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Integrating Family Planning Services and HIV Treatment :

An Overview

By Emily J. Erbelding, MD, MPH

Identifying women who are HIV-infected through counseling/ testing, then providing antiretroviral (ARV) drugs during pregnancy, is the standard approach to preventing maternal to child transmission (PMTCT) of HIV. However, many women living with HIV do not wish to become pregnant at all, or they wish to plan their pregnancy timing so that their own health and that of their families will be optimal. Providing accessible family planning services to these women—ideally at the site where they access HIV treatment--will also prevent maternal to child transmission of HIV by preventing unintended pregnancies. In this article we will summarize some of the main considerations in integrating family planning services with HIV treatment services.

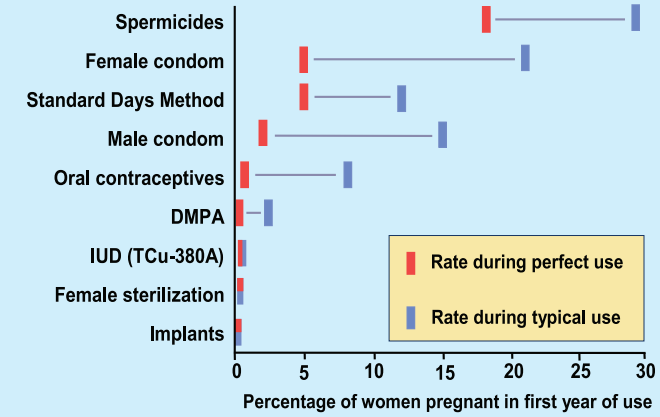
Unintended Pregnancy and HIV:

Extent of the Problem

In African countries heavily impacted by HIV/AIDS, women of childbearing age may comprise up to 61% of the population of those living with HIV infection. This proportion is increasing in some parts of Sub-Saharan Africa. Young women 15-25 years of age are often disproportionately impacted by high rates of HIV compared to that of other age groups. The integration of PMTCT services into antenatal care has been promoted as a public health goal.

However, large gaps remain in the availability of family planning. Among African countries with PEPFAR programs, the proportion of unplanned births to all women may be as great as one-third to one-half of all births. Countries with the greatest unmet needs for family planning services tend to be the countries with the highest rates of HIV prevalence among women of childbearing age. Delivering reproductive health services, including family planning services, along with HIV treatment services in the same setting, will be an essential part of addressing this gap in HIV prevention.

Effectiveness



Source: CCP and WHO, 2007.

Figure 1. Comparative effectiveness of various family planning methods

Family Planning Promotes Healthier Families

There are a number of benefits to women—both HIV-infected and uninfected-- and children when family planning services are readily accessible. Women and men can limit the size of their families and have only the number of children that they want and are able to support economically. Mothers can space pregnancies to reduce the health risks associated with too many pregnancies or pregnancies occurring at very close intervals. Serodiscordant couples (couples in which one partner is HIV-positive and the other is HIV-negative) can also use family planning methods to control the timing of conception so that it occurs when the risk of HIV transmission to the uninfected partner is the lowest.

Pregnancy and HIV

There are many reasons that a woman living with HIV may consider becoming pregnant. Her partner or family may put pressure on her to have children, and she may be concerned that if she doesn't become pregnant, these people will be suspicious about her HIV status. She may be optimistic about the ability of ARVs and other PMTCT interventions to decrease the chance of a child being HIV infected. She may have experienced restored

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INSIDE stories

EDITORIAL

According to WHO, reproductive health addresses the reproductive processes, functions and systems. This means having a responsible, satisfying and safe sex life. It also means the freedom to decide if, when and how often to have children.

To achieve this both men and women must be well informed and have access to safe, effective, and affordable methods of family planning. Excuse the cliché, but 'Knowledge is Power', indeed.

In recent decades, tremendous advances have been made in the development of safer and more effective contraceptives, and in the provision of affordable and accessible family planning services. Yet, still millions of individuals and couples around the world are unable to plan their families as they wish.

The ability to make informed decisions can be achieved by cascade information to communities. It is imperative that the risks of frequent pregnancies, especially in HIIV/AIDS infected people, be emphasized to couples and information on PMTCT disseminated.

Increased access to appropriate health care services will enable women to safely go through pregnancy and childbirth and provide couples with the best chance of having a healthy child.

The myth that family planning methods are dangerous to women's health should be demystified. People's perspectives on issues are influenced by culture, education, religious beliefs, etc. These influences create prejudices that make it difficult to appreciate a different point of view, or understand any practice that challenges their underlying assumptions. As health workers disseminating family planning information, we ought to understand that these too present a challenge.

In this ATIC News issue we are glad to bring to you a review on reproductive health.

health from ARVs and may be optimistic about the possibilities of staying well and raising her own children. At the most basic level, she may simply want to have children. And lastly, disclosure of her HIV status to her partner, along with taking control of family planning choices, may result in violence, abandonment, and loss of economic support. Though pregnancy may impose physiologic stress on a woman, such as anemia and added nutritional needs, research has shown that pregnancy does not accelerate rate of CD4 cell decline or progression to clinical AIDS in women living with HIV infection. But some studies have shown an increased risk of poor pregnancy outcomes such as stillbirth or infant low birth weight. However, with good medical care and proper access to PMTCT services, an HIV-positive mother can be optimistic about delivering a healthy baby.

Specific Contraceptive Methods: Considerations in HIV-infected Women

Estimates on effectiveness of the range of contraceptive options available are shown in Figure 1. WHO consensus guidelines state that HIVinfected women can use nearly all contraceptive methods safely, regardless of WHO stage of HIV disease1.

The most commonly chosen methods of hormonal contraception are oral combination agents (OCAs), which contain varying amounts of estrogen and progesterone and prevent pregnancy by suppressing ovulation. Another common oral method used is progestin-only pills (POPs). Injectables, such as depot medroxyprogesterone acetate (DMPA, or Depo-Provera) and implants, such as Implanon, are progestin-only methods that provide a longer duration of contraceptive coverage for every dose given. Injectables and implants may be particularly convenient and useful when a woman prefers to not take a pill daily for contraception.

Though all available hormonal methods can be used for women with HIV, there are some important ARV drug interactions for the clinician to know. The most significant interaction between ARV drugs and hormonal contraceptives occurs through the hepatic metabolism of ethinyl estradiol (circulating estrogen), which may be altered by ARV drugs in the protease inhibitor and non-nucleoside reverse transciptase inhibitors (NNRTIs) classes. The direction of these interactions by specific protease inhibitors and NNRTIs—either reduced or increased levels of circulating estrogens—is summarized in Table 1 on page 3

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1. Continuous use of nevaripine leads to reduced levels of both ethinyl estrodiol and norethisterone, but the clinical significance of this interaction is unclear. Given what is known from pharmacokinetic data and clinical observations, current WHO recommendations for use of hormonal contraceptives and ARVs state only that ritonavir (in any dose) should be avoided in women prescribed contraceptive methods which contain estrogens. The WHO does not recommend against use of NNRTIs, which often comprise the backbone of the most common ARV regimens prescribed in Sub- Saharan Africa, with combination hormonal agents or with progestin-only agents.

There are no known interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and circulating estrogens or progestins. Also, studies focusing on progestin-based methods (DMPA specifically) indicate that there are no significant interactions between these agents and ARVs. Women living with HIV who choose either OCA , injectables, or implants as their family planning method should be advised to also use condoms to prevent transmission of STI/HIV. Efavirenz (EFV) exposure during the first trimester of pregnancy has been associated with birth defects in nonhuman primates. Therefore, it is generally recommended to avoid use of this ARV agent in women who may be at risk for becoming pregnant, including those women who are fertile but not using family planning reliably. It is especially important to ask a woman of her pregnancy intentions if she is taking EFV. However, inclusion of EFV in the regimen of a woman of childbearing age may be appropriate based upon her individual health status and the availability of other options.

Emergency contraception

Emergency contraception (EC) is a method of contraception taken orally after unprotected intercourse has occurred in order to prevent implantation and pregnancy. EC prevents pregnancy from occurring but does not act on an existing pregnancy. EC options include progestin only pills and OCAs. Either formulation can be used up to 5 days following the event, though the method will be most effective when used early. EC is safe for women with any stage of HIV/AIDS; it can be used with any ARV regimen.

Other considerations in HIV

The intrauterine device (IUD) has been a common family planning choice method of women in many geographic settings for decades. Some features and side effects of the IUD have raised theoretical concerns among clinicians for use in HIV-infected women: One common side effect is longer duration of menses with greater blood loss than other contraceptive methods. This may lead to worsening of anemia, a complication more significant in HIV infection. Also, infectious complications, such as chronic pelvic inflammatory disease, have been described with long-term IUD use. It was unknown whether this risk would be greater in women living with HIV. However, results from a recent clinical trial done among HIV-infected women in Zambia suggests that a copper IUD can be significantly more effective in pregnancy prevention than OCAs2. Results also suggested that the IUD may be safer for HIV-infected women than OCA; a more complete understanding of this difference will need to be explored through future research. Given these findings, the WHO guidelines rank IUD as a preferred method of contraception and likely to be safe for most HIVinfected women.

Summary Points:

Providing effective family planning to women living with HIV is critical to HIV prevention, especially PMTCT. The vast majority of contraceptive options are safe for women with HIV/AIDS including those on ARV. However, given pharmacologic interactions between ritonavir and estrogens, avoiding use of ritonavir along with oral combination agents (or other estrogen containing contraceptive) is recommended.

References:

1. World Health Organization (WHO). Medical Eligibility Criteria for Contraceptive Use. Third Edition. Geneva: WHO, 2004.
2. Stringer EM et al: A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol Aug;197(2):144 e1-8, 2007.

Additional resources for clinicians and counselors are available at:

Family Health International:
http:// www.fhi.org/training/en/modules/FPHIV_toolkit/interface.pdf

The World Health Organization:
http://www.who.int/reproductivehealth/publications/mec/mec_update_2008.pdf and http://www.who.int/reproductivehealth/ publications/family_planning. html

EngenderHealth
http://www.engenderhealth.org/pubs/family-planning/reversible-methods. php

Jhpiego
http://www.jhpiego.org/resources/pubs/index.asp

Antiretroviral agent	Blood contraceptive hormone level	Blood ARV level
Nelfinavir	Decreased	No data
Ritonavir	Decreased	No data
Lopinavir/ritonavir	Decreased	No data
Atazanavir	Increased	No data
Indinavir	Increased	No data
Saquinavir	No data	No change
Nevaripine	Decreased	No change
Efavirenz	Increased. *Eestradiol is increased but information on proesterone is not known. Thus it should not be assumed that oral contraceptive prevent pregnancy wirh EFV*	No change

Table 1

Syphilis in Pregnancy

By Edith Nyangoma Senior House Officer, Internal medicine. Mulago Hospital

Introduction.

"He who knows syphilis, knows medicine" Sir William Osler.

Syphilis is a chronic disease with a waxing and waning course, the manifestations of which have been described for centuries. It is relatively common in Uganda, and its prevalence among pregnant women varies between 4% in western region and 8% in north western regions. It is a chronic infection caused by the spirochete Treponema pallidum (TP). TP is a delicate, motile spirochete bacterium and humans are its only natural source.

Syphilis is mostly transmitted by sexual contact through exposure to mucocutaneous syphilitic lesions that contain infectious spirochetes except for the cases of vertical transmission. After inoculation, the incubation period is around 3 weeks (10–90 days), at the end of which a primary sore develops at the site of infection, usually the genitalia. In people who practice oral sex, the mouth may be involved.

Classification of Syphilis

In the absence of treatment, syphilis occurs in different stages, over time. Each stage has characteristic clinical features. None of these stages is altered by pregnancy.

Primary syphilis

The first manifestation of syphilis is a papule (small elevation of skin, without pus), which is typically painless, at the site of inoculation. The papule soon ulcerates to produce the classic chancre of primary syphilis, a 1 to 2 centimeter painless ulcer with a raised, indurated margin that may be genital or extra genital e.g in the mouth. The ulcer is associated with mild to moderate regional lymphadenopathy that is often bilateral. Chancres heal spontaneously within three to six weeks, even in the absence of treatment.

Secondary Syphilis

Secondary syphilis is a disseminated systemic process that begins six weeks to six months after the appearance of the chancre in approximately 25 percent of untreated patients. A generalized maculopapularskinrashinvolvingthepalms and soles and mucous membranes, but usually sparing the face, is characteristic of this stage of the infection. Generalized lymphadenopathy accompanies the skin rash. Additional clinical features include fever, pharyngitis, weight loss, and large genital lesions called condylomata lata. Although spirochetes can be found in the cerebrospinal fluid (CSF) of around 40 to 50 percent of patients with early syphilis, neurological manifestations are rare.

After the secondary phase,

patient's symptoms may spontaneous resolve. Patients are then described to be in the latent phase. Approximately 60% of patients remain latent for the rest of their lives. In the early latent stage, 25% will relapse with a secondary syphilitic manifestation, whereas the likelihood of such relapses in the late latent stage is small.

Tertiary syphilis. This occurs in approximately one-third of untreated patients and is characterized by slowly progressive signs and symptoms. Clinical manifestations include gumma formation, cardiovascular disease, and/or CNS changes (neurosyphilis). Such manifestations usually develop 5 to 20 years after the disease has become latent. Vertical Transmission of Syphilis T. pallidum readily crosses the placenta, thereby resulting in fetal infection. Pregnancies complicated by untreated syphilis are at increased risk of several adverse outcomes, although approximately 20 percent of children born to mothers with untreated syphilis will be normal. Adverse outcomes include; Intrauterine growth restriction, Intrauterine fetal death, Abortions, Early neonatal death, Preterm birth,and Congenital infection and anomalies Vertical transmission can occur at any time during pregnancy and at any stage of the disease but the risk of congenital syphilis is directly related to the stage of syphilis in the mother and the risk is extremely high for the first four years after maternal acquisition of infection when spirochetemia is relative high in pregnancy. The newborn can also be infected by contact with an active genital lesion at the time of delivery. Perinatal transmission occurs in 50 percent of patients with primary or secondary syphilis, with fewer congenital infections among women with early latent, late latent, and tertiary disease respectively. Seventy to one hundred per cent of infants born to untreated infected mothers are infected.

Maternal Screening:

The problems associated with syphilis in pregnancy can be almost completely eliminated by universal early ante partum screening and treatment with appropriate antibiotics. It is recommended that all pregnant women be screened for syphilis; the cost and morbidity associated with testing for syphilis is low and the benefit of detecting and treating the disease is high for both mother and child. Serologic testing should be performed at initial antenatal visits and then repeated during the third trimester and again at delivery in populations with a high prevalence of syphilis or for selected patients at high risk e.g HIV positive patients. Women who deliver stillborns after 20 weeks should also be tested. A pregnant woman with positive syphilis test should be considered actively infected unless an adequate treatment history is clearly documented and sequential antibody titers have declined.

Diagnosis of syphilis in Pregnancy:

Currently in Uganda, serological tests are now available widely used in the diagnosis of syphilis as they are cheap to perform and require little human resource. Techniques for Polymerase chain reaction and direct fluorescence can only be done in research settings. Nontreponemal antibody tests (eg, Venereal Disease Research Laboratory [VDRL] test and the Rapid Plasma Reagin [RPR] test) are performed on serum and used as the screening test for syphilis in most settings. Positive tests are usually reported as a titer

of antibody and can be used to follow the response to treatment in many patients. These tests are relatively inexpensive, easy to perform, and can also be done on other body fluids, such as CSF.

Treponemal antibody tests (eg, fluorescent treponemal antibody absorption [FTA-ABS] and the Treponema pallidum particle agglutination assay [TPPA]) are confirmatory tests that detect antibodies specifically directed at treponemal cellular components. These tests are sensitive and specific, but expensive and correlate poorly with disease activity, since they remain positive despite treatment. It is important to remember that there is a high rate of false positives among pregnant patients with HIV infection.

Treatment of syphilis in pregnancy;

Penicillin is the drug of choice for treating all stages of syphilis in pregnancy as it is effective for treating maternal disease, preventing transmission to the fetus, and treating established fetal disease. Parenteral rather than oral treatment has been the route of choice as the therapy is supervised and bioavailability is guaranteed.

Most women treated during pregnancy will deliver before their serological response to treatment can be assessed definitively. Neonates born to such women should be evaluated for congenital syphilis.First-line therapy: intramuscular (i.m.) procaine penicillin 750 mg daily for 10 days or Penicillin G (benzathine) 2.4 million units IM weekly for 3 weeks.

Patients with penicillin allergy:

erythromycin 500 mg four times a day should be given for 14 days. Alternatively, azithromycin 500 mg should be given daily for 10 days. In addition to this, examination, tests, and treatment of all babies at birth should be carried out. Desensitization to penicillin may be considered, followed by the first-line treatment. Mothers treated with erythromycin or azithromycin may be considered for retreatment with doxycycline after delivery and when breast-feeding is stopped.

References

1. Syphilis in Pregnancy; up-to- Date 15.1

2. Sexually Transmitted Diseases Treatment Guidelines, 2006. MMWR Recomm Rep 2006 (RR-11); 55:1- 95

3. D.L Brown and J.E. Frank; Diagnosis and Management of Syphilis. American family physician. 2003; 68. 2.

Vulvovaginal candidiasis

By Francis Kalemeera, Bsc, BPharm, MPS

Introduction

Vulvoginal candidiasis occurs in many women (27-60%). The incidence is the same in HIV infected and non HIV infected women. Vulvovaginal candidiasis can be a nuisance to the patient especially because of frequent recurrences. Also recurrences may be a challenge for you as the health care worker, seeing patients with the same complaint month after month. However, recurrences can be reduced. The reduction is propagated by giving appropriate treatment of episodes, and providing maintenance therapy. We would like to share information with you on appropriate treatment of vulvovaginal candidiasis and maintenance of treatment outcome.

As you may already know, the signs and symptoms of symptoms of vulvovaginal candidiasis include mucosal burning (pain that feels hot, like it were on fire) and marked pruritus (itching). Patients also suffer with dyspareunia (painful sexual intercourse); peripheral lesions; and external dysuria (painful urination). On examination the mucosa is erythematous (reddened, due to dilatation of small blood vessels in the mucosa); there is a yellow white curd-like adherent (sticky) discharge; and the labia are swollen.

Treatment: Treatment may be topical or systemic Topical (applied at site of infection)

- Clotrimazole 1% cream 5g per dayfor 7 to 14 days.
- Clotrimazole 100mg tab vaginal tab per day for 7 to 14 days or 100mg tab twice daily for 3 days or 500mg tab once
- Nystatin 100,000 units per day for 14 days
- Miconazole 2% cream 5g per day for 7 days or 100mg of pessary per day for 7 days or 200mg pessary twice daily for 3 days Systemic (Oral or injectable administration)
- Fluconazole 150mg orally once
- If available, Itraconazole 200mg orally twice daily for 3 days may be used

Maintenance: Vulvoginal candidiasis can have very frequent recurrences in women. To avoid these recurrences maintenance regimens are recommended. And by the way, this information is based on recommendation in women without HIV infection. The following are the regimens recommended for maintenance:

- Clotrimazole 500mg orally every week (for 6 months) or
- Fluconazole 100-150mg orally weekly (for 6 months) or
- Ketoconazole 200mg orally weekly (for 6 months)
- Itraconazole 400mg every month or 100mg every week for 6 months

Note:

1. The same treatment should be given to HIV infected and non infected women
2. If the disease is severe
   - topical therapy should be given for 7 to 14 days,
   - while oral fluconazole should be given 150mg once and again 72hours later
3. In pregnancy, only topical azoles should be used to treat vaginal candidiasis

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2. Sha B, Benson C, Pottage J, et al: HIV infection in women: a six year longitudinal, observational study. In: Proceedings of the IX International Conference on AIDS, Berlin, 1993, Vol I, Abstract No. PO-B01-0891:283.

3. Schuman P, Capps L, Peng G, Vazquez J, el-Sadr W, Goldman AI, Alston B, Besch CL, Vaughn A, Thompson MA, Cobb MN, Kerkering T, Sobel JD. Weekly fluconazole for the prevention of mucosal candidiasis in women with HIV infection. A randomized, double-blind, placebo-controlled trial. Terry Beirn Community Programs for Clinical Research on AIDS. Ann Intern Med. 1997 May;126(9):689-96 [PubMed ID: 9139554]

4. Medical Management of HIV Infection 2005-2006

SCALING UP HIV PREVENTION AT IDC

Focusing on HIV discordant couples

By Florence Namimbi, Counsellor, Discordant couples.

Sexual intercourse remains the epidemic's driving force in Sub Saharan Africa (UNAIDS report, 2008). According to the Uganda national Sero Behavioral Survey in 2005, the most important source of new infections continues to be sexual transmission, accounting for up to 76% (MoH report, 2007). The recent epidemiological evidence has revealed the region's epidemic to be more diverse than previously thought.

According to Demographic and Health surveys in 5 African countries (Burkina Faso, Cameroon, Kenya, Tanzania and Ghana), two thirds of HIV infected couples were serodiscordant, that is only one partner was infected. Similar surveys in East Africa indicate that more than 40% of married individuals with HIV have un infected spouses (UNAIDS report, 2008).

A follow up analysis of the Sero Behavioral Survey suggests that up to 65% of new infections are occurring among married people; and discordant couples may compromise up to 50% of these transmissions (MoH, MACRO, 2005).

This data underscores the vital importance of effective, targeted prevention work with married adults, especially discordant couples. Currently at IDC, over 150 clients (friends) have so far been identified and confirmed to be living in discordant relationships with their partners.

It is likely that these numbers will double in the next few years as the screening process is still on going. A vigorous campaign by staff, the drama team and peer educators calling on all clients in sexual relationships (married, cohabiting, or those who have been in a sexual relationship for over six months) to bring their partners for HIV testing has yielded results.

The major goal of creating the Dis cordant Couples (DISCO) cohort at IDC is to try and prevent HIV transmission to the negative partners. A community based study in Uganda, Rakai, has shown that, among sero discordant heterosexual couples, the negative partner has an estimated 8% annual chance of contracting HIV (UNAIDS report, 2008).

The discordant couples at IDC are therefore given counseling sessions together whenever they come to the clinic, they are also attended to by the medical officers attached to the DISCO cohort. The negative partners benefit from free medical consultation and free treatment of STIs here at IDC. Peer support meetings are also organized on a quarterly basis and issues raised by discordant couples are thoroughly handled by the facilitators. Condom use remains an important tool of HIV prevention among discordant couples. Condoms are therefore availed to discordant couples at every given opportunity. Negative partners in discordant relationships are re-tested after every six months. Since various studies have cited the positive relationship between HIV testing and less risky behaviors to contracting HIV, its also assumed that with the six monthly interval follow up testing given to couples, those who remain will be encouraged to continue protecting themselves against contracting HIV.

We are looking forward to our next peer support group meeting on 28-02-2009.
For more information contact; Doctors: Fred Sewankambo, Liz Matovu, Timothy Muwonge,
Counsellors:Florence Namimbi, Wakabi Leila, Susan Nakate and Phoebe Nabongo.

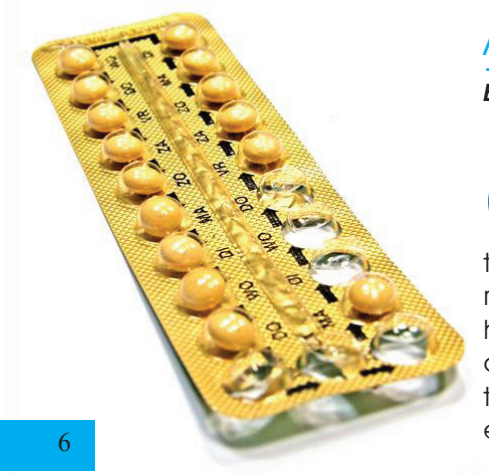
FOOD FOR THOUGHT

When was the last time you took an HIV test together with your partner? Don't make any assumptions about him/her. You may be living in a discordant relationship. Seek couple HIV counseling and testing from the nearest testing facility!

Combined Oral Contraceptives

A review of combined oral contraceptives

By Pharmacist Mrs. Robinah. N.Lukwago (BPharm, MPH, MPS)



Combined oral contraceptives (OCP's) contain estrogenic and progestinic steroids. They were developed to prevent ovulation by suppressing the release of gonadotropins. Combined hormonal contraceptives, inhibit follicular development and prevent ovulation as their primary mechanism of action. Either estrogen or progesterone alone is capable of inhibiting both Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) sufficiently to prevent ovulation. The combination of the two steroids creates a synergistic effect that greatly increases their antigonadotropic and ovulation-inhibitory effects. They also alter the consistency of cervical mucus, affect the endometrial lining, and alter tubal transport.

Administration

To ensure maximum contraception efficacy, OCP's should be taken as near as possible to the same time each day (i.e. at regular 24 hour intervals). To minimize nausea, oral contraceptives should be taken after the evening meal or at bedtime.

Missed tablet: If a woman misses 1 or 2 pills, she should take 1 tablet as soon as she remembers. She then takes 1 tablet twice daily until coverage of the missed pills is achieved. Women who have missed more than 2 consecutive pills should be advised to use a backup method of contraception (e.g. condoms) simultaneously to finishing up the packet of pills until their next menses.

Side Effects

Common adverse effects of OCP's appear to be mainly caused by estrogen, are usually most pronounced during the first oral contraceptive cycle, and disappear or diminish after 3 or 4 cycles.

Gastrointestinal (GI) effects: The most frequent adverse effect is nausea. Other GI adverse effects include vomiting, abdominal cramps, abdominal pain, bloating, diarrhea, and constipation. Changes in appetite and changes in weight may also occur.

Dermatologic effects: the most frequent dermatologic reaction is melasma (pigmentation of the face most commonly on the upper cheek, bridge of the nose and forehead). Women who have had melasma during pregnancy appear to be most susceptible. The irregular brown macules may develop slowly on the face within 1 month to 2 years following initiation of oral contraceptive therapy. Another common dermatologic reaction is acne. The severity of acne may increase in some women and may develop in some women who have not previously had acne.

Cardiovascular effects: a positive association between the amount of estrogen and progestin in oral contraceptives and the risk of adverse cardiovascular effects has been observed.

a) Elevated blood pressure- increases in blood pressure may occur in women receiving OCP's . Blood pressure elevations are usually minor, but clinically important hypertension may occur in some women. Some women develop hypertension within 1-3 weeks after initiation of oral contraceptive therapy and become normotensive during the part of the cycle when they do not receive the drugs. Elevated blood pressure may gradually decrease or persist after the oral contraceptive is discontinued. The precise cause of the increased blood pressure is not known but it may result from a stimulatory effect of the estrogen on the rennin-angiotensin system.

b) Thromboembolic disorders- oral contraceptive use is associated with an increased risk of thromboembolic and thrombotic disorders. One study has shown an increased relative risk of fatal venous thromboembolism.

c) Other cardiovascular effects- oral contraceptives may cause some degree of fluid retention and edema They should be used with caution in patients with conditions that might be aggravated by fluid retention.

Endocrine and metabolic effects:

a) Effects on glucose- decreased glucose tolerance has been observed in a significant percentage of patients receiving oral contraceptives. Fasting blood glucose concentrations are not altered in most patients; however increased plasma insulin and blood pyruvate concentrations may occur.

b) Effects on lipids and lipoproteins increased concentrations of plasma triglycerides, low-density lipoproteins and total phospholipids may occur.

Hepatic effects: Liver function tests may be altered in patients receiving oral contraceptives and if results of these tests are abnormal, they should be repeated 2 months after the drugs have been discontinued. Increased sulfobromophthalein retention occurs frequently. Less frequently increased serum aminotransferase and alkaline phosphotase concentrations may occur. Liver function test results usually return to normal within several weeks after oral contraceptives are discontinued.

Genitourinary effects: Breakthrough bleeding and/or spotting (especially within the first 3 months of use), changes in menstrual flow, missed menses (during use), or amenorrhea (after use) may occur in women receiving hormonal contraceptives. An increased incidence of candida vaginitis has been associated with oral contraceptive therapy.

Nervous System effects: Mental depression may occur in women receiving oral contraceptives. In a few cases mental depression has been so severe and has led to suicidal behaviour. Fatigue, dizziness, nervousness, aggressiveness, anxiety, emotional liability, and irritability have been reported in women receiving estrogen progestin contraceptives; changes in libido may also occur.

Drug Interactions

Drugs affecting Hepatic Microsomal Enzymes: clinically important drug interactions may occur when OCP's are administered with other drugs metabolized by the hepatic microsomal cytochrome (CY) P-450 enzyme system.

Metabolism of estrogens is mediated by the CYP3A4 isoenyme and the possibility exists that drugs that induce this isoenzyme may reduce ethinyl estradiol concentrations. Rifampicin reportedly decreases contraceptive efficacy and increases breakthrough bleeding during concomitant use with OCP's. These effects have been attributed to enhanced metabolism of both the estrogenic and progestinic components of OCP's, presumably by induction of hepatic microsomal enzymes.

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It has been suggested that similar effects may occur during concomitant therapy with other known inducers of hepatic microsomal enzymes, including barbiturates, carbamazepine, griseofulvin and phenytoin. Therefore it has been suggested that alternate methods of contraception e.g. condom be considered when these drugs must be administered to a patient on oral contraception. Estrogens are inhibitors of the CYP enzyme and may alter the pharmacokinetics of drugs metabolized by this isoenzyme.

Anti-infective Agents

a) Antiretroviral agents: concomitant use of OCP's with some HIV-protease inhibitors and non-nucleoside reverse transcriptase inhibitors may result in substantial changes in the area under the plasma concentration curve of the estrogen and/or progestin. This is because some antiretroviral drugs are enzyme inducers (such as efavirenz, nevirapine, lopinavir, nelfinavir, ritonavir and tipranavir). It is advised that caution and additional/barrier methods are required when OCP's are administered with efavirenz, indinavir/r, lopinavir/r, nelfinavir, nevriapine, ritonavir, saquinavir and atazanavir. There are no clinically significant drug interactions expected between OCP's and nucleoside reverse transcriptase inhibitors.

b) Other anti-infective agents: it has been suggested that anti-infective agents which alter the GI bacterial flora may decrease the contraceptive efficacy of OCP's and increase breakthrough bleeding. The estrogen is thought to be affected by drugs which reduce colonic bacteria (such as antibiotics) which in turn reduces enterohepatic circulation and reduces the re-absorption of the estrogen and its metabolites from the gut. There is no enterohepatic circulation of progestins so these drugs are not affected by antibiotics. Manufacturers caution that concomitant use of anti-infective agents (e.g. ampicillin, chloramphenical, sulphonamides, nitrofurantoin) with oral contraceptives may result in decreased efficacy of the contraceptives. However the level of evidence that broad spectrum antibiotics reduce contraceptive effectiveness is generally poor.

c) Benzodiazepines Oral contraceptives appear to decrease oxidative metabolism by the liver of some benzodiazepines (e.g. diazepam), while they may increase metabolism of other benzodiazepines (e.g. lorazepam, temazepam) that undergo glucuronide conjugation in the liver. Although the clinical importance of these potential interactions between oral contraceptives and benzodiazepines has not been determined, alterations in benzodiazepine dosage may be necessary in some patients.

Conclusion

OCP's provide a cheap and effective means of birth control. In the setting of HIV, it is important for the health care provider managing a patient to discuss available options with the patient before deciding on prescribing COC's as the method for birth control. It is important to consider;

a) Issues of pill burden and thus drug adherence in patients that may already be receiving antiretroviral drugs and drugs for opportunistic infections. Sticking to a stringent timetable is pertinent for the success of OCP's.

b) The possibility of drug interactions between OCP's and antiretroviral drugs commonly used in first line therapy e.g. efavirenz and nevirapine.

c) Side effects that may potentially affect adherence must be discussed with the patient before initiation of OCP's. It is also important to monitor liver function tests in patients that are on antiretroviral drugs that are hepatotoxic and OCP's.

d) The patient must also be informed that OCP's do not offer protection from sexually transmitted diseases such as syphilis and gonorrhea.

OCP's are available free of charge at government health centers with family planning units and for minimal fees (e.g. 500/= per cycle) in private pharmacies across the country. It is important for a health worker to consider patient specific facts such as weight, current pill burden, history of heart disease, habits such as smoking and commitment to strict drug adherence before helping the patient decide on the most appropriate means of birth control.

For a detailed list of references used for this article please write to queries@atic.idi.co.ug

THE COMMONEST CANCER IN HIV:

Kaposi's Sarcoma

By Miriam Laker Opwonya-Oketta, MB ChB, DTH&H, MSc TMIH, DPPM. Coodinator ARV-Kaposi's Sacoma Study

What is Kaposi's sarcoma?

Kaposi's sarcoma (KS) is the most common cancer worldwide in people who are HIV positive. In Uganda it is also the most common cancer and accounts for 6 out of every 10 cancer diagnoses made in the cancer institute. It is a cancer of mainly the blood vessels and because blood vessels are found throughout the body, any organ may be attacked. Most of the time, KS affects the skin and the inside of the mouth. Many times it also grows in the intestines and the lungs. In some people it may be in the eyes, the bones and even the spinal cord.

Where did Kaposi's sarcoma come from?

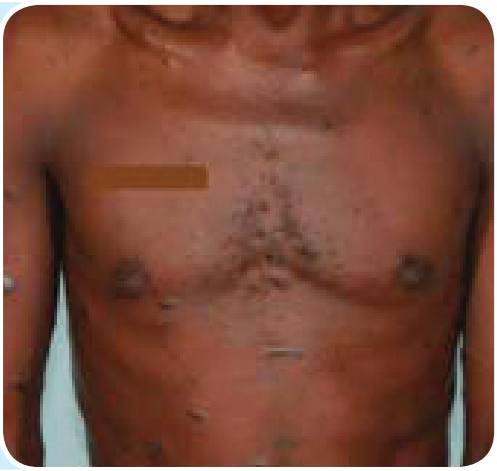
In the past, KS was known as a disease for older men. It was first discovered by a Hungarian professor called Moritz Kaposi in 1862 in elderly men in the Mediterranean area. This form of KS became known as "classic" KS. Subsequently, KS was found to occur in tropical Africa, where it became known as "endemic" KS. In Uganda, KS mainly affected men from areas with volcanic soils like around Mt. Muhavura in southwestern Uganda and around Mt Elgon in eastern Uganda. In the 1960's, as medicine advanced to transplanting organs, like kidneys, KS began to emerge among people receiving transplants. In these patients, KS was believed to have occurred because of medicines given to reduce the patient's immune system in order to allow the patient's body to accept the new organ. Looking back, the fact that "transplant-associated" KS occurred in people with a weakened immune system was the first sign that KS would become a substantial complication in HIV/AIDS. Up until 1981, the three known forms of KS (classic, endemic, and transplant-associated) were mainly just known to a limited number of interested doctors. This all changed in 1981 when KS began to appear in both young men and women in parts of the world which had never seen it before, such as the United States. These individuals were subsequently found to be infected with HIV, and the occurrence of KS was the sign of what became known as the HIV/AIDS epidemic. Today, KS is the most common cancer associated with HIV worldwide. In sub-Saharan Africa, the HIVassociated form of KS is also known as "epidemic" KS, which occurs in men and women in equal frequency. In part because of the HIV epidemic, KS is now the most common cancer among adults in Uganda and one of the most common forms of cancer in children.

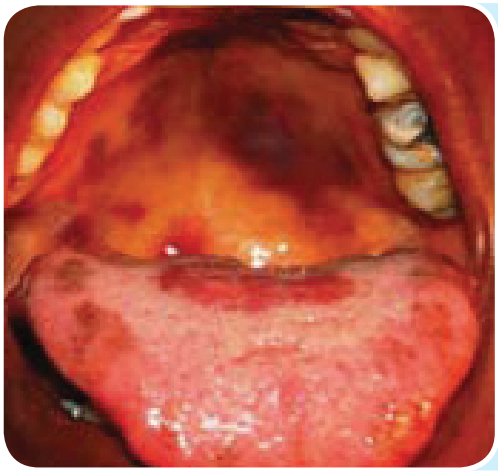
What causes Kaposi's sarcoma?

Although most people who have KS also have HIV, we now know that KS is caused by a virus called human herpesvirus type 8 (HHV-8), which is also known as Kaposi's sarcoma-associated herpesvirus (KSHV). This virus was discovered in 1994 after scientists had spent over a decade searching for an infectious cause for KS. Although HHV-8 was discovered only recently, we now know it has been circulating in humans for at least 10,000 years. In contrast, HIV is thought to have been introduced into humans sometime in the past 50 to 75 years. This helps to explain why KS was known to occur long before the HIV epidemic.

Who is infected with HHV-8?

While all persons who have KS are infected with HHV-8, many more people than just those with KS are also infected with the virus. In fact, in Uganda, about 4 out of 10 adults are infected with HHV-8. Other parts of Africa also have high a frequency of HHV-8, which is about 2 or 3 out of 10 persons. While HHV-8 infection is common in Africa, it is interestingly uncommon in most other parts of the world such as the Americas, Europe, and Asia. It is not known why Africans are so commonly infected with HHV-8 while persons in other parts of the world are not.



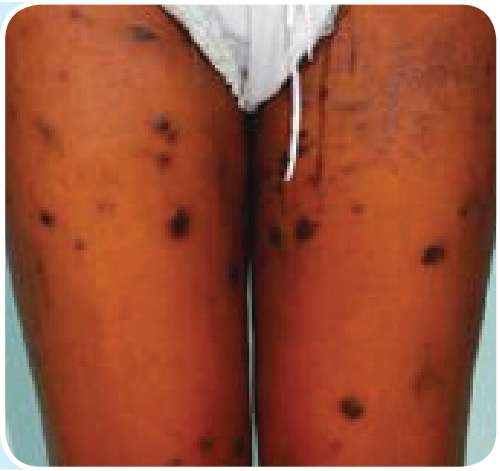


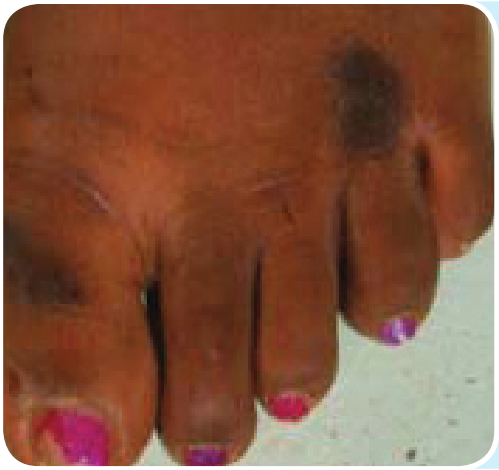
How is HHV-8 spread?

HHV-8 is found only in humans. It is not found in animals nor can it be picked up from the environment. Therefore, scientists know that HHV-8 is spread person-to-person among humans by exchange of body fluids. HHV-8 can be found in blood and genital secretions but is most commonly found in saliva. It is for this reason scientists believe that passage of saliva from one person to another is the most common way that HHV-8 is spread. Exactly how saliva is exchanged that allows HHV-8 to spread is unknown, but what is known is that most infection occurs in childhood. Indeed, about 3 out of 10 Ugandans are infected with HHV-8 by age 12, with most infections occurring between the ages of 2 and 8. Another 1 out of 10 Ugandans become infected in their adult years. Other less common ways to contract HHV-8 are by sharing injection drug use equipment or by receiving an organ transplant.

How come not every one has KS?

With such a large percentage of the population being infected with HHV-8, a big question is why does not everyone get KS? The answer to this intriguing question is that most persons who acquire HHV-8 are able to keep it quiet for the rest of their lives. HHV-8 is felt to never actually leave a person's body entirely, meaning that scientists can find traces of it even in older persons. However, most persons are able to keep the virus in check in a dormant (quiet) phase for all of their lives. It is only when the body's immune system is weakened does HHV-8 awaken and go on to cause KS. Because HIV/AIDS is one of the most harmful assaults on the immune system, it is no surprise that persons with HIV/ AIDS are at highest risk to develop KS.





How does one know that they have Kaposi's sarcoma?

KS can appear anywhere on the skin, where it may appear as a flat black or dark brown spot, patch or round swelling. It is usually not painful and not itchy. In the early stages these growths may be very small and innocent looking, causing no problems except for concern about their appearance. As the lesions progress, they may become raised, patch-like, and may join to form bigger patches. Later on, the lesions may develop wounds and start to produce fluids. When the growths are in the legs, or feet or on the arms or face, they may lead to swelling of the whole limb, the face and may also extend to the genitals. In the lungs KS may cause a dry cough, cough streaked with blood, or a person may run out of breath after mild exercise. If it is in the intestines, KS may cause one to vomit blood or pass blood with stool. Among persons who have KS in their lungs or intestines, the skin can in almost all cases be found to be affected as well.

The speed of development of KS varies from person to person. In some people it grows slowly while in others, it grows very fast with new spots occurring almost every week. In some people the tumor grows in only one part of the body while in others they spread to every part of the body. The different pattern of KS in each person is one of the most striking aspects of the illness.

Because virtually everyone with KS will have at least some spots on their skin, the best way for people to look out for themselves is to examine their skin. If you do notice any new spots on your body, you should inform your nurse, counselor or doctor about them. When your healthcare provider suspects that you have KS, he/she will send you to a doctor so that a small piece of skin, called a biopsy sample, can be taken and looked at under a microscope to confirm whether or not the growth is indeed cancer.

Can KS be treated?

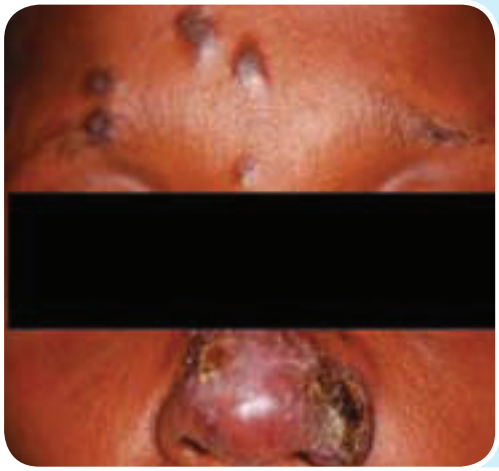
The good news about KS is that although it is the most common cancer in HIV, it can in many cases be treated. In the past, the typical way that KS was treated was with anti-cancer drugs, known as chemotherapy. Unfortunately, these drugs are not widely available in Africa,
are expensive and also tend to lower immunity by interfering with the cell manufacturing processes of the bone marrow. Interestingly, once antiretroviral drugs (ARVs) became available to treat persons with HIV/ AIDS, doctors began to observe that some patients with AIDS and KS had a shrinking in their KS lesion. This is especially encouraging as ARVs are becoming more and more available throughout the world. What is not known, however, is what percentage of patients with the HIV-associated form of KS will have their KS lesions shrink with ARVs and exactly which types of patients will have this good response. Furthermore, some scientists believe that particular forms of ARVs, known as protease inhibitors (PIs), may be especially powerful at treating KS.

Kaposi's sarcoma Immune reconstitution syndrome (IRIS):

Although many patients with KS will have a good response to ARVs, some may get temporarily worse. This phenomenon is called KS IRIS. Scientists do not know how often this happens or which patients are most prone. It has been seen that some people's existing KS lesions increase in size rapidly or they may develop new lesions, they may get pain or abnormal sensations like burning, pin pricks or numbness in their KS lesions, sometimes they may develop difficult breathing, dry cough or cough up blood after starting ARVs, others may experience swelling which may be limited only to the lesions of KS or may involve the legs, genitals, arms, face and sometimes that entire body. All these occur to varying degrees ranging from mild in some to fatal in others. When KS IRIS happens two things may occur

1. It may spontaneously resolve

2. It may progress to require anticancer treatment

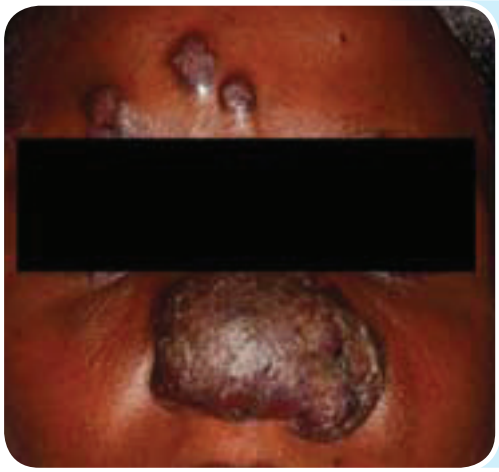


KS IRIS: Before

While there are still many questions about the best way to treat KS, one fact remains true, and it is that the earlier KS is diagnosed the better chances doctors have to successfully treat it. In this sense, KS is very much like other cancers: finding KS early and treating it early gives the patient the best chance at success.

THE ARVS FOR KAPOSI'S SARCOMA RESEARCH STUDY

Because there are so many questions about the best way to treat KS, doctors at the Infectious Diseases Institute and Uganda Cancer Institute at Mulago Hospital are conducting research on the topic. The Antiretrovirals for Kaposi's sarcoma (ARKS) research study is trying to find the best ARV drug for treating KS and which patients will get a good response to ARVs.



KS IRIS: After

People from all over Uganda who are not yet on ARVs and think they may have KS are encouraged to visit the research study at new Mulago Hospital or to mention this to their health care provider who can then make a referral to the study. When patients come to the research study, they are first given a skin examination. Those patients who are thought to have KS receive a biopsy of one of their skin spots to confirm if they have the cancer.

Persons who are found to have KS are then divided into two groups and provided free-ofcharge ARV therapy that contains a protease inhibitor (Aluvia) or a non-nucleoside reverse transcriptase inhibitor (Efavirenz). These are the most powerful drugs used to treat HIV. If patient's KS does not respond to ARVs, chemotherapy is also available free-of-charge. Each patient is closely examined every month for one year to see which group improves most. This study is also trying to find out how often HIV positive people with KS who are started on ARVs will develop KS IRIS and what determines whether one will develop IRIS or not. This is the first study of its kind in the world and hence promises to be able to inform the world about the best way to treat this common cancer. .

Our contacts

If you think you have KS and want to know more about this cancer you can send an email to

mlaker@idi.co.ug

or call 0751 940 010 or 0772312 326

Muteesi Brenda

I am Muteesi Brenda aged 21 years. Iam a primary seven candidate and I live at Makindye. I came to know of my HIV status in 2006 after testing in Rubaga Hospital following a long episode of fever and cough, I was given Septrin but there was no change until I was admitted in Mulago hospital. Investigations were done and the results showed I had TB, and then I was started on TB treatment immediately and discharged from the ward later. Although I was on TB treatment my health status continued to decline with my CD4 count decreasing and my heamoglobin level in blood was dropping: 2.0 mg/dl. Secondary to my poor health I was referred to IDC in July 2008 for further treatment hence joined the transition clinic. During my clinic appointment the doctor stopped me from the TB treatment for some time due to liver toxicity and then later switched me to injections and some tablets. I got a bit better and then I was put on ARV'S (CBV/EFV) for a month but these drug combinations worsened my health status with vomiting and diarrhea and dizziness, I was found to be anemic hence the doctor changed my ARV treatment to Truvada/Efv. Therefore having changed my drug combinations (ARV's) I started losing hope of getting any better but continued to take the medicine religiously. With the care and support from my family, fellow friends in the transition clinic and the home visit by the medical team. With lots of counseling and the help from two of spouses of the board members of IDI who visited me at the time when I was bed ridden , and agreed to pay for my nutritional fees, beddings and suit case were I would keep my clothing, I started regaining my hope. I am now healthy and continuing ARV medication and looking forward to resume school.

Ask ATIC

Francis Kalemeera, BSc, BPharm, MPS, HIV Clinical Pharmacist

Do you know how to use antiretroviral medicines to prevent transmission of HIV from the mother to the child during pregnancy?

We have written this article because you might be out there with ARVs for PMTCT and you have rather sketchy information on how to use them. As a medicines information centre, we are more than glad to give you practical and easily usable information on PMTCT. The information we give you is based on the Uganda PMTCT Guidelines.

Our guidance is based on zidovudine, lamivudine, and nevirapine, which are the recommended drugs for PMTC in the Uganda PMTCT guidelines. This is how they are used.

Information of the regimen

For the mother:

Zidovudine (AZT) and lamivudine (3TC) are given twice daily starting at 32-36 weeks of pregnancy. When labour starts a single dose of nevirapine (NVP) is given (Do not give NVP more than once). AZT and 3TC are continued twice daily for seven days after the single dose of nevirapine. (If the mother comes after 36 weeks of pregnancy, wait for labour. Give the single dose of nevirapine during labour and at the same time start AZT and 3TC twice daily for seven days.)

For the neonate:

When the baby is born, be sure that you give a single dose of NVP within 72 hours of life. On that same day that you give NVP, start the AZT which you should give twice daily for seven days.

Information on the doses

For the mother:

The mother should receive 300mg of AZT twice daily and 150 mg of lamivudine twice daily. Frequently, a combination of AZT and 3TC is available. This combination contains the amount of AZT and 3TC in the amount that is required, i.e. AZT/3TC: 300/150. The single dose of NVP is 200 mg, i.e. one tablet.

For the neonate:

NVP is given at a dose of 2mg per kg of body weight, while AZT is given at a dose of 4mg per kg of body weight. As an example let's take a neonate of 3.3kg.

For each kg of body weight, the child should be given 2mg of nevirapine. This is calculated as follows:

3.3 x 2 = 6.6mg

And 4mg of AZT, which is calculated as:

4 x 3.3 = 13.2mg

How to get this amount of drug for the neonate.

Because the preparations of NVP and AZT are syrups you can get the amount of drug you need based on the concentration of the syrup. For this example, we will consider only NVP.

NVP syrup concentration is 50mg/5ml. This means that 1 ml contains 10mg. But, you want 6.6mg. This is how you calculate the amount of syrup this baby needs:

10mg is equivalent to 1ml

Which means that 1 mg is equivalent to 1ml divided by 10mg (1/10)_

6.6mg is therefore equivalent to (6.6mg x 1ml/10mg)

$$\frac{6.6 \times 1}{10}$$

The answer is 0.66mls *(You can round this off to 0.7mls).*

Get a measuring instrument graded or marked well (e.g. a suitable syringe) to enable you see the amount of syrup between 0.1 and 1 ml. Measure off 0.7ml, since 0.66 may be difficult. At this point, you can measure the amount of NVP in the 0.7ml through a backward calculation. We recommend the backward calculation because with it you can ensure that you are giving the right dose. Do the backward calculation like this:

5mls contains 50mgs

1 ml contains 1 mls x 50mg/5ml which is equal to 10mg

0.7mls therefore contains 0.7 x 10 which is equal to 7mg

NB: Use the same principles to determine the dose of AZT in the child.

If you would like, do the following:

1. Calculate the dose of AZT for the baby in the example above

2. Carry out a calculation for the dose of AZT and NVP for a baby weighing 2.6 kg.

When you are through and this has been a good learning session for you, **BEEP 0414-307-245 or 0414-307-228 or 0312-307-245 or 0312-307-228** to give your answer.

Please note: Single dose nevirapine can still be used if the other drugs are not available or if there is clinically sound reason why the other drugs cannot be used. ATIC is ready to share any information on PMTCT (and others) with you.