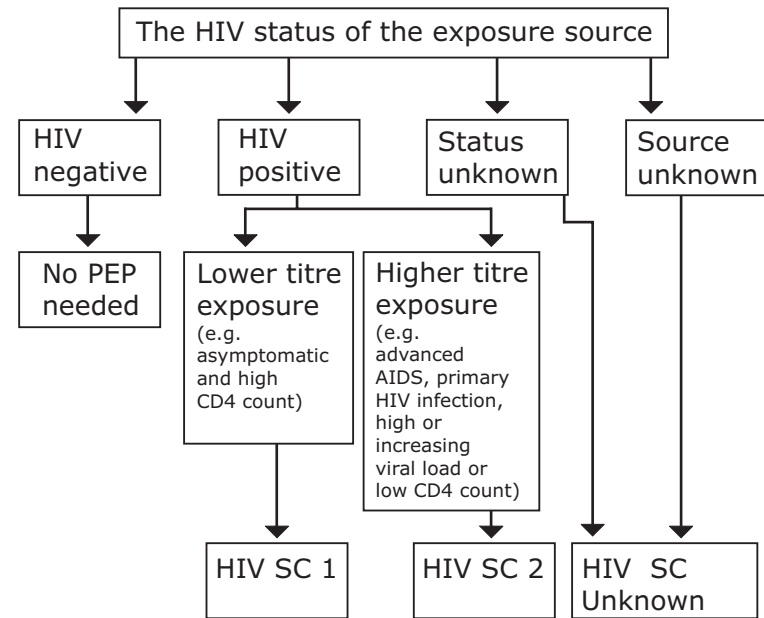
Most occupational exposures do not lead to HIV infection. The chance of possible serious side effects (toxicity) of the drugs used to prevent infection may be much greater than the chance of HIV infection from some kinds of exposures. Both, risk of infection and possible side effects of drugs, should be carefully considered when deciding whether to take post-exposure prophylaxis.

Exposures with a lower infection risk may not be worth the risk of the side effects associated with these drugs. The decision to start PEP is made on the basis of degree of exposure to HIV and HIV status of the source from which exposure/infection has occurred:

Determination of the Exposure Code (EC)



Determination of the HIV Status Code (HIV SC)



EC	HIV SC	PEP recommendation
1	1	PEP may not be warranted
1	2	Consider basic regimen. Exposure type poses a negligible risk for HIV transmission.
2	1	Recommend basic regimen. Most HIV exposures are in this category; no increased risk for HIV transmission has been observed but use of PEP is appropriate.
2	2	Recommend expanded regimen. Exposure type represents an increased HIV transmission risk.
3	1 or 2	Recommend expanded regimen. Exposure type represents an increased HIV transmission risk.
Unknown		If the source, (in the case of an unknown source), the setting where the exposure occurred suggests a possible risk for HIV exposure and the EC is 2 or 3, consider PEP basic regimen.

Basic regimen : Zidovudine (ZDV/AZT) - 600 mg in divided doses (300mg/twice a day or 200 mg/thrice a day for 4 weeks) + Lamivudine (3TC) - 150 mg twice a day for 4 weeks)

Expanded regimen : Four weeks therapy: Basic regimen + Indinavir (800 mg/thrice a day) or any other protease inhibitor. (4 weeks therapy)

Testing and Counselling

The health care provider (HCP) should be tested for HIV as per the following schedule-

1. Base-line HIV test - at time of exposure
2. Repeat HIV test - at six weeks following exposure
3. 2nd repeat HIV test - at twelve weeks following exposure

On all three occasions HCP must be provided with a pre-test and post-test counselling. HIV testing should be carried out on three E/R/S (ELISA/Rapid/Simple) test kits or antigen preparations.

The HCP should be advised to refrain from donating blood, semen, or organ tissues and abstain from sexual intercourse. In case sexual intercourse is undertaken a latex condom should be used consistently. In addition women HCP should not breast-feed their infants during the follow up period.

Counselling and Testing of the Source Patient

HIV testing should be offered to all source patients, with their informed consent. Where such consent is not available (for example in a comatose or anaesthetized patient), this consent should be obtained from a relative or senior medical staff member. Where the source patient

does not wish to know the HIV result, it may be acceptable to offer to take blood for the test (for the protection of the health care worker), without disclosing the result to the source patient. In practice, very few patients refuse consent and most are extremely concerned about health worker risk.

Duration of PEP

PEP should be started as early as possible after an exposure. It has been seen that PEP started after 72 hours of exposure is of no use and hence is not recommended. The optimal course of PEP is not known, but 4 weeks of drug therapy appears to provide protection against HIV.

If the HIV test is found to be positive at anytime within 12 weeks, the HCW should be referred to a physician for treatment

Pregnancy and PEP

Based on limited information, anti-retroviral therapy taken during 2nd and 3rd trimester of pregnancy has not caused serious side effects in mothers or infants. There is very little information on the safety in the 1st trimester. If the HCW is pregnant at the time of exposure to HIV the designated authority/physician must be consulted about the use of the drugs for PEP.



12. Classification Of HIV Infection

(Centres for disease control and prevention. United States public health service, 1986 and 1987)

Group 1	Acute syndrome*
Group 2	Asymptomatic infection
Group 3	Persistent generalized lymphadenopathy (PGL)**
Group 4	Other diseases
Subgroup A	Constitutional diseases
Subgroup B	Neurologic diseases
Subgroup C	Secondary infectious diseases
Subgroup D	Secondary neoplasms
Subgroup E	Other conditions

*Acute infection: occurs in 30% to 70% of individuals infected with HIV. Incubation period: 4 to 8 wks; Syndrome: fever, myalgia, lymphadenopathy, pharyngitis, maculopapular erythematous rash,hepatosplenomegaly, aseptic meningitis, peripheral neuropathy, etc.

** Presence of one or more lymph nodes(> 1 cm) in two different extragenital locations for more than one month.

CLASSIFICATION OF HIV INFECTION IN ADOLESCENTS AND ADULTS (CDC,1993)

CLINICAL CATEGORIES

CD4 Cell Categories	A Asymptomatic, PGL, or acute HIV infection	B Symptomatic (not A or C)	C* Conditions indicative of AIDS (1987)
>500/ mL (29%)	A1	B1	C1
200-499/mL (14%-28%)	A2	B2	C2
<200/mL (<14%)	A3	B3	C3

* All patients in categories A3,B3, and C1-3 are classified as having AIDS, based on the indicator conditions of AIDS (see last table in this section) and/or a CD4 count <200 cells/mL.

AIDS indicator conditions include three new diseases: recurrent bacterial pneumonia, invasive cervical cancer, and pulmonary tuberculosis.

Symptomatic conditions not included in category C are:
a) attributed to HIV infection or indicative of defect in cell-mediated immunity, or
b) considered infections whose management might be complicated by HIV infection.

Examples of category B conditions include, but are not limited to, bacillary angiomatosis, oral candidiasis, persistent vulvo-vaginal candidiasis (frequent or with little response to therapy), cervical dysplasia(moderate or severe), cervical carcinoma in situ, constitutional

symptoms such as fever(38.5 °C) or diarrhoea (>1 month) oral hairy leukoplakia, two episodes of herpes zoster in more than one dermatome, idiopathic thrombocytopenic purpura, listeriosis, pelvic inflammatory diseases (especially if complicated by a tubo-ovarian abscess), and peripheral neuropathy.

(Adapted from Bartlett J. *Medical Management of HIV Infection 1996*)

INDICATOR CONDITIONS OF AIDS (ADULTS)

Candidiasis (oesophagus, trachea, bronchi, or lungs)
Cervical cancer (invasive)*
Coccidioidomycosis (extrapulmonary)
Cryptococcosis (extrapulmonary)
Cryptosporidiosis with diarrhoea (>1 month)
Cytomegalovirus (any organ other than liver, spleen, or lymph nodes)
Herpes simplex with mucocutaneous ulcers(>1 month) or bronchitis, pneumonitis, or oesophagitis
Histoplasmosis
HIV-associated dementia (cognitive and/or motor dysfunctions interfering with occupation or activities of daily living)
HIV-associated wasting (involuntary weight loss >10% of baseline plus chronic diarrhoea[>2 loose stools/ day for >30 days])
Isosporiasis with diarrhoea (>1 month)
Kaposi's sarcoma in patients <60 yrs old (or >60 yrs old)
Lymphoma of brain in patients < 60 yrs old (or >60 yrs old as in Kaposi's sarcoma)
Lymphoma (non-Hodgkin's of B cells or unknown immunologic phenotype and histology showing small, non-cleaved lymphoma or Immunoblastic sarcoma)
Mycobacterium avium or *M. kansasii* (disseminated)
Mycobacterium tuberculosis (disseminated)
Mycobacterium tuberculosis (Pulmonary)**

Nocardiosis

Pneumocystis carinii pneumonia

Pneumonia (recurrent- bacterial, >/=2 episodes in 12 months)

Progressive multifocal leukoencephalopathy

Salmonella septicaemia

Strongyloidiasis (extraintestinal)

Toxoplasmosis (internal organ)

Wasting syndrome due to HIV (as defined in "HIV associated wasting")

* Added to the revised case definition, 1993

** Requires positive HIV antibody test

(Adapted from Bartlett J. *Medical Management of HIV Infection 1996*)



13. Criteria For Beginning Antiretroviral Therapy During Pregnancy

Clinical status	CD4 count cells/mL	(Viral load (RNAcopies/mL)	Recommendation
Asymptomatic Asymptomatic Asymptomatic	NA >500 <500 >200	NA NA or <5000 >5000	Offer ZDV* Offer ZDV* Offer ZDV*+ NRTI + NNRTI
Asymptomatic	<200	Regardless	Offer ZDV*+ NRTI and protease inhibitor or NNRTI
Symptomatic	Regardless	Regardless	Offer ZDV*+ NRTI and protease inhibitor or NNRTI

* Refer to ACTG protocol 076.

NA- not available NRTI - nucleoside reverse transcriptase inhibitor
NNRTI - non nucleoside reverse transcriptase inhibitor

PRINCIPAL ANTIRETROVIRALS

Name	Dose	Frequency	Principal side effects
NRTI Zidovudine (ZDV)	300 mg	1, bid	Headache, anemia, neutropenia, myalgia, GI intolerance
Lamivudine (3TC)	150 mg	1, bid	GI intolerance, anemia, pancreatitis
Didanosine (ddI)	100 mg	2, bid	Pancreatitis, Peripheral neuropathy, GI intolerance

Zalcitabine (ddC)	0.75 mg	1, tid	Peripheral neuropathy, Stomatitis
Stavudine (d4T)	40 mg	1, bid	Peripheral neuropathy
PI Ritonavir	100 mg	6, bid	GI intolerance, perioral paresthesias, taste disturbances, hepatotoxicity
Saquinavir	200 mg	3, tid 6, tid	GI intolerance, Headache
Indinavir	400 mg	2, tid	Nephrolithiasis, GI intolerated elevated indirect bilirubin
Nelfinavir	250 mg	5, bid	Diarrhea
NNRTI Nevirapine	200 mg	1, qd x 14 days ,	Rash fever; oedema arthralgia, malaise
		then 200 mg	Hepatitis, nausea, headache
Delavirdine	100 mg	4, tid	Rash, headache

*Nucleoside reverse transcriptase inhibitor (NRTI).
' Protease inhibitor(PI)
Nonnucleoside reverse transcriptase inhibitor (NNRTI).

Lamivudine (3TC) is the only NRTI besides ZDV for which a pharmacokinetics study has been completely performed in pregnant women and newborn infants. It is well tolerated and has the potential for good patient adherence (1 tablet of 150 mg every 12 hours). Monthly testing of complete blood counts, platelet counts,

transaminases, and amylase can be used to monitor 3TC therapy. Other NRTIs such as ddI, d4T and ddC may be used, as well as nonnucleoside reverse transcriptase inhibitors such as nevirapine or delavirdine in combination with ZDV, but there is no information regarding their safety for pregnant women, foetuses, and newborns or their efficacy in reducing vertical transmission of HIV.

Because of the lack of information on the safety of protease inhibitors during pregnancy and in newborns, their use may be postponed, depending on the time of gestation, until after delivery.

The benefits, potential risks, and side effects of protease inhibitor use during pregnancy should be discussed with each woman, and any decision to prescribe these drugs must be individualized. The goal of antiretroviral therapy in HIV-infected adults is suppression of viral replication to undetectable levels. During pregnancy, the achievement of undetectable viral load will benefit both the mother (good health) and her unborn infant (no HIV transmission).

Suggestions

1. ZDV 300 mg PO two times a day is more convenient, and adherence is more likely to result. Monotherapy is for infant prophylaxis, not for treatment.
2. Three-drug therapy should be offered to all women who are being treated for their health and the health of their babies. Many women will opt only for two-drug therapy. Fixed dose ZDV 300 mg/3TC 150 mg PO two times a day is well tolerated, and one can easily adhere to it.
3. A well tolerated, non - protease inhibitor - containing three-drug regimen is ZDV + 3TC one tablet PO two times a day and nevirapine 200 mg PO two times a day. (Begin 200 mg once a day for 1 - 2 weeks, and then

increase to two times a day to minimize the risk of rash.)

4. A well-tolerated three-drug regimen (including a protease inhibitor) is ZDV + 3TC one tablet PO two times a day and nelfinavir 250-mg tablet, five tablets (1250 mg) PO two times a day.
5. If a woman is not taking ZDV when she becomes pregnant, ZDV should be added back to her regimen.
6. Stop ZDV monotherapy for the woman once she has delivered the baby, since long-term monotherapy can result in viral resistance to this agent.



14. Common Opportunistic Infections

CANDIDIASIS

Candidiasis is the most Common infection in HIV patients. It usually appears when the CD4 count is below 500 cells/ml.

Oral candidiasis:

Frequently, oral candidiasis appears as white patches (thrush) covering part of the oral mucosa. The resulting discomfort can interfere with eating. Other presentations are angular cheilitis and atrophic erythematous candidiasis of the tongue. Clinical diagnosis is confirmed by the presence of hyphae in a scraping of the lesion, as seen on direct microscopic examination with 10% potassium hydroxide.

Treatment: Fluconazole 50mg/d to 100 mg/d PO for 14 days avoid in first trimester whenever possible. Local application of 1% clotrimazole may help temporarily.

Oesophagitis:

Dysphagia, odynophagia, and retrosternal pain are the clinical manifestations of oesophagitis. Oesophagitis occurs more frequently in women. The diagnosis can be confirmed with endoscopy and biopsy. Upper gastrointestinal endoscopy reveals whitish pseudomembranous plaques that may involve the whole oesophagus. When diagnostic endoscopy cannot be done, a clinical treatment may be initiated and response to therapy evaluated.

Treatment: Fluconazole 200 mg/d for 2 to 3 weeks

Vulvovaginal candidiasis :

The most common candidial manifestation among HIV-infected pregnant women, vulvovaginal candidiasis, can occur without significant alterations in the CD4 count. Relapses are frequent. Clinically, patients complain of white or yellowish cheesy discharge, vulvar pruritus, burning, and dysuria. On physical examination, hyperaemia, oedema, and fissures in the vulva are seen. Speculum exam can reveal hyperaemic vaginal walls coated with white plaques. Direct microscopic exam of this material reveals the presence of hyphae and spores.

Treatment:

Local: Miconazole 2% vaginal cream or vaginal inserts for 10 days, or Clotrimazole 1% vaginal cream for 7 to 14 days.

Systemic: Fluconazole 150-mg single dose (longer treatment may be necessary in refractory or recurrent cases)

TUBERCULOSIS

Tuberculosis is one of the most common opportunistic infections seen in HIV- infected individuals. Its clinical presentation is usually insidious but can be abrupt, with or without productive cough, fever, night sweats, weight loss, asthenia, etc. It is a common cause of fever identified while niveptigating unknown aetiology.

Diagnosis:

The chest X ray may show the classic picture of an inflammatory infiltrate in the superior lobes with or without cavitations, miliary nodules, pleural effusion, or atypical forms such as diffuse or localized interstitial infiltrate, hilar adenopathy, or focal infiltrate. The X ray may even appear to be normal in very immunosuppressed patients.

Frequently, other organs can be involved, such as the liver, spleen, kidneys, bone marrow, central nervous system, and/or lymph nodes.

Microbiologic examinations:

Depending on clinical symptoms, microbiologic examinations can include scraping or sputum for acid-fast staining; sputum culture for tubercle bacilli; bronchoalveolar lavage; pleural fluid; cerebrospinal fluid (CSF); biopsies of liver, lymph nodes, and bone marrow; and blood cultures, etc. Because of the possibility of resistance to antitubercular drugs, it may be needed that we determine drug sensitivities of the isolates. Multiple drug resistance refers to resistance to two or more first-line drugs.

Treatment :

Isoniazid (INH) 5 mg/kg/d PO (maximum 300 mg/d) plus Rifampin (RMP) 10 mg/kg/d PO (maximum 600 mg/d) plus Ethambutol (EMB) 15 mg/kg/d to 25 mg/kg/d PO (maximum 2.5 g) plus Pyrazinamide (PZA) 15 mg/kg/d to 30 mg/kg/d PO (maximum 2 g/d)

Therapeutic regimen: INH, RMP, EMB, PZA: 2 months

INH, RMP: 6 to 10 months

Oral pyridoxine (vitamin B6) 50 mg/d should be added to isoniazid therapy to avoid peripheral neuropathy. For HIV-infected pregnant women, the anti-tuberculosis treatment is the same as for non-pregnant women. Alternate treatment regimens necessary because of drug intolerance or allergy should include three drugs, avoiding streptomycin, which is contraindicated because of foetal ototoxicity. Other options are ethambutol 1200 mg/d and ethionamide 750 mg/d. Hepatic toxicity is common, principally because of the concomitant use of other hepatotoxic drugs. Minimum combined treatment is 6

months, and many clinicians recommend up to 12 months of therapy because of higher relapse rates associated with 6 months of treatment.

NOTE: RMP accelerates the metabolism of protease inhibitors, decreasing their serum concentrations and effectiveness. Protease inhibitors slow the metabolism of RMP, increasing its serum concentration, which may lead to toxicities.

DO NOT USE Thiacefazole

Side effects:

INH : neuritis, hepatitis

RMP : GI intolerance, rash, hepatitis

EMB : ocular toxicity, GI intolerance

PZA : arthralgia, hepatitis, rash, hyperuricemia, digestive intolerance, uveitis, neutropenia

TOXOPLASMOSIS

Toxoplasmosis is caused by the protozoan *Toxoplasma gondii*. Clinical presentation is extremely variable and influenced by characteristics such as age, immune status, pregnancy, and associated illnesses. When toxoplasmosis occurs during pregnancy, the difficulty of treatment increases, because, in addition to changes that occur in the mother, the infection is capable of affecting the embryo, foetus, and newborn. Furthermore, the best medications available for treatment of active maternal infection can adversely affect the foetus.

Two distinct scenarios need to be addressed for HIV-positive pregnant women infected with *T. gondii* : chronic and acute infection.

Chronic infection: Among patients who have had toxoplasmosis prior to the current pregnancy, i.e. chronic infection (IgG positive, IgM negative), overt toxoplasmosis can develop in those with severe immunodeficiency (CD4 counts below 200 cells/ml).

Clinical findings: In such cases, encephalitis with *T. gondii* is one of the most common causes of infection of the central nervous system and occurs, in most instances, as a relapse of a chronic latent infection. Most cases of neurotoxoplasmosis occur when the CD4 count drops to 100 cells/ml or less. Headaches are a frequent complaint, and about 50% of patients manifest focal neurological signs such as convulsive crises, hemiparesis, or ataxia.

Diagnosis: Diagnosis is achieved through cerebral computed tomography (CT) or magnetic resonance imaging (MRI), the latter of which has greater sensitivity in detecting small lesions. Single lesions or, more characteristically, multiple lesions are observed, sometimes with surrounding annular enhancement of contrast material, localized in the basal nuclei and with perilesional oedema. Lumbar puncture should not be done.

Differential diagnosis: Tuberculoma, central nervous system lymphoma, cryptococcoma, abscess, etc.

Treatment:

First choice: Sulfadiazine 4 g/d to 8 g/d PO plus Pyrimethamine 100 mg to 200 mg PO loading dose, then 50 mg/d to 100 mg/d PO plus Folinic acid 10 mg/d PO for 6 to 8 weeks. If folinic acid is not available, brewer's yeast two tablets bid can be substituted.

Alternative: Clindamycin 900 mg to 1200 mg IV or 300 mg to 450 mg PO every 6 hours plus Pyrimethamine 100 mg to 200 mg loading dose, then 50 mg/d to 100 mg/d PO

plus Folinic acid 10 mg/d. If there is a response to treatment in 7 to 10 days, as measured by clinical response or evidence of improvement by CT/MRI at 2 weeks, then the diagnosis of neurotoxoplasmosis is confirmed; a full course of therapy should be undertaken, and suppressive treatment is indicated for the remainder of the patient's life. In the event of therapeutic failure, brain biopsy and histopathological study are indicated to exclude other diagnostic possibilities.

Suppressive (lifelong):

Preferred: Sulfadiazine 0.5 g/d to 1.0 g/d PO every 6 hours plus Pyrimethamine 25 mg/d to 75 mg/d PO plus Folinic acid 10 mg/d.

Alternative (patients allergic to or intolerant of sulfadiazine): Clindamycin 300 mg to 450 mg PO every 6 to 8 hours plus Pyrimethamine 25 mg/d to 75 mg/d PO plus Folinic acid 10 mg/d to 25 mg/d.

Trimethoprim-sulfamethoxazole, one tablet (DS) once a day typically indicated for primary prophylaxis of *P. carinii* infection when the CD4 count is below 200 cells/ml or when oral candidiasis or hairy leukoplakia is present, can be used to prevent toxoplasma encephalitis.

Ocular toxoplasmosis is rarely seen in AIDS patients. However, the diagnosis is possible with the appearance of characteristic lesions on fundoscopy. In this stage of serious immunologic compromise, serologic tests are not useful.

Acute infection with *T. gondii* during pregnancy or reactivation of a chronic latent infection (related to immunodeficiency, resulting in parasitaemia and infection of the placenta) can cause congenital infection. In immunocompetent pregnant women, the risk of primary infection transmission to the foetus is about 40%. In the first trimester of pregnancy this risk is proportionately

lower (<15%); however, the risk of abortion or serious illness is greater. The probability of infection increases during the course of pregnancy (60% in the third trimester). The newborn usually has subclinical manifestations (e.g. ocular lesions, or chorioretinitis) in the first year of life or later. Serologic evaluation with the objective of determining exposure to *T. gondii* is useful in the diagnosis of acute toxoplasmosis in pregnant women. A positive diagnosis indicates that treatment is necessary to attempt prevention of infection in the foetus. However, in pregnant women simultaneously infected with *T. gondii* and HIV, serologic tests can be unreliable.

Clinical: Acute toxoplasmosis is asymptomatic in approximately 90% of cases. The most commonly observed clinical manifestation is lymphadenopathy. Occasionally, the clinical presentation in pregnant women can be similar to that of infectious mononucleosis.

Diagnosis: Pregnant women showing prior positive serologic tests with the presence of IgG titres, characterizing old infection need not undergo subsequent serologic follow-up. Positive IgM titres indicate recent infection by *T. gondii* protozoa and, therefore, risk of congenital infection. Negative serologic reactions for *T. gondii* imply the possibility of acquiring infection during pregnancy. In such cases, it is important to inform patients about the various routes of infection. Ingestion/handling of raw/undercooked meat and unwashed fruits and vegetables, as well as contact with cats and changing of cat litter boxes, should be avoided by patients at risk.

Treatment: Patients with acute or reactivated infection need pyrimethamine and sulfadiazine and folinic acid. In cases of acute infection during pregnancy, maternal treatment reduces the incidence and severity of foetal infection. Spiramycin (1 g PO every 8 hours taken while

fasting) is a macrolide that does not pose a risk to the foetus and has been shown to prevent foetal infection in about 60% of cases. However Spiramycin, because it does not cross the placental barrier, is effective only for prophylaxis of the foetus and cannot be used to treat confirmed foetal infection. It is emphasized that Spiramycin does not reach therapeutic levels in the central nervous system, and therefore it is contraindicated in the treatment of pregnant women with neurotoxoplasmosis. The most effective regimen, sulfadiazine (4 g/d) with pyrimethamine (25 mg/d to 50 mg/d) and folinic acid (5 mg/d to 10 mg/d), can be used only after the first trimester, as pyrimethamine has potential to be teratogenic. If the second regimen is used, weekly follow-up with complete blood count is necessary.

Prophylaxis: Patients without a clinical diagnosis but with newly acquired infection, as defined by positive IgM or IgA, should receive Spiramycin.

PNEUMOCYSTIS CARINII PNEUMONIA (PCP)

PCP is the second most common opportunistic infection in AIDS. Without primary prophylaxis, 80% to 85% of AIDS patients will develop PCP during the course of this illness. Without secondary prophylaxis, more than 50% will have recurrence of PCP within 1 year. As a rule, PCP is seen only in patients with CD4 counts below 200 cells/ml.

Clinical manifestations:

Clinical manifestations usually include fever, cough (slightly productive or with mucus expectoration), exertional dyspnea, fatigue, and weight loss. Although generally insidious, the onset may also be abrupt, proceeding quickly to respiratory insufficiency.

Physical examination findings: Weight loss, tachycardia, tachypnoea, and, with progression of the disease, cyanosis of the lips and extremities due to respiratory insufficiency.

Chest X-ray findings: In 80% of patients, the classic finding is a diffuse bilateral interstitial infiltrate in the perihilar and/or basilar regions of the lungs, commonly of heterogeneous density. In more fulminant cases there may also be evidence of alveolar consolidation. Chest X ray can be normal in early stages in 15% to 20% of patients. Atypical findings include focal infiltrate, nodules, pneumatocele, pneumothorax, or, rarely, miliary nodules.

Laboratory findings: Mild to severe hypoxemia (PO₂<60 mm Hg). Lactate dehydrogenase (LDH) levels above 500 U/L are suggestive of PCP, but non-specific and normal values do not exclude the diagnosis.

Definitive diagnosis: *P. carinii* in a sputum smear (commonly silver methenamine stain). Sputum can be obtained by ultrasonic nebulization with hypertonic saline solution (3% to 5%) after fasting and oral and dental hygiene. Fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) has a sensitivity of approximately 90%, which can be increased further by adding a transbronchial biopsy.

Treatment

First choice: Trimethoprim-sulfamethoxazole (TMP-SMX): TMP 15 mg/kg/d and SMX 75 mg/kg/d PO or IV for 21 days in three or four divided doses. Typical oral dosage is two tablets (DS) three times a day. IV administration is preferred for initial therapy in very ill patients.

Alternative (patients allergic to sulfa): Pentamidine 4 mg/kg/d single dose, diluted in 100 mL to 250 mL 5% dextrose infused IV over 1 to 2 hours for 21 days or Clindamycin 600 mg IV every 8 hours or 300 mg to 450 mg PO every 6 hours plus Primaquine 30 mg (base)/d PO for 21 days or Atovaquone for mild to moderate PCP: 750 mg oral suspension two times a day with food for 21 days.

Adjunctive corticosteroids: Indicated in serious cases (PO₂ <70 mm Hg or an A-a gradient of >35 mm Hg measured on room air) to decrease the inflammatory process and pulmonary fibrosis. Prednisone 40 mg PO two times a day for 5 days, then 40 mg/d for 5 days, then 20 mg/d until completion of treatment.

Prophylaxis

Primary (all patients with CD4 counts below 200 cells/L):

Preferred: TMP-SMX one (DS) tablet daily

Alternative: TMP-SMX one (DS) tablet three times per week or one (SS) tablet daily
or Dapsone 100 mg once a day
or Dapsone 50 mg/d PO plus pyrimethamine 50 mg/wk PO plus folinic acid 25 mg/wk PO
or Aerosolized pentamidine 300 mg/every 4 weeks.

Secondary (required for all patients with prior PCP):

Preferred: TMP-SMX one (DS) tablet daily

Alternative: Dapsone 100 mg once a day or Aerosolized pentamidine 300 mg/every 4 weeks.

Side effects:

TMP-SMX: nausea, vomiting, rash, neutropenia, thrombocytopenia, anaemia, abnormal liver function tests, pruritus, hyperkalemia (found in 20% to 25% of

patients receiving TMP-SMX >15 mg/kg/day).

Atovaquone: rash, liver function abnormalities, vomiting, diarrhoea

Clindamycin: nausea, vomiting, diarrhoea, pseudomembranous colitis

Dapsone: haemolytic anaemia, rash, fever, nausea, headache, methemoglobinemia, and GI intolerance

Primaquine: haemolytic anaemia (in G6PD-deficient persons), methemoglobinemia, neutropenia, nausea, vomiting, headache

Systemic pentamidine: hypotension, hypo/hyperglycaemia, pancreatitis, myelotoxicity, GI intolerance, nephrotoxicity, and hypocalcemia

CRYPTOCOCCOSIS

This fungal infection caused by *Cryptococcus neoformans* can affect HIV-infected patients, especially those with advanced disease (CD4 count <200 cells/mL). Meningitis is the most serious clinical manifestation. Disseminated disease (isolation of the fungus in blood, urine, lymph nodes, pulmonary secretions, skin lesions, and liver) is seen with increased frequency.

Clinical manifestations: The clinical picture of cryptococcal meningitis is variable. Patients may have prolonged fever and discrete constitutional symptoms or histories of convulsions and coma. Often there are complaints of headache, which progresses to intense pain, nausea, vomiting, and photophobia. Sudden visual loss occasionally occurs.

Diagnosis: Patients thought to have cryptococcal meningitis, based on symptoms, low immune status, and

neurological examinations, should undergo lumbar puncture for examination of CSF. Patients with papilloedema and focal neurological deficits should first undergo cerebral CT or MRI to rule out the presence of a parenchymal mass (cryptococcoma or other space-occupying lesions such as toxoplasmosis or lymphoma).

The CSF exam should include wet preparation of the fungus using India ink stain, exam for cryptococcal antigen, and fungal culture, along with cell counts and chemistries. Cryptococcal meningitis in AIDS patients characteristically presents with a large number of fungal organisms, few cells, and relatively normal protein levels (i.e. little inflammatory response).

Disseminated disease can be diagnosed by positive blood cultures and detection of cryptococcal antigen in the blood.

Treatment:

Meningitis:

Preferred regimen: Amphotericin B 0.7 mg/kg/d IV for 10 to 14 days, then fluconazole 400 mg PO 2 times a day for 2 days, followed by 400 mg/day for 8 to 10 weeks. Amphotericin B is always diluted in 5% dextrose and infused IV over 4 to 6 hours. The liposomal form of the product, because it has less toxicity than other forms, obviates the need to gradually increase the dose; thus the full therapeutic dose can be reached more rapidly. Pre-medication with acetaminophen (650 mg), promethazine (25 mg), meperidine (0.7 mg/kg), or diphenhydramine (50 mg) can be given 30 minutes before infusing amphotericin B to reduce the occurrence of adverse effects (fever and chills).

Alternate regimens: In situations where amphotericin B is not available or contraindicated: fluconazole 400 mg/d PO for 6 to 10 weeks as initial therapy only for patients with mild disease

or
Following amphotericin B 0.7 mg/kg/d for 10 to 14 days:
itraconazole 200 mg PO three times a day for 3 days, then
200 mg PO two times a day for 8 weeks

Without meningitis

Preferred regimen: Fluconazole 200 mg PO two times a day for 6 to 10 weeks

Alternative: Itraconazole 200 mg PO two times a day or
100 mg oral suspension once daily for 6 to 10 weeks

Maintenance treatment

Meningitis (lifelong, required for all patients):

Fluconazole 200 mg/d to 400 mg/d PO

or

Amphotericin B 0.6 mg/kg to 1.0 mg/kg IV once to three times a week

Systemic cryptococcal disease without meningitis

(Need for maintenance not established):

Fluconazole 200 mg/d PO

or Itraconazole 200 mg/d PO

or Amphotericin B 0.6 mg/kg to 1.0 mg/kg IV once or twice a week

Laboratory monitoring: During treatment, complete blood count, platelet count, and serum chemistries (glucose, urea, creatinine, sodium, and potassium) should be obtained twice weekly.

Side effects

Amphotericin B:

Immediate effects: fever, chills, hypotension, convulsive crises, cardiac arrhythmias

Delayed effects: phlebitis, elevated serum urea nitrogen,

renal tubular acidosis, hypocalcemia, anaemia; also nausea, vomiting, hypomagnesemia, nephrotoxicity, and thrombophlebitis

Fluconazole: GI intolerance, hepatotoxicity, rash, Stevens-Johnson syndrome, and reversible alopecia

Itraconazole: hepatitis, GI intolerance, rash, hypokalemia, fluid retention

CYTOMEGALOVIRUS

Cytomegalovirus (CMV), a herpesvirus, is potentially pathogenic and responsible for a wide variety of clinical manifestations. Once the infection occurs, usually early in life, patients are chronically and latently infected with CMV. CMV may also reactivate in patients with long-standing and advanced HIV. Intrauterine infection results in devastating destruction of the central nervous system, while encephalitis from postnatal CMV is rare. Primary CMV infection developing late in life is usually asymptomatic, but can occasionally result in a mononucleosis-like syndrome with hepatic involvement.

Reactivation of latent CMV infection can produce serious clinical manifestations, especially in immunosuppressed patients. In AIDS patients, CMV infection can cause retinitis, colitis, oesophagitis, central nervous system disease, and pneumonia. Less common manifestations include adrenal infection and oral mucosal ulcers. Patients who have CD4 counts below 100 cells/mL and, more specifically, those with CD4 counts below 50 cells/mL are at high risk for developing symptomatic CMV disease.

CMV retinitis: Patients complain of spots (floaters) in their visual fields and/or blurred vision. Usually the complaints are unilateral and can evolve into bilateral

symptoms, including loss of vision, if not treated. The diagnosis is made by fundoscopic examination, which initially shows granular white lesions and, later, hemorrhagic lesions.

CMV colitis: Patients usually have abdominal pain, diarrhoea, and fever. Complications may include intestinal perforation and gastrointestinal haemorrhage. The diagnosis is made by endoscopy (colonoscopy or rectosigmoidoscopy) and biopsy.

CMV oesophagitis: Most patients complain of pain and difficulty in swallowing. Fifty percent of patients have epigastric pain independent of swallowing complaints, and about one third experience significant weight loss. Illness caused by CMV can affect the entire digestive tract including, in addition to the mouth, the oesophagus, colon, stomach, small intestine, and appendix. Hepatitis, cholangitis, and pancreatitis also should be considered.

Diagnosis is made by upper gastrointestinal endoscopy and biopsy of the intestinal ulcers or other affected organs, histopathological features of multinucleated giant cells confirms diagnosis.

Treatment

First choice: Gancyclovir 5 mg/kg IV every 12 hours for at least 14 to 21 days. Initial maintenance therapy should be 6 mg/kg IV once a day, five times a week. The drug should be diluted in 5% dextrose or normal saline and infused over 1 hour. Weekly complete blood counts should be obtained because of the haematotoxicity of this drug.

Alternative (in case of toxicity to gancyclovir or therapeutic failure): Foscarnet 60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours for 14 to 21 days, followed by long-term maintenance therapy

or

Cidofovir 5 mg/kg IV two times a week, then 5 mg/kg IV every 2 weeks, plus Probenecid 2 g PO 3 hours before each dose, and 1 g PO at 2 and 8 hours post-dose.

Both foscarnet and cidofovir are nephrotoxic.

Maintenance therapy (lifelong for patients with retinitis): Gancyclovir 5 mg/kg/d to 6 mg/kg/d IV infused over 1 hour five to seven times a week or 1000 mg PO three times a day or Foscarnet 90 mg/kg/d to 120 mg/kg/d IV infused over 2 hours or Cidofovir 5 mg/kg IV every other week.

Side effects

Cidofovir: nephrotoxicity, neutropenia, metabolic acidosis; Concurrent use of other nephrotoxic drugs (aminoglycosides, amphotericin B, foscarnet, non-steroidal anti-inflammatory drugs [NSAIDs]) must be avoided.

Foscarnet: nephrotoxicity, hypocalcemia, hypomagnesemia, hypokalemia, anaemia, and hypophosphatemia

Gancyclovir: Granulocytopenia is the most common and serious side effect; thrombocytopenia and anemia are less common, as is cutaneous rash. Myelotoxicity is potentiated by the concomitant use of other bone marrow toxic drugs such as ZDV. Gancyclovir should be interrupted in patients with absolute neutrophil counts below 500/mL; it may be restarted when counts rise above 750/mL. An alternative is to add granulocyte colony-stimulating factor when the white blood cell count drops below 500/mL. Initial dose should be 5mg/kg once a day and titrated upwards based on the response of the white blood cell count.

VARICELLA ZOSTER INFECTION

Varicella zoster infection begins with a short prodromal period of fever and malaise, followed by a maculopapular rash that rapidly becomes vesicular and then pustular, followed by crusting of lesions. Skin lesions demonstrate regional polymorphism with centripetal distribution and commonly evolve in clusters. Varicella zoster infection may be more severe in pregnant women, causing greater morbidity and mortality secondary to visceral dissemination, interstitial pneumonia, encephalitis, etc.

Incubation period:

13 to 17 days, with the most transmissible period 2 days before onset of rash; infectivity continues until all skin lesions have crusted over (mean, 5 days). Systemic illness is associated with viremia in the mother, which has three potential outcomes in the foetus: 1) intrauterine infection with infrequent congenital abnormalities; 2) post-natal infection with disseminated infection of the newborn; or 3) herpes zoster infection occurring months or years following the mother's viremia. Perinatally transmitted varicella zoster infections occur most often 4 days prior to and 2 days after delivery and may cause severe disseminated disease in the newborn.

Clinical manifestations:

Herpes zoster manifestations are uncommon in pregnancy and are not associated with congenital disease. In immunocompromised patients, cutaneous disease may be found on multiple dermatomes or be disseminated; disseminated visceral disease is more common in this setting.

Diagnosis:

Usually based on clinical appearance.

Treatment :

Ideally, treatment should begin within 72 hours of the appearance of rash. Disseminated varicella zoster: acyclovir 10 mg/kg IV every 8 hours, infused over 1 hour (diluted in 100 mL of 5% glucose) for 10 days or until 48 hours post defervescence or crusting of lesions.

Dermatomal herpes zoster: acyclovir 800 mg PO five times daily for 7 days, or as above. Treatment (IV therapy, topical antivirals) should be more aggressive in cases of ocular herpes zoster.

Prophylaxis:

Newborns should receive varicella zoster immune globulin (VZIG) if their mothers have contracted chickenpox within 5 days of or 48 hours following delivery. Dose: 125 U IM (one vial)

HIV-infected pregnant women with no prior history of chickenpox and recent exposure to varicella zoster virus should receive VZIG 125 U IM per 10 kilograms of body weight (maximum dose, 625 U [five vials]), as soon as possible, preferably within 48 hours of exposure, and not beyond 96 hours of exposure.

BACTERIAL INFECTIONS OF THE RESPIRATORY TRACT

HIV-infected pregnant women, as with other patients infected by HIV, have a higher frequency of bacterial respiratory infections. However, the clinical presentation, diagnostic workup, and response to treatment for HIV-positive patients are generally the same as for HIV-uninfected patients.

Community-acquired pneumonia

The most common etiologic agent is *Streptococcus pneumoniae*. The clinical presentation usually includes sudden onset of fever, chills, pleuritic chest pain, and a productive cough with purulent sputum or haemoptysis. Patients may complain of dyspnea and have tachypnoea at initial presentation. Chest X ray may initially be normal but commonly shows evidence of consolidation or a bronchopulmonary infiltrate. Gram stain of the sputum reveals a large number of polymorphonuclear leukocytes and gram-positive intracellular diplococci. Thirty percent of patients will have bacteraemia, and a percentage may develop pleural effusion and empyema.

Treatment should be guided by the severity of a patient's disease. In ambulatory cases, in areas where penicillin resistance is low, ampicillin (500 mg PO every 6 hours), amoxicillin (500 mg PO every 8 hours), or procaine penicillin (600,000 U IM every 12 hours) may be used. In more severe cases, crystalline penicillin (2 million U IV every 4 hours) ceftriaxone 1g IV/IM every 24 hours, or erythromycin 500 mg IV every 6 hours is indicated. Duration of treatment is commonly 7 to 14 days, with length of therapy adjusted according to the patient's clinical improvement. For patients with penicillin-resistant pneumonia, a good approach is to treat for at least 72 hours following the resolution of fever with an appropriate agent, for example, ceftriaxone 1 to 2 g IV/IM every 24 hours or vancomycin 1 g IV every 12 hours.

Haemophilus influenzae pneumonia may also occur in HIV-infected pregnant women. Its presentation may be similar to that of pneumococci but with a slower onset of symptoms. Gram stain of sputum shows a predominance of pleomorphic gram-negative bacilli. Treatment options include amoxicillin-clavulanate (500/125 mg PO every 8 hours) or cefuroxime axetil (500 mg PO every 8 hours). For

more severely ill patients, ceftriaxone (1 to 2 g IV every 24 hours) is used for 10 to 14 days.

Staphylococcus aureus may cause pneumonia or bronchopneumonia; it may or may not be associated with bacteraemia and skin lesions, which may be the portal of entry to the bloodstream. Gram stain of the sputum may show clusters of gram-positive cocci. X-ray may reveal a bronchopneumonic infiltrate with or without pneumatoceles. Blood cultures are frequently positive. Treatment is best started in the hospital, using oxacillin or nafcillin (100 mg/kg/d to 150 mg/kg/d IV in four or six divided doses). Duration of therapy should be 4 to 6 weeks. For patients allergic to penicillin (non-life threatening), use of a first-generation cephalosporin or vancomycin may be considered (vancomycin pregnancy category B).

Other etiologic agents include gram-negative bacilli, particularly *Pseudomonas aeruginosa*. Gram-negative organisms may cause primary pneumonias in HIV-infected pregnant women, especially those with advanced immunosuppression; more often, they cause nosocomial infections, typically in neutropenic patients. Definitive diagnosis is made using blood cultures, but empiric treatment, based on clinical suspicion, should be initiated prior to availability of blood culture. Therapy should include a third generation cephalosporin or semisynthetic penicillin agent active against *Pseudomonas* spp in combination with an aminoglycoside.

Duration of therapy is 2 to 3 weeks. Patients should give prior informed consent to the use of an aminoglycoside in pregnancy, as these medications are classified as category C and associated with congenital abnormalities.

NOTE: Proper use of aminoglycosides may be lifesaving for pregnant women with severe infection and therefore medically necessary.

OTITIS AND SINUSITIS

Common aetiologic agents of acute otitis media and sinusitis include *S. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*, and *Streptococcus spp.* Patients with more advanced immunosuppression may harbour other uncommon pathogenic organisms (Gram-negative bacteria, fungi). The clinical presentation is similar in HIV-infected and uninfected patients; however, recurrences and relapses are more common in HIV-infected patients.

Diagnosis:

In patients with otitis media who do not respond to conventional therapy, tympanocentesis may be useful to establish an etiologic diagnosis. An aggressive diagnostic evaluation, including sinus lavage, drainage, and/or biopsy (for culture and histopathological studies), must be considered for patients who do not improve with empiric treatment for sinusitis. Additional organisms isolated from patients with chronic otitis and sinusitis include *S. aureus*, *P. aeruginosa*, and anaerobic bacteria.

Treatment: Ampicillin or amoxicillin in usual dosages may be used; however, patients not responding to treatment within 48 to 72 hours will require a change in therapy; in such cases, amoxicillin-clavulanate or TMP-SMX is commonly prescribed. Many clinicians would "spare" treatment with sulfa and reserve it for treatment of PCP because of the risk of sensitization that occurs with repeated use of this agent.

Duration of therapy for otitis media: 10 to 14 days, possibly longer in recurrent cases.

Duration of therapy for sinusitis: a minimum of 21 days.

In the appropriate clinical setting, where there is no improvement with the previously described treatment, a cephalosporin active against *Pseudomonas spp.* in combination with an aminoglycoside and clindamycin may

be initiated. Metronidazole is contraindicated during the first trimester of pregnancy.

Decongestants, indicated in the treatment of sinusitis, should be used with caution during pregnancy. Increasing fluid intake will help loosen secretions.

URINARY TRACT INFECTION

Asymptomatic bacteriuria occurs in 4% to 7% of pregnant women, and of these, 20% to 40% will develop symptomatic urinary tract infection. HIV infection does not increase the incidence of asymptomatic bacteriuria during pregnancy. Even asymptomatic bacteriuria should be treated in pregnant women, because of the risk of pyelonephritis and subsequent stillbirth and prematurity of the infant.

Symptomatic urinary tract infection usually occurs in pregnant women with persistent bacteriuria. The clinical presentation of fever, dysuria, polyuria, and back pain is similar to that of nonpregnant women.

Complications of pregnancy related to urinary tract infection

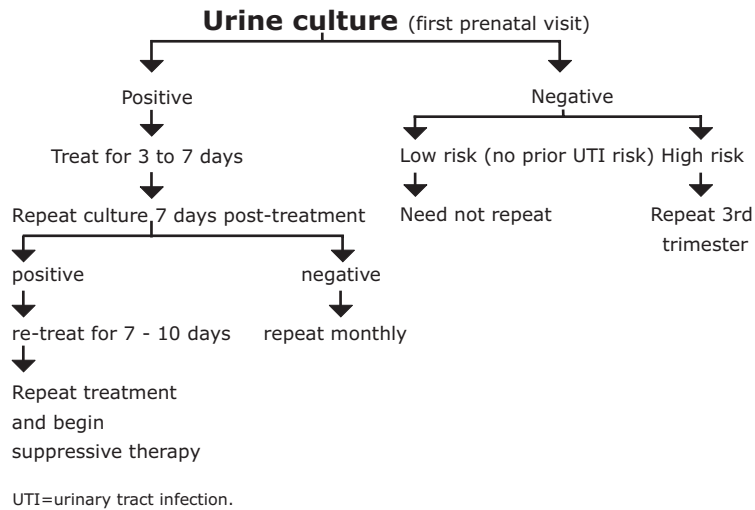
- Premature delivery
- Low birth weight
- Intrauterine growth retardation

Aetiology:

The coliforms are the most common: *Escherichia coli*, the *Klebsiella-Enterobacter* group, and *Proteus spp.* Gram-positive organisms include *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, and enterococci.

Diagnosis:

Urine culture is preferred for the diagnosis of bacteriuria. It should be performed at the first prenatal visit.



Therapeutic regimens for symptomatic and asymptomatic bacteriuria:

- Amoxicillin 250 mg to 500 mg three times a day for 7 days
- Nitrofurantoin 100 mg four times a day for 7 days
- Cephalexin 500 mg four times a day for 7 days
- Amoxicillin-clavulanic acid 250 mg/125 mg three times a day for 7 days

Acute Dysuria

Urine cultures should be obtained in acutely dysuric women. In women with sterile cultures, acute dysuria, and pyuria; chlamydia urethritis should be suspected. Sexually active women should have pelvic exams, cultures, and appropriate treatment.

Treatment: Azithromycin 1g as a single dose or Erythromycin 500 mg orally four times a day for 7 days.

TREATMENT OF INTESTINAL PARASITES IN HIV-INFECTED PREGNANT WOMEN

Parasite	Drug of Choice (Any Period of Pregnancy)	Drug of Choice (After 1st trimester)	Drugs With Potential Risk During Pregnancy (Their Use May Be Considered)
E histolytica	Paromomycin 500 mg PO tid for 5 - 7 d	Metronidazole 750 mg tid for 5 d	Metronidazole 750 mg tid for 5 d
D fragilis	Paromomycin 500 mg PO tid for 5 - 7 d		Metronidazole 750 mg tid for 5 d
G lambia	Paromomycin 500 mg PO tid for 5 - 7 d	Metronidazole 250 mg tid PO for 7-10d	Metronidazole 250 mg tid PO for 7-10d
E coli			Metronidazole 750 mg tid for 5 d
Cryptosporidium spp	Spiramycin 1-3 g/d for 14 d Paromomycin 500-750 mg PO tid for 10 d to several mo		
I belli			TMP-SMX 160 mg/800 mg PO qid for 10 d
E bieneusi			Albendazole 200-400 mg bid for 1 mo
A lumbricoides	Piperazine 100 mg/kg PO as first dose, then 65 mg/kg PO bid (max. 4 g/d) for 4 d		
T trichiura			Mebendazole 100 mg PO bid for 3 d
A duodenale			Mebendazole 100 mg PO bid for 3 d
N americanus			Mebendazole 100 mg PO bid for 3 d
S stercoralis			Thiabendazole 25 mg/kg (max. 15 g) PO bid for 2d
E vermicularis	Piperazine 65 mg/kg (max. 2.5 g)		
T solium	Niclosamide 2 g po		Praziquantel 10-20 mg/kg (max. 600 mg) PO (single dose)
T saginala	Niclosamide 2 g po		Praziquantel 10-20 mg/kg (max. 600 mg) PO (single dose)
H nana	Niclosamide 2 g po		PO Praziquantel 25 mg/kg (max. 600 mg) PO (single dose)
S mansoni			Treatment contraindicated



15. Prevention Of Opportunistic Infections In HIV-infected Pregnant Women

PNEUMOCYSTIS CARINII PNEUMONIA (PCP)

Primary prophylaxis: Pregnant women should receive chemoprophylaxis against PCP if their CD4 counts are below 200 cells/mL or percentage of CD4 cells is less than 15%, or if they have unexplained fever ($>37.7^{\circ}\text{C}$) for more than 2 weeks, histories of oral candidiasis, an opportunistic infection, or other manifestations of immunodeficiency.

First choice:

TMP-SMX one DS tablet (160 mg/800 mg) daily or three times weekly, or one SS tablet (80 mg/400 mg) daily (TMP-SMX one DS tablet daily is preferred because it also has efficacy against bacterial infection and toxoplasmosis). Patients intolerant of or allergic to TMP-SMX should be switched to dapsone.

Second choice:

Dapsone 100 mg/d PO
or

Aerosolized pentamidine 300 mg every 4 weeks, diluted in 6 ml physiologic solution or filtered water and nebulized with humidified oxygen 6 L/min

Secondary prophylaxis: same as primary prophylaxis

TOXOPLASMA GONDII ENCEPHALITIS

Primary prophylaxis: Pregnant women with reactive serology for Toxoplasma antibodies (negative IgM, positive IgG) and CD4 counts below 100 cells/mL should receive TMP-SMX

Secondary prophylaxis: Pyrimethamine 25 mg to 75 mg PO once a day plus Sulfadiazine 0.5 g to 1.0 g PO every 6 hours plus Folinic acid 10 mg PO once a day

TUBERCULOSIS

Indication: Chemoprophylaxis is recommended for HIV-infected pregnant women with PPD >5 mm or histories of exposure to *M. tuberculosis* without clinical evidence of active tuberculosis. Active tuberculosis can be evaluated through a patient's clinical history and physical signs. Chest radiography should be avoided when possible during pregnancy but may be performed (with shielding of the abdomen) after the first trimester.

Preferred regimen: Isoniazid (INH) 300 mg/d PO plus pyridoxine (vitamin B6) 50 mg/d PO for 1 year beginning after the first trimester of pregnancy

DISSEMINATED INFECTION WITH MYCOBACTERIUM AVIUM COMPLEX (MAC)

Indication: HIV-infected pregnant women with CD4 counts below 50 cells/mL

Regimens: Azithromycin 1200 mg/wk PO or Clarithromycin 500 mg PO two times a day

HEPATITIS B

Indication: All pregnant women with negative anti-HBc or HBsAg should receive hepatitis B vaccine.



Regimen: three doses (0, 1, and 6 months) of the vaccine

NOTE: Infants born to HBsAg-positive mothers should receive 0.5 mL of hepatitis B immunoglobulin (HBIG) and the first dose of hepatitis B vaccine (0.5 mL/dose IM) at separate sites within 12 hours of birth. The second dose should be administered at 1 to 2 months of age and the third at 6 months.

16. Sexually Transmitted Diseases

SYPHILIS

Patients with syphilis may have no signs or symptoms of the illness, making serologic testing necessary for all pregnant women. Signs and symptoms that suggest syphilis include an oral or urogenital lesion, localized or generalized exanthem on the palms and soles, mucosal plaques, lymphadenopathy, etc.

Primary syphilis :

Presence of a chancre, a painless, ulcerated lesion with regional adenopathy in the genital or oral region. Incubation period ranges from 9 to 90 days.

Secondary syphilis:

Presence of maculopapular rash on palms and soles, generalized lymphadenopathy, headache, mucosal plaques, flat condyloma. Usually occurs 2 to 8 weeks after appearance of chancre.

Latent syphilis :

Defined as the period after infection with *T pallidum*, in which patients are seroreactive but without any other evidence of infection; early latent syphilis: lasts for less than 1 year; late latent syphilis: lasts for more than 1 year

Neurosyphilis :

Meningeal manifestations, tabes dorsalis, cranial nerve disturbances, ophthalmologic and auditory disturbances, psychiatric disturbances, etc

Tertiary syphilis :

Aortitis, gummas, bone and/or visceral involvement, neurosyphilis

Laboratory Diagnosis :

All HIV-infected pregnant women should be tested for syphilis with the nontreponemal antibody titre rapid plasma reagin (RPR) test initially in the prenatal period, then in the third trimester, at the time of delivery, and when the patient is exposed to the disease or shows symptoms and signs of any sexually transmitted disease.

Treatment :

Successful treatment of syphilis in HIV-infected pregnant women should ideally be finished at least 4 weeks before delivery. All infants born to women with a diagnosis of syphilis should be evaluated for congenital syphilis, even if the mothers were treated in the last trimester, because treatment failures are more common in this setting.

For pregnant women primary, secondary, or latent syphilis should be treated with three doses of 2.4 million U of benzathine penicillin G IM given 1 week apart. Although oral therapy with erythromycin can be adequate for pregnant women, it is not effective for fetuses and therefore should not be used.

Tetracycline adversely affects foetal bone and dentition and thus is contraindicated in pregnancy.

Pregnant women with abnormal CSF (pleocytosis, elevated protein, or positive VDRL) should be treated with aqueous penicillin G 3 to 4 million U IV every 4 hours for 10 to 14 days. Patients who refuse IV treatment can be treated with 2.4 million U of procaine penicillin IM concurrently with probenecid 500 mg four times a day for 10 to 14 days. Ceftriaxone is a less efficacious alternative to penicillin but has been used in doses of 250 mg IM for 5 days for primary or secondary syphilis and in doses of 1 g

IM/IV for 14 days for neurosyphilis. Some authors suggest using ceftriaxone IM or IV for 10 days when penicillin desensitization is not possible.

Treatment Follow-up :

Pregnant women should have post-treatment RPR testing at 1, 3, 6, 9, and 12 months and then annually. The titre should fall fourfold in 3 months in cases of primary and secondary syphilis and after 6 months in cases of latent syphilis of less than 1 year's duration. In patients with late latent disease, the titre should drop fourfold in 12 months.

GNOCOCCAL INFECTION

The aetiologic agent *Neisseria gonorrhoeae* is a gram-negative diplococcus. It is characteristically identified intracellularly within neutrophils on microscopic exam.

Incubation period: 3 to 7 days (asymptomatic or symptomatic). Major sites of infection in women are the endocervix, urethra, anal canal, and pharynx. Symptoms of acute pelvic infection are most commonly caused by extension of the infection from the endocervix to the endometrium and fallopian tubes, resulting in endometritis and salpingitis; extension of infection into the peritoneum may be followed by gonococcal perihepatitis (Fitz-Hugh-Curtis syndrome). Infection of the urethra may extend to the bladder, producing dysuria, urinary urgency, and frequency.

Management of gonorrhoea includes positive identification of gonococcus and treatment of all sexual partners, whether or not they are symptomatic

The incidence of gonococcal ophthalmic neonatorum can be reduced by 90% with the prophylactic

use of 1% silver nitrate eye drops, 0.5% erythromycin ophthalmic ointment, or 1% tetracycline ophthalmic ointment.

Laboratory Diagnosis :

Gram's stain of a smear from the endocervix will show polymorphonuclear (PMN) cells with intracellular gram-negative diplococci.

All sites (genitourinary tract, cervix, rectum, pharynx) should be cultured with selective media (Thayer-Martin). It is possible to identify gonococcal infection by PCR or Ligase Chain Reaction (LCR) from urine and genital secretions.

Treatment :

Preferred:

Ceftriaxone 125 mg IM one time Cefixime 400 mg PO one time

Alternative:

Spectinomycin 2 g IM one time

CHLAMYDIAL INFECTION

The principal sites of chlamydial infection in women are the cervix and endocervix. Chlamydial infection often coexists with other sexually transmitted diseases. Asymptomatic or latent infection appears to be common and may be chronic. Symptomatic and even asymptomatic genital infection by Chlamydia spp is associated with a higher risk of premature rupture of foetal membranes, pre-term labour, and intrauterine growth retardation. 40% to 55% of infants born to untreated mothers develop pneumonia.

Screening and treatment for chlamydial infection should be performed in women in the following situations:

Purulent or mucopurulent cervicitis
Past history of any sexually transmitted disease
Partner with gonococcal urethritis

Diagnosis :

Laboratory methods available to confirm the diagnosis include cytology, serology, antigen detection, cultures, PCR, and LCR.

Treatment:

Important considerations concerning chlamydial

treatment: Because of the life cycle of C trachomatis, long-term treatment is required. Sexual partners must be treated concurrently. If patients have sexual intercourse, condoms must be used.

1. The safest agents available for the treatment of mucopurulent cervicitis and urethritis during pregnancy are oral erythromycin and oral amoxicillin (see below for doses).
2. Tetracyclines should not be given during pregnancy. The new macrolide antibiotics clarithromycin and azithromycin have excellent activity, but experience with these agents in pregnant women is limited.
3. Treatment of gonococcal infection with penicillin, cephalosporin, or spectinomycin will not eradicate chlamydiae.

Preferred regimens:

Erythromycin base 500 mg PO four times a day for 7 days or Amoxicillin 500 mg PO three times a day for 7 days

Alternative regimens:

Erythromycin base 250 mg PO four times a day for 14 days, or

Erythromycin ethylsuccinate 800 mg PO four times

a day for 7 days or
Erythromycin ethylsuccinate 400 mg PO four times
a day for 14 days or
Azithromycin 1 g PO (single dose)

NOTE: Erythromycin estolate is contraindicated during pregnancy.

TRICHOMONIASIS

The etiologic agent is *Trichomonas vaginalis*

Clinical characteristics: Yellow vaginal discharge (low viscosity, foul odor), vulvar and perineal itching and discomfort, dyspareunia, dysuria, urinary hesitancy and frequency, vulvar and vaginal erythema, lower abdominal pain. Vaginal mucosae are typically erythematous and granular, "strawberry cervix."

Diagnosis: Organisms identified by examination of the wet preparation with saline show flagellated organisms
Papanicolaou smear
Giemsa stain
Vaginal pH 6 - 7

Treatment:
Metronidazole: 2 g PO (single dose) or 500 mg PO two times a day for 7 days. Metronidazole gel (intravaginal therapy) given for 10 to 14 days is another, albeit less effective, option.

NOTE: Systemic treatment with metronidazole should be avoided in the first trimester of pregnancy. Topical therapy, while less effective, is the treatment of choice for pregnant women. Sexual partners should be treated at the same time as the patient. Partners should avoid sexual intercourse while receiving treatment.

BACTERIAL VAGINOSIS (NONSPECIFIC VAGINITIS)(BV)

In bacterial vaginosis (BV), there is an increasing amount of foul-smelling secretions associated with replacement of the normal H₂O₂ producing *Lactobacillus sp* in the vagina with high concentrations of anaerobic bacteria (*Prevotella spp* and *Mobiluncus sp*), *Gardnerella vaginalis*, and *Mycoplasma hominis*. BV is a common cause of vaginal infection, and 50% of women may be infected without symptoms. Usually there is no pruritus or irritation; when present, these suggest other causes.

Diagnosis :

(Requires three out of the following four clinical criteria):

1. Homogeneous, thin vaginal discharge
2. Positive whiff test (a fishy odour is detected following addition of 10% KOH)
3. Presence of "clue cells" (large epithelial cells with granular cytoplasm covered by small gram-negative bacilli) on microscopic exam
4. Vaginal pH > 4.5

Treatment

Preferred:

Metronidazole 250 mg PO three times a day for 7 days

Alternatives:

Metronidazole 2 g PO one time or Clindamycin 300 mg PO orally two times a day for 7 days or Metronidazole gel 0.75%, one full applicator intravaginally two times a day for 5 days

NOTE: Metronidazole should be avoided during the first trimester of pregnancy. Lower doses are recommended to minimize exposure of the drug to the foetus. Clindamycin vaginal cream is not recommended during pregnancy.

GENITAL HERPES INFECTION

Caused by herpes simplex virus type 2, genital herpes is a sexually transmitted disease that affects adolescents and adults. Primary infection may occur without symptoms. In women, a primary lesion most frequently develops in the cervical or vulvar region. Recurrent lesions usually occur in the vulva, perineum, and buttocks. Primary infection manifests with vesicles that evolve into shallow, painful, ulcerative lesions. Patients may complain of fever, headache, myalgia, general malaise, and tender inguinal lymphadenopathy.

During secondary recurrence, systemic symptoms are usually mild or absent, and lesions are less pronounced. There may be a prodrome of itching or burning in areas where lesions will later develop. Vaginal delivery by women with active genital herpes is associated with a high risk of infection in the newborn with severe central nervous system and disseminated disease. In such high-risk situations, Caesarean section is mandatory.

Incubation period: 2 to 12 days. Primary genital lesions are infectious for 7 to 12 days following onset. In recurrences, the period of infectivity is shorter (4 to 7 days).

Diagnosis :

Multinucleated giant cells with cytoplasmic inclusions in scrapings or biopsied material taken from the lesions.

Treatment

Primary infection:

Acyclovir 200 mg PO five times a day or 400 mg PO three times a day for 7 to 10 days

Severe or disseminated disease: Acyclovir 5 mg/kg to 10 mg/kg IV every 8 hours, diluted in 100 mL of

glucose 5% solution and infused over 1 hour, for 5 to 7 days

Recurrent infection:

For immunocompromised patients, acyclovir may be used at dosages of 200 mg PO five times a day, 400 mg PO three times a day, or 800 mg PO two times a day for 5 days. More severely immunocompromised patients may require higher doses and/or longer duration of therapy.

For HIV-infected pregnant women, acyclovir treatment should be limited to those with severe or disseminated disease and those with primary infection; clinicians may consider treatment for patients with very frequent recurrences.

CHANCROID

Also known as "soft chancre" (in contrast to the "hard chancre" of syphilis), chancroid occurs more often in men than in women and is more prevalent in tropical and subtropical regions than in other areas. Caused by *Haemophilus ducreyi*, it is transmitted by sexual contact with infectious secretions from the ulcerative lesion or via contact with pus from an inguinal lymph node.

Incubation period: 3 to 14 days (mean of 5 days). Initial lesion usually occurs in the genitalia and presents as a small papule with erythema. Lesions may be single or multiple and progress rapidly to pustules, which are well delineated, painful, and ragged. The ulcer base is generally covered by gray, necrotic secretions and bleeds easily when manipulated. A genital ulcer that is painful but without induration helps differentiate chancroid from primary syphilis. Occasionally, lesions may enlarge and progress to necrotic ulcers.

Autoinoculation may cause additional lesions in areas contiguous to the genitalia. Unilateral painful

inguinal lymphadenitis occurs in 50% of patients with chancroid. These nodes should not be drained because of the risk of infection disseminating along the borders of the surgical incision. Lymph nodes should be aspirated. 12% to 15% of chancroid lesions may also harbour *Treponema pallidum*.

Diagnosis:

Diagnosis is confirmed by culture of ulcerative lesion secretions or by lymph node aspiration.

Treatment: Erythromycin base 500 mg PO four times a day until lesions heal (minimum of 7 days) or Ceftriaxone 250 mg IM (single dose) or Azithromycin 1 g PO (single dose)

NOTE: Ciprofloxacin is contraindicated in pregnant and lactating women.

PELVIC INFLAMMATORY DISEASE

Pelvic inflammatory disease (PID) is generally considered a polymicrobial infection. The main etiologic agents are *N. gonorrhoeae*, *C. trachomatis*, *M. hominis*, *U. urealyticum*, anaerobes (*Peptostreptococcus spp*, *Bacteroides spp*, *Actinomyces israelii*), and aerobes (*Streptococcus faecalis*, *E. coli*, *Klebsiella spp*, *Proteus spp*). PID is rarely caused by *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, or *Campylobacter spp*. It usually results from the ascent of pathogenic organisms from the lower genital tract; it occurs only rarely during pregnancy (after 10 weeks gestation) because the developing foetus, placenta, and foetal membranes are able to protect against ascending infection.

Clinical manifestation/diagnosis

Minimum criteria:

Lower-abdominal tenderness, adnexal tenderness,

cervical motion tenderness, and absence of alternative conditions, such as appendicitis or ectopic pregnancy

Additional criteria: Fever above 38.3°C (>101°F), abnormal cervical/vaginal discharge, elevated erythrocyte sedimentation rate, elevated C-reactive protein, positive test for gonorrhoea or chlamydia, tubo-ovarian abscess diagnosed by ultrasound

Diagnosis:

Pregnant women should meet the minimum criteria plus one or more additional criteria. Laparoscopy should be avoided in pregnant women except during early gestation in cases with severe clinical manifestations and an unclear diagnosis following therapeutic failure.

Differential diagnosis:

Ectopic pregnancy, acute appendicitis, ovarian cyst (ruptured or hemorrhagic), endometriosis, and torsion of adnexal structures

Treatment:

Immunosuppressed HIV-infected women with PID should be treated aggressively with parenteral antibiotics.

Criteria for hospital admission:

HIV infection, unclear diagnosis, pregnancy, infection that does not respond to outpatient treatment in 48 hours, tubo-ovarian abscess, severe disease, nausea and vomiting, high fever, signs of peritonitis observed during examination (surgical emergency), probability of non-adherence to oral therapy, and inability to follow or tolerate outpatient regimen. As a rule, all pregnant women with PID should be hospitalized for treatment with parenteral antibiotics.

Outpatient treatment:

Ceftriaxone 250 mg IM (single dose) plus erythromycin base 500 mg PO four times a day for 14 days (clindamycin 450 mg PO four times a day for 14 days)

Inpatient treatment with parenteral antibiotics:

Cefoxitin 2 g IV every 6 hours or ceftriaxone 2 g IV/IM once a day plus erythromycin 500 mg IV every six hours or azithromycin 500 mg IV once a day until at least 48 hours after observation of clinical improvement. Patients becoming afebrile are switched to clindamycin 450 mg orally four times a day to complete a total of 14 days of therapy. Clindamycin 900 mg IV every 8 hours plus gentamicin, loading dose of 2 mg/kg IV/IM followed by 1.5 mg/kg IV every 8 hours (adjust dose according to renal function and gentamicin levels) Patients becoming afebrile for 48 hours are switched to oral antibiotics, clindamycin 450 mg orally four times a day to complete a total of 14 days of therapy

Indications for surgery:

Suspected rupture of tubo-ovarian abscess, progression of abscess despite treatment as demonstrated by ultrasonography, failure of clinical treatment, peritonitis, septicaemia, abscess larger than 8 to 10 cm as determined by ultrasonography

PAPILLOMAVIRUSES

Among the more than 60 types of human papillomavirus (HPV), HPV types 6 and 11 are more frequently associated with benign genital warts (condyloma acuminata), and HPV types 16, 18, 31, 33, and 35 have been implicated as causes of cervical cancer. Women infected by HIV may have bigger and more numerous HPV lesions; immunosuppression facilitates the development of lower-genital tract neoplasia. Recurrence

of dysplasia after treatment can occur in more than 50% of HIV-infected women compared with usually less than 10% of non-infected women. As a rule, the lower the CD4 cell count, the more frequent the HPV recurrences.

Occasionally, HPV lesions may develop ulceration, secondary infection, or bleeding. Condyloma acuminata can grow during pregnancy. Biopsy of atypical-appearing lesions is therefore mandatory.

Diagnosis:

Observation of lesion and confirmation of HPV by Papanicolaou smear (cytopathologic study), colposcopy, biopsy, DNA hybridization, and PCR

Treatment:

There is no treatment currently available to eradicate HPV. Clinical studies have reported efficacy with numerous therapies for HPV, but many patients continue to have recurrence of lesions following treatment. Moreover, spontaneous resolution of symptoms may occur in up to 20% to 30% of patients. For treatment of condyloma acuminata, trichloroacetic acid 80% to 90% can be applied carefully to warts; other options include electrocoagulation, cryotherapy, and surgical excision. Podophyllin, Imiquimod, and Podofilox are contraindicated in pregnancy.

There is no contraindication to vaginal delivery by pregnant women with active HPV lesions. Caesarean section should be performed only in patients with large lesions that obstruct vaginal delivery.

SEXUALLY TRANSMITTED AGENTS AND VERTICAL INFECTION

AGENT	SEQUELAE	
	PREGNANT WOMAN	NEWBORN
β- hemolytic Streptococcus Bacterial vaginosis <i>Chlamydia trachomatis</i> Hepatitis B (chronic carrier, acute and chronic) Herpes simplex HIV HPV <i>Mycoplasma hominis</i> <i>Neisseria gonorrhoeae</i> <i>Treponema pallidum</i> <i>Trichomonas vaginalis</i> <i>Ureaplasma urealyticum</i>	Endometritis Chorioamnionitis, endometritis (postpartum) Cervicitis, PID early in pregnancy (<10 wk), ectopic pregnancy, fertility Chronic carrier Local exacerbation Changes in clinical course Condyloma exacerbation Endometritis Bacteremia, Fitz-Hugh-Curtis syndrome, cervicitis, PID early in pregnancy (<10 wk) Syphilis Vaginitis Chorioamnionitis	Meningitis, septicemia Premature rupture of membranes, prematurity Conjunctivitis, pneumonia Acute and chronic hepatitis Local and disseminated infection HIV infection Laryngeal polyposis Septicemia Conjunctivitis, septicemia, disseminated infection Congenital syphilis Pneumonia Chronic premature lung disease,

HPV=human papillomavirus; PID=pelvic inflammatory disease. Adapted from Lee RV. Sexually transmitted infections. In: Burrow G, Ferris T, eds. Medical Complications During Pregnancy. 4th ed. Philadelphia, Pa.; WB Saunders Company; 1995:406.

ETIOLOGY, MANIFESTATIONS, AND DIAGNOSIS OF GENITAL LESIONS IN PREGNANCY

LESION	DISEASE	AGENT	LESION CHARACTERISTICS	LYMPH NODE	DIAGNOSIS
Painful ulcer	Herpes Chancroid	Herpes simplex <i>H. ducreyi</i>	Vesiculopustular Friable ulcers (not indurated)	Yes (painful) Yes (painful)	Culture, Tzanck tests, immunofluorescence Gram stain, culture PCR, culture
Painless ulcer	Lympho- granuloma Syphilis	<i>C. Trachomatis</i> <i>T. pallidum</i>	Shallow ulcer (short duration) Ulcer with induration	Yes (painful) Yes (painless)	Dark field exam, serologies Stain of crushed tissue
Painless, progressive ulcers	Granuloma inguinale	<i>Calymmato- bacterium granulomatis</i>	Small, ulcerated nodules	Rare	

SYNDROMIC MANAGEMENT OF STDs

Sexually transmitted infections require special attention because they share the same risk factors as those associated with sexual transmission of HIV. Presence of STIs increases the risk of acquiring and transmitting HIV by manifolds. In patients with advanced immunodeficiency the clinical presentation may be different and multiple STDs may be present simultaneously. In most resource poor settings adequate laboratory diagnosis facilities are not available and clinical diagnosis may be difficult in majority of the cases. Because STD control is an important aspect of HIV prevention programmes the health authorities have been promoting 'syndromic approach' for management of STDs.

Most STD patients consult a doctor or health care provider with complaints related to one of the following syndromes:

1. Urethral discharge
2. Vaginal discharge
3. Genital ulcer
4. Inguinal swelling
5. Lower abdominal pain

SYNDROME BASED TREATMENT GUIDELINES

1. Urethral discharge

Male patients complaining of urethral discharge and/or dysuria should be examined for evidence of discharge. If none is seen, the urethra should be gently massaged from the ventral part of the penis towards the meatus.

Urethral discharge is usually due to gonococcal or non-gonococcal urethritis. Unless gonorrhoea can be definitely excluded by laboratory tests (negative Gram-

stain) the treatment should be for both the causes.

Recommended treatment

Norfloxacin 800 mgm in a single dose orally and Doxycycline 100 mgm orally twice daily for 10 days

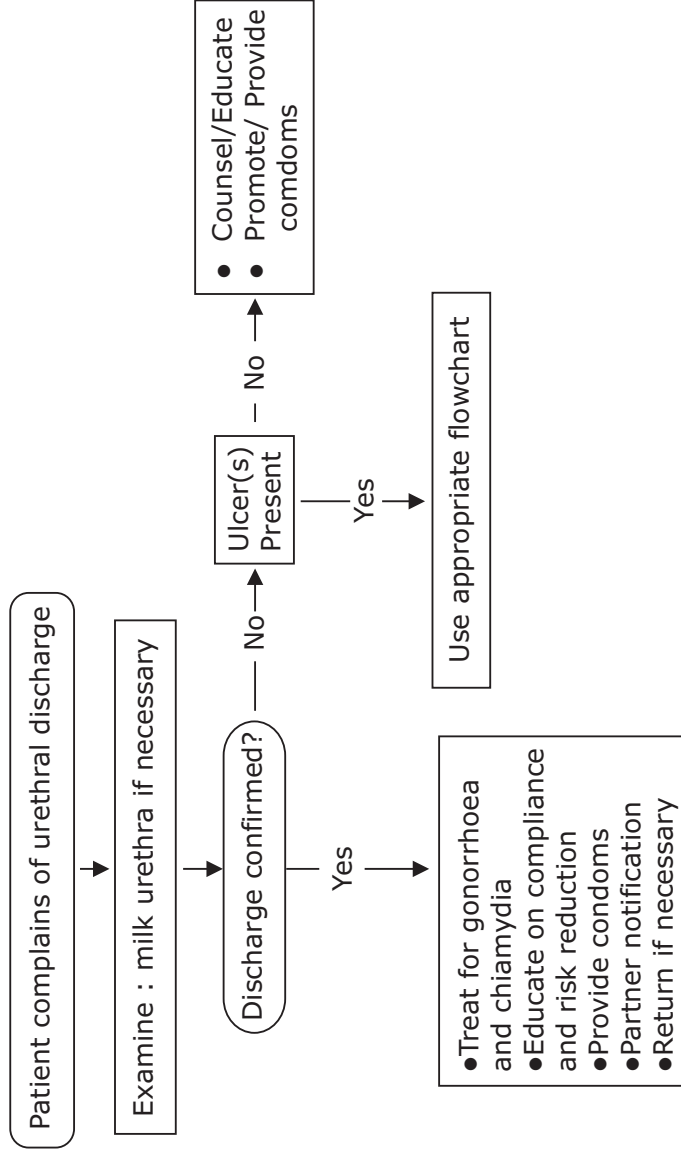
In case of treatment failure re-treat with Spectinomycin 2 gm I.M. stat.

Persistent and recurrent symptoms

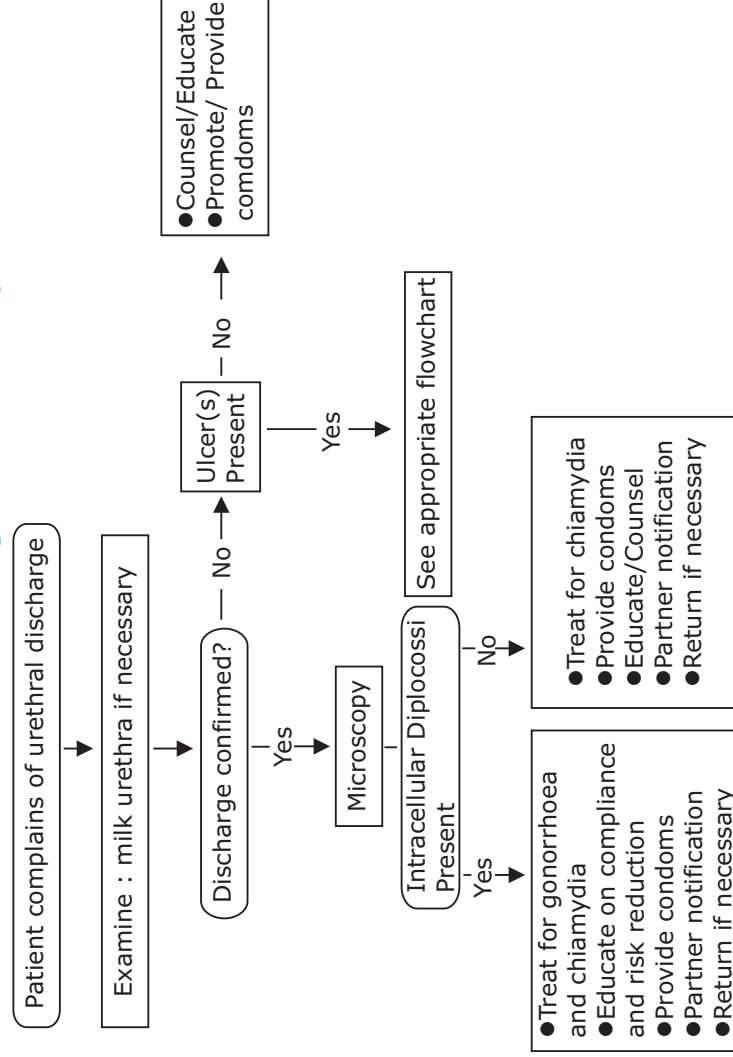
Recurrent and persistent symptoms may be due to poor compliance, reinfection or infection with the resistant strain of *N. gonorrhoeae*, or infection with *T. vaginalis*. Where symptoms persist or recur after adequate treatment of both patient and partner(s), they should be referred to laboratory investigation.

Investigation should include a Gram-stain to conform the presence of urethritis and to look for *N. gonorrhoeae*. Urethritis is defined as the presence of >5 polymorphonuclear leukocytes/1000x field in areas of maximum cellular concentration. *T. vaginalis* may be identified by microscopy of first voided urine sample, although the sensitivity of this test is fairly low as compared to culture. If presence of *T. vaginalis* is conformed, metronidazole 2 gm should be given as a single oral dose.

Flow chart for urethral discharge



Flow Chart for Urethral discharge with microscope



2 Vaginal discharge

Vaginal discharge can be due to either a cervical discharge, such as caused by Gonococcal or non-gonococcal cervicitis or can be due to vaginitis. The latter can be due to trichomoniasis, candidiasis or Bacterial Vaginosis. Cervicitis and vaginitis can occur together and a speculum examination is essential to distinguish between these two. Where no speculum examination is possible, the patient should at least be asked if her partner is symptomatic. If so then treatment should be given for both cervicitis and vaginitis. If he is not symptomatic, then treatment for only vaginitis should be given.

2a. Cervical discharge on speculum examination

Recommended treatment (non-pregnant women):

Norfloxacin 800 mgm in a single dose orally and Doxycycline 100 mgm orally twice daily for 10 days

In case of pregnancy:

Norfloxacin 800 mgm in a single dose orally and Erythromycin stearate 500 mgm orally four times day for 7 days

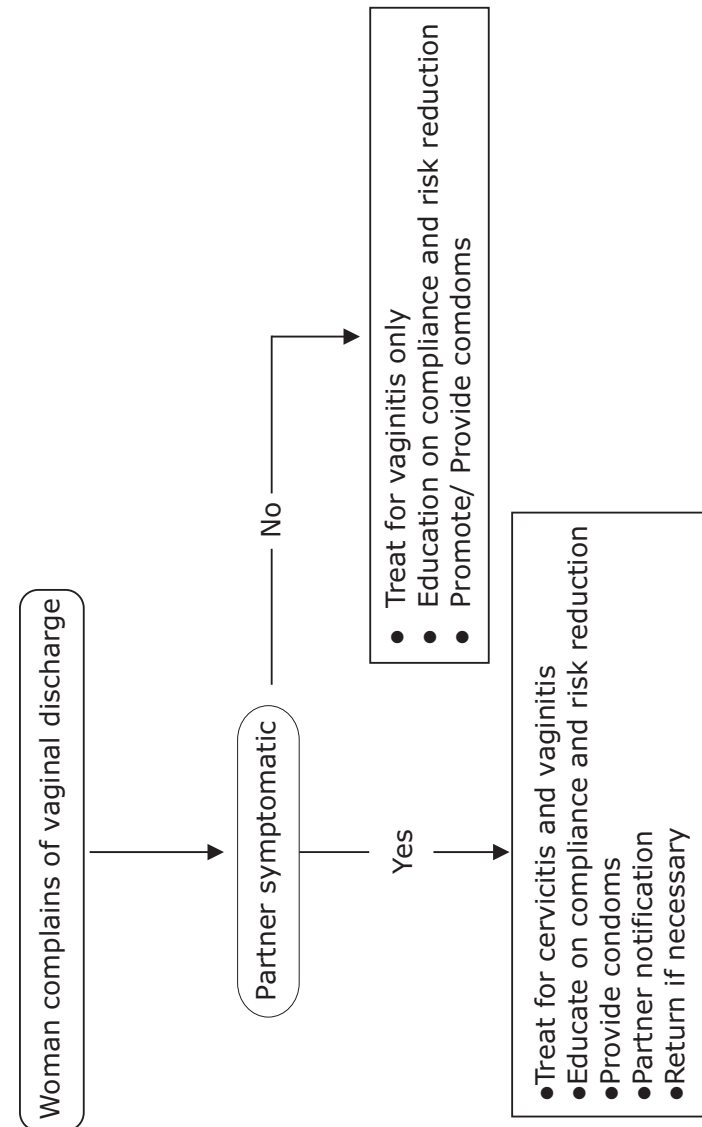
2b. Vaginal discharge on speculum examination

Recommended treatment: Metronidazole 200 mgm three times a day for 7 days

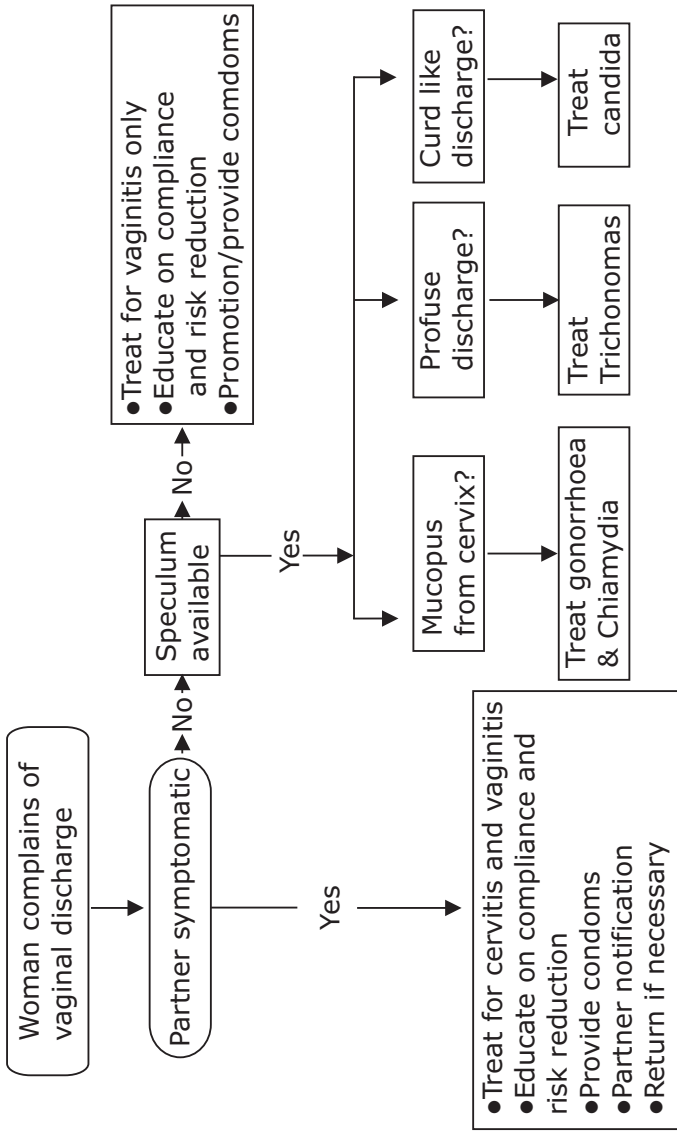
Miconazole 100 mgm intravaginally once daily for 6 days

During the first trimester of pregnancy no Metronidazole must be given and treatment is by Miconazole only.

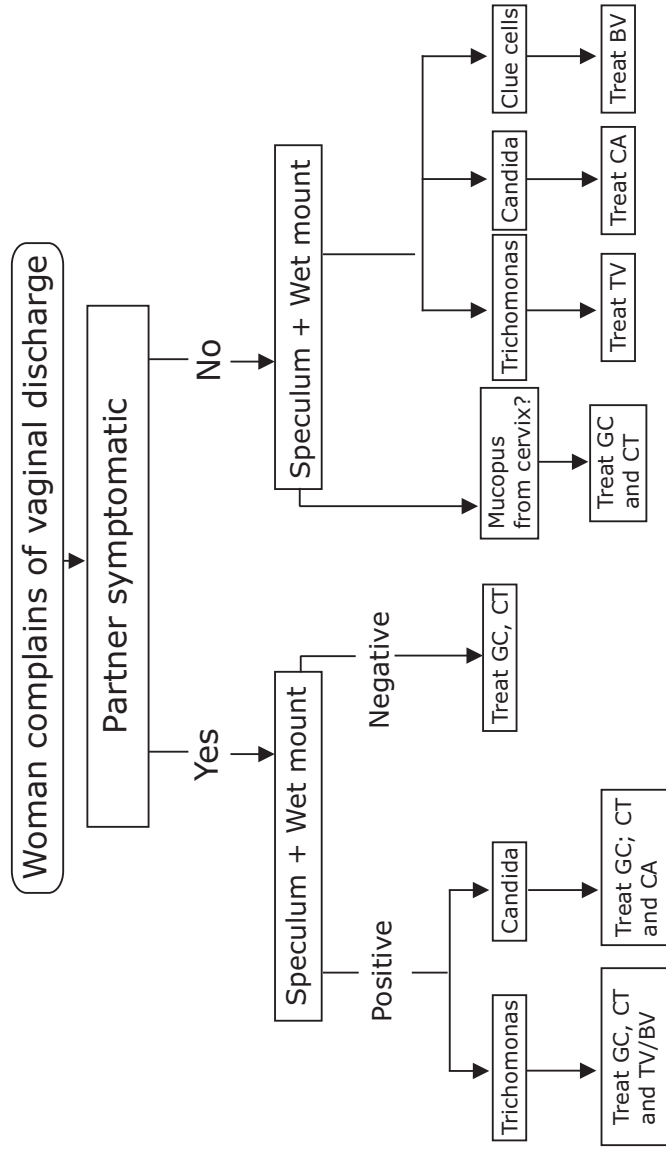
Flow chart for vaginal discharge



Flow chart for vaginal discharge with speculum



Flow chart for vaginal discharge with speculum and microscope



3. Genital ulcer :

Genital ulcer can be caused by syphilis, chancroid, lymphogranuloma venereum or granuloma inguinale. In addition to these, genital ulcers can be caused by genital herpes infection. The treatment recommended below will cure all ulcers, except those caused by herpes.

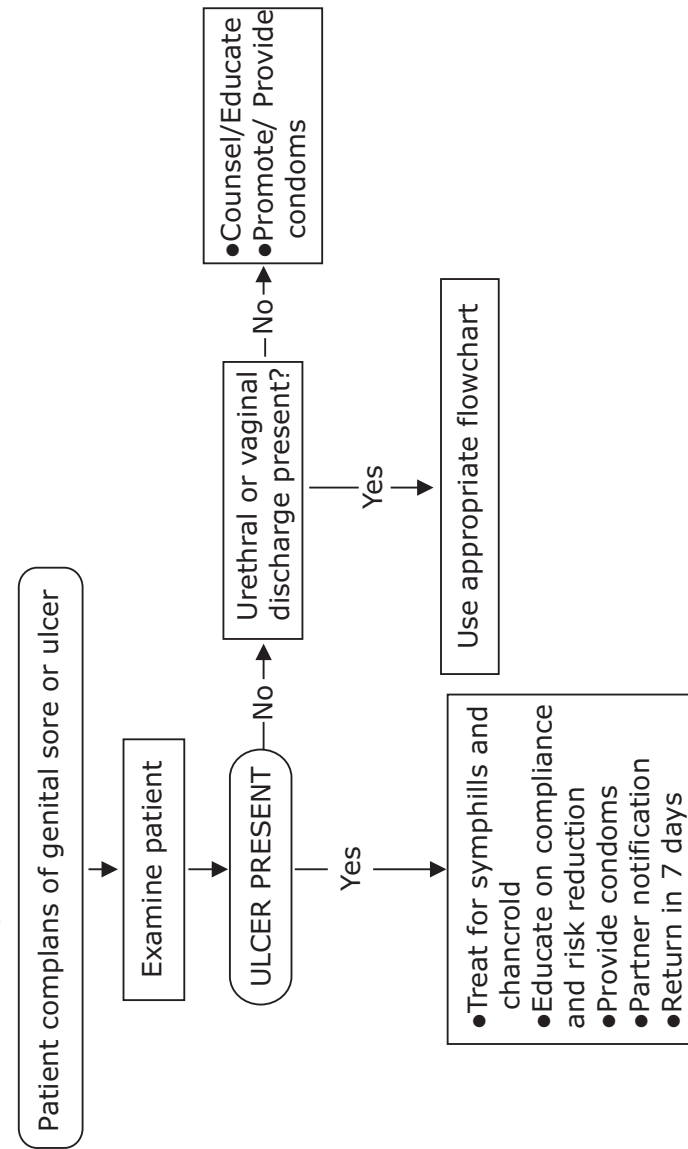
Recommended treatment (non-pregnant patients):

Benzathine benzyl penicillin 2.4 Mega Units I. M. in a single dose
and
Doxycycline 100 mgm orally twice daily for 15 days

Pregnant patient :

Benzathine benzyl penicillin 2.4 Mega Units I.M. in a single dose
and
Trimethoprim (80 mgm)/ Sulphamethoxazole (400 mgm) 2 tabs twice daily for 15 days

Flow chart for genital ulcer



4. Inguinal swelling (bubo) :

The most common cause for inguinal swelling, without the presence of genital ulcer is Lymphogranuloma Venereum (LGV)

Recommended Treatment :

Doxycycline 100 mgm orally twice daily for 15 days

5. Lower abdominal pain - pelvic inflammatory disease (PID)

All sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence of salpingitis and/or endometritis. In addition, routine bimanual examination should be done on all women with a presumptive STD since some women with PID or endometritis will not complain of lower abdominal pain. Women with endometritis may present with complaints of vaginal discharge, and/or bleeding and/or have uterine tenderness on pelvic examination. Symptoms suggestive of PID include abdominal pain, dyspareunia, vaginal discharge, meno-metrorrhagia, dysuria, onset of pain in association with menses, fever, and sometimes nausea and vomiting.

PID is difficult to diagnose. However, PID becomes highly probable when one or more of the above symptoms are seen in a woman with adnexal tenderness, evidence of lower genital tract infection, and cervical motion tenderness.

Hospitalisation of patients with acute pelvic inflammatory disease should be considered when (a) the diagnosis is uncertain, (b) surgical emergencies such as appendicitis and ectopic pregnancy need to be excluded; (c) a pelvic abscess is suspected (d) severe illness makes outpatient management impossible, (e) the patient is

pregnant, (f) the patient is unable to follow or tolerate an outpatient regimen, (g) the patient has failed to respond to outpatient therapy; or (h) if clinical follow-up 72 hours after the start of the antibiotic treatment can not be guaranteed

Because of the fact that many organisms can cause PID, and because it is difficult to establish aetiology for individual infections, it is recommended that PID is treated with concurrent treatments for gonorrhoea, non-gonococcal infection and anaerobic infection.

Recommended treatments are:

Kanamycin 2 gm I.M. in a single dose

or

Spectinomycin 2 gm I. M. in a single dose

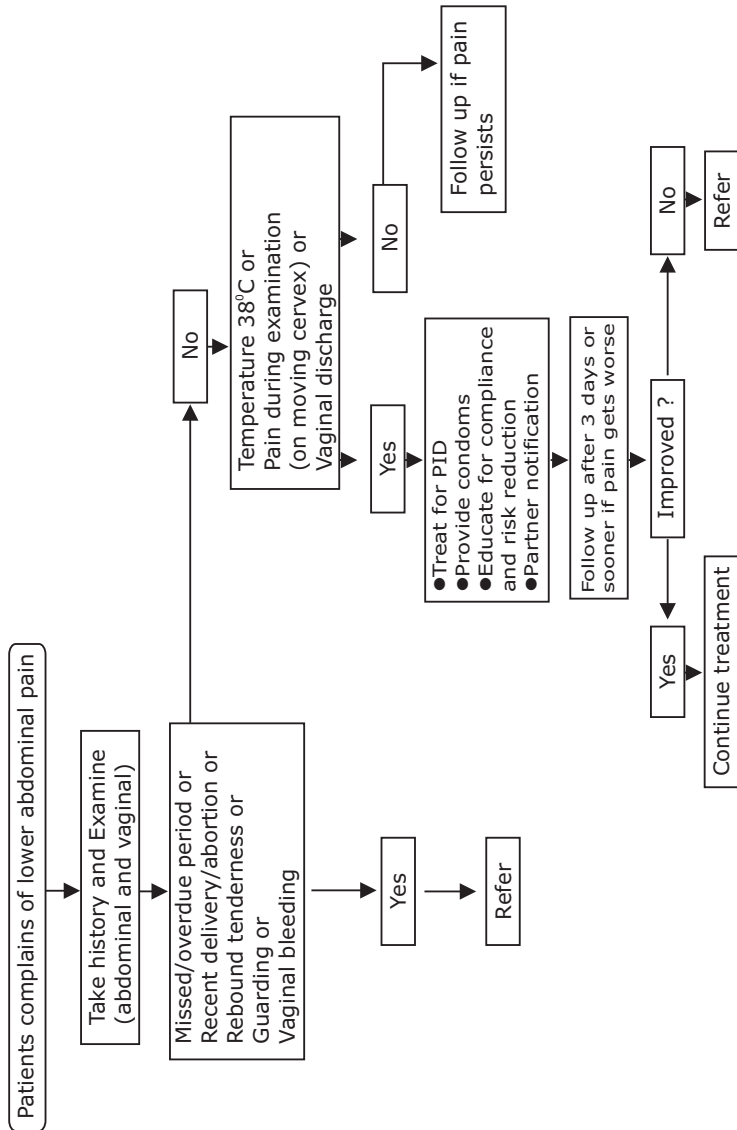
and

Doxycycline 100 mgm orally twice daily for 2 weeks and

Metronidazole 400 mgm orally twice daily for 10 days

All patients treated on an outpatient basis should be followed up after 72 hours, and admitted if not improved.

Flow Chart For Lower Abdominal Pain



17. Contraceptive Methods for HIV-infected Women

CONDOM (MALE)

Currently, the condom is the best contraceptive method available, next to abstinence, for HIV-infected women (and men, too). Additionally, condoms provide protection against transmission of HIV and other sexually transmitted diseases. It is important to keep in mind that some women will not want to use condoms if they are using other contraceptive methods. The importance of using condoms should always be emphasized. Some women will require more security, and the healthcare worker should be able to assist them in choosing additional contraceptive methods, explaining the advantages and disadvantages of each method.

Advantage:

Protects against HIV and other sexually transmitted diseases

Disadvantages :

1. Must be used during every act of intercourse
2. Allergic reactions to latex occur rarely
3. Male controlled method; women have little control over the partner's preference

FEMALE CONDOM (FEMIDOM)

These are not freely available, are costly. Feasibility studies are going on. If effective, are likely to provide an excellent woman controlled barrier contraception and also protection against STIs including HIV.

SPERMICIDE

Advantages :

1. May protect, to some extent, against sexually transmitted diseases and can be used with condoms and diaphragms
2. Partner participation not necessary
3. Can be used as a backup in the event of condom breakage

Disadvantages:

1. May result in allergic reactions (especially with frequent use)
2. Must be used during every act of intercourse

DIAPHRAGM

Advantages:

1. Offers some protection against sexually transmitted diseases, especially when used with spermicidals.
2. Partner participation not necessary
3. Useful to women who have infrequent intercourse
4. Inexpensive

Contraindications:

1. Allergic reactions to latex
2. Anatomic abnormalities of vagina
3. Inability to place diaphragm correctly
4. Previous history of toxic shock syndrome
5. Recurrent urinary tract infections
6. Gynaecologic neoplasm

ORAL CONTRACEPTION

Advantages:

1. Offers excellent contraceptive protection - efficacy greater than 95%
2. Is easy to use
3. Reduces pelvic discomfort and menstrual flow
4. Partner participation not necessary
5. Does not require any action at the time of intercourse
6. Use is associated with a decreased incidence of uterine and ovarian cancers

Disadvantages:

1. Does not protect against sexually transmitted diseases, including HIV
2. Risk of side effects headache, nausea, thrombophlebitis, mood swings, cyclic weight gain, oedema, acne

Contraindications:

1. History of thrombophlebitis or thromboembolism
2. History of hormone-dependent neoplasms
3. High blood pressure
4. Currently smoking (more than 15 cigarettes a day) and older than 35 years of age
5. Liver function abnormalities
6. Hemoglobinopathy
7. Family history of hyperlipidemia

INTRAUTERINE DEVICE (IUD)

This is not a good contraceptive method for women who are HIV positive or at risk for HIV infection, because the IUD increases the risk of PID and potentially increases the risk of infection/transmission.

Books for References:

- Lambert John S, Noguera Susie A, Anderson E. H. *"Manual for the clinical care of HIV infected pregnant women."* Paediatric AIDS Foundation.
- NACO guidelines for *"Prevention of Mother -to -Child Transmission Programmes"*.
- NACO *"Simplified STD Treatment Guidelines"*. 1993
- Powderly William G. *"Manual of HIV Therapeutics"* 2nd Ed. Lippincott Williams & Wilkins 2001
- UNAIDS. *"HIV in pregnancy: A Review"* 1999