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PMTCT : THE UGANDAN JOURNEY

By Dr. John Bwanika MBChB, Medical Officer – IDI

For close to a decade following the first discovery of the existence of the HIV virus, not much was known regarding prevention of new infection from a mother to her child.

Prevention of Mother To Child Transmission (PMTCT) constitutes all the measures put in place to ensure that babies born to HIV +ve mothers can be free from the disease.

According to WHO, this constitutes of 4 main approaches

- Primary Prevention of HIV in the general population
- Prevention of unintended pregnancies in HIV infected women
- Prevention of Mother to Child transmission of HIV
- Care and support for women living with HIV and AIDS.

WHERE WE HAVE BEEN……

The first major breakthrough for PMTCT was in 1994 when American and French researchers proved that Zidovudine (AZT) in pregnancy could reduce vertical transmission by 65% in the ACTG 076 Study.

Initial studies used AZT starting at 14 weeks of gestation, through labour and then 6 weeks postnatally for the infant. Later, commendable reduction in vertical transmission of up to 50% was demonstrated even when AZT was used from 36 weeks with or without infant dosing! However, the simplest and perhaps the most feasible PMTCT regimen was adopted from the HIVNET 012 Study..

The HIVNET 012 study carried out in Uganda between 1997 and 1999. It's main objective was to determine the efficacy of oral AZT and the efficacy of oral NVP for prevention of HIV-1 vertical transmission.

Pregnant HIV-1 infected women enrolled in the study were randomly assigned to receive either NVP (200 mg to the mother and 2 mg/kg for neonates within 72 h of birth) or AZT (600 mg at labor onset and 300 mg every 3 h until delivery, and 4 mg/kg twice daily for neonates for 7 days) to prevent vertical HIV transmission from mother to child. A total of 645 mothers were enrolled in the study. 313 were part of the NVP arm, 313 were part of the AZT arm. Infants were tested for HIV-1 by RNA PCR at birth, 6-8 weeks, 14-16 weeks, and at 12 months of age. At 18 months of age, the children were tested by HIV-1 antibody. HIV-1 free survival and HIV-1 transmission were then assessed.

There was significant reduction in the risk of perinatal HIV transmission among breast feeding women in Uganda by 47% at 14-16 weeks and by 41% at 18 months. Based on its simplicity, low cost, and efficacy, single dose NVP (sd-NVP) provided at the onset of labour and NVP syrup provided to the infant within 72 hours of delivery provided a deliverable regimen which became the cornerstone for expansion of prevention of mother-to-child transmission (PMTCT) activities throughout much of the developing world.

Despite the favourable results of the HIV012 NET Study, concerns over the emergence of NVP resistant mutations after single dose NVP made its suc-

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INSIDE STORIES

EDITORIAL

In the 80's and 90's many of us lost loved ones to the AIDS scourge that had seemingly overwhelmed Uganda. It seemed then like all we ever did as Ugandans was bury, bury and bury more loved ones. We lost so many people to the mysterious slimming disease that was finally found to be AIDS; this disease that did not distinguish between doctor, minister, priest, teacher, or peasant Ugandan but killed all in the same painful way.

In this December issue of The ATIC Newsletter, we look at HIV Prevention which has since grown from 1987 when the first AIDS Control Program was introduced with the backing of the Government.

We revisit the old HIV Prevention methods like the ABC's (Abstain, Be faithful, Use Condoms) that brought us relief against AIDS as HIV prevalence rates were lowered from 29% in the 80's, 15% in the 90's and even further down to about 6.4% by 2006.

Even as we feature the progress Uganda has made in HIV Prevention, we can not ignore the growing signs of new HIV infections that could push the prevalence rates back up to high numbers. That is why in this issue, we also examine the strength of the evidence for novel prevention methods. We look at new methods like Circumcision, Microbicide gels, and Pre Exposure Prophylaxis.

The reality of an HIV free world is still possible, and we hope you will read on, as we further discuss the old and new issues pertaining to HIV Prevention in Uganda.

Sheila Karamagi - Editor

There was significant reduction in the risk of perinatal HIV transmission among breast feeding women in Uganda by 47% at 14-16 weeks and by 41% at 18 months.

cess controversial in some circles.
Follow up studies of this trial found that 25% (70 out of 279) of NVP-exposed women had evidence of NVP resistance at six weeks postpartum, as did 46% (11 out of 24) infants who became infected with HIV.
Because cross -resistance with other agents in the NNRTI class, such as EFV, is very common, this caused concerns about the reduced effectiveness of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI's) in future HAART regimens.

In Uganda, the Ministry of Health began offering PMTCT services in a small number of ANC clinics in January 2000.
The trial PMTCT program included counseling and rapid testing for all women attending ANC clinics as well as provision of sd-NVP for the mother and NVP syrup to the baby.

With increasing need and more resources being channeled towards PMTCT, the number of PMTCT delivery service sites was greatly expanded between 2005 and 2007 with emphasis on providing services to rural populations.
Consequently, the number of health facilities providing routine HIV counselling and testing for pregnant women increased, raising the uptake of HIV testing to 80% of all women attending antenatal clinics and increasing the proportion of HIV positive pregnant women receiving antiretrovirals for PMTCT from 12% in 2005 to 34% in 2007 and to 53% in 2009

In 2006, the WHO released new recommendations for PMTCT (Table 1) following findings from clinical trials done in Asia. The trials revealed that there was an 80% reduction in MTCT when sd-NVP for the mother and child were given in addition to the standard AZT regimen that started at 28 weeks.

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Table 1: 2006 WHO recommendations for PMTCT

MOTHER	INFANT
AZT prophylaxis starting at 28 weeks through delivery. AZT/3TC instead of AZT if mother captured after 32 weeks. In both cases above, give single dose NVP during delivery and AZT/3TC for 7 days postpartum. * If mother has CD4+< 350 or is stage III or IV, initiate on lifelong HAART	• single dose NVP within 72 hours of birth • AZT syrup for 1 week after birth.
INFANT FEEDING : Exclusive breastfeeding for the first 6 months unless replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) • At 6 months, continue breastfeeding with additional complementary food if AFASS is not met • Wean within a period ranging from about 2–3 days	

Uganda quickly adopted these guidelines: AZT/3TC (Combivir) + single dose NVP followed by single dose NVP to the infant and a week of AZT syrup were used for PMTCT in higher level facilities.

Lower level health centers with fewer resources continued to use single dose Nevirapine only for the mother and single dose NVP to the infant within the first 72 hours of delivery for the infant.

WHERE WE ARE HEADING TO……

In the past few years, new evidence has emerged on;

- Benefits of earlier initiation of ARV prophylaxis during pregnancy in reducing mother to child transmission.
- Effectiveness of ARV prophylaxis provided during breast feeding in reducing MTCT.
- Benefits of breast feeding as opposed to replacement feeding in babies born to HIV positive mothers in developing countries

In response to this evidence, WHO has produced revised guidelines for PMTCT (Table 2). New WHO recommendations consist of 3 major changes intended to substantially reduce MTCT.

1. Initiation of ARVs much earlier in pregnancy (14 weeks instead of 28 weeks)
2. Provision of ARV prophylaxis during breast feeding (ARVs to mother or baby)
3. Breast feeding strongly recommended as preferred infant feeding method and for a longer time (12 months)

TABLE 2: 2010 WHO recommendations for PMTCT

OPTION A	OPTION B
Mother If CD4+ > 350, Antepartum AZT (from 14 weeks) sdNVP+ AZT/3TC at delivery AZT/3TC for 7 days post partum	Mother If CD4+> 350 Triple ART from 14 weeks of pregnancy until 1 week after breastfeeding has stopped. If CD4+< 350; Lifelong ART.
Infant If breast feeding; daily NVP from birth until 1 week after breastfeeding has stopped. If not breastfeeding or mother on ART---give NVP for 6 weeks	Infant NVP for 6 weeks (regardless of whether mother is breastfeeding or not.)
INFANT FEEDING: Where breastfeeding is judged to be the best option: • Exclusively breastfeed for the first 6 months, introduce appropriate complementary food thereafter, and continue breastfeeding for 12 months • Wean gradually within 1 month	

Uganda as a country has adopted Option B but due to limited resources is practicing Option A with plans to phase into Option B when resources become available

Overall, we can see that Uganda has made big strides in the campaign to prevent HIV spread through MTCT. According to the latest figures, new HIV infections in Uganda occurring from MTCT have dropped from 25% in 2008 to 18% in 2009. These figures however may be higher since many births in Uganda occur away from the health centers.

In Uganda's 2010 country progress report, PMTCT has been placed high on the agenda with a target of halving mother-to-child transmission rates by 2012.

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THE MICROBICIDE VAGINAL GEL: NEW AMMUNITION FOR AN OLD BATTLE

By Dr. Moses Nsubuga Kakyama
MBChB, Medical Officer- IDI

The HIV/AIDS juggernaut moves relentlessly forward, ploughing adults, youth and children alike, and, in its wake, leaving a sea of suffering, shattered dreams and futures that never will be.

The advent of life prolonging antiretroviral therapy has done its best to reverse this trend.
According to the UNAIDS Report 2010, an additional 1.2 million people received antiretroviral therapy in 2009,bringing the total number of people receiving treatment in low and middle income countries to 5.2 million, a 30% increase over 2008.

This is the good news, the flip side of the coin is that this figure represents only 36% (about 5.2 million) of the 15 million people in need of antiretroviral therapy in these countries.
With the slowing down of global funding for HIV programs in low and middle income countries, this percentage may not significantly improve in the short term.

SubSaharan Africa's main hope in stemming the HIV epidemic therefore still lies in primary prevention.
Traditionally there have been 3 main prevention strategies which have come to be commonly known as the ABCs and which have resulted in a noted reduction in global HIV incidence rates. An estimated 2.6 million people became newly infected with HIV in 2009, nearly 20% fewer than the 3.1 million people infected in 1999.

However, despite this decrease in overall incidence, Primary prevention still remains a major challenge in women, who constitute 52% of the global total of people living with HIV and up to 60% in SubSaharan Africa.
This is mainly because all the existent prevention methods are male intiated or male controlled. In SubSaharan Africa, gender norms related to masculinity can encourage men to have more sexual partners and older men to have sexual relations with much younger women while norms related to femininity can prevent women – especially young women – from accessing higher education or HIV information and services.

These two factors contribute to higher infection rates among young women (15-24 years) compared to young men.
Although the use of condoms reduces the risk of HIV transmission through sexual contact, using condoms requires the co-operation of the male partner. This disadvantages women who are sometimes dependent financially and socially on the men and therefore can not negotiate or insist on condom use

This makes the need for prevention methods that give women a chance to have full control of their lives important for the successful fight against HIV acquisition.

One of the first international advocates for female initiated prevention techniques was South African epidemiologist Zena Stein who published "HIV Prevention: The Need for Methods Women Can Use," in the American Journal of Public Health in 1990. In her paper, she proposed that the empowerment of women was crucial for the prevention of HIV transmission to women, and that prophylaxis must include procedures that rely on the woman and are under her control.

In response to this and other concerns, work on the microbicide vaginal gel began.

The microbicide vaginal gel is a new product that women can insert vaginally to protect themselves from HIV . A number of vaginal gel studies have been conducted over the years with mostly disappointing results.

Microbicide gel trials carried out in Nigeria, Uganda and South Africa either showed that their-micorbicide vaginal gels were not effective in preventing HIV transmission during vaginal sex (Uganda, South Africa) or that they slightly increased the risk of aquiring HIV(Nigeria)

However, at the annual International Aids Conference held in Vienna earlier this year, findings from the CAPRISA Study gave scientists a glimmer of hope that an efficacious microbicide gel could yet be licensed that would forever change the scope of HIV prevention.

The CAPRISA 004 trial, conducted in South Africa, looked at the effect of a vaginal microbicide gel containing Tenofovir disoproxil fumarate, an NRTI, in the prevention of HIV in women.

The study was a randomized double-blinded controlled trial involving 889 women aged 18 to 40 years, who were HIV negative and not pregnant at the beginning of the trial.

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The study participants were randomized to the two arms of the study, one arm receiving 1% tenofovir gel and the other arm receiving placebo. Participants in both arms received treatment of STDs, routine counseling and condoms and were followed up to for at least one year up to a total of 30 months with monthly HIV tests.

Findings from the trial showed that the Tenofovir gel reduced HIV acquisition by an estimated 39% and up to 54% in women who adhered well (more than 80% adherence). Tenofovir gel was also shown to reduce the incidence of vaginal herpes simplex, which could also potentially reduce further the risk of acquiring HIV.
News of the findings of this study were received with much jubilation across the scientific world as it opened a whole new window of opportunity for prevention.

Other microbicide gels in development, mostly still in the laboratory and animal stages have also shown positive results and were presented at the Microbicide Conference 2010 held in Pittsburgh, USA.
Papers were presented on gels containing the protease inhibitor darunavir, integrase inhibitors, fusion inhibitors, entry inhibitors and a combination gel containing darunavir and dapivirine, an NNRTI.

Studies on the combination gel containing both darunavir and dapivirine showed impressive results in its ability to reduce HIV infection of human genital and colorectal tissue samples.

Laboratory studies on the entry inhibitor, maraviroc, which binds to the CCR5 receptors thereby preventing entry of the virus, showed that it was most effective when given on a continuous basis. This has laid ground for investigations into sustained release forms of the drug such as a vaginal ring. This mode of delivery, if successful would a go a long way in tackling adherence issues in future microbicide gel trials.

As a result of all this work being done, the future looks bright, especially for the women who will for the first time have a chance in truly determining their destiny.

PARTNERS PrEP STUDY

Dr. Fridah Gabona, MBChB
IDI-Jinja Prep Trial

The study is testing two types of antiretroviral drugs; tenofovir disproxil fumarate (TDF) and Truvada®, which is a co-formulation of emitricitabine/tenofovir disproxil fumarate (FTC/TDF), for safety and efficacy in pre-exposure prophylaxis. These are given to the HIV negative person in a discordant relationship.

PrEP is Pre- exposure prophylaxis. The Partners PrEP Study is a three arm study were by a computerised system is used to randomly assign patients to one of the study arms. This study is being conducted among HIV-1 discordant couples and it is one of the eight large trials of PrEP that are ongoing or planned worldwide, reflecting a high enthusiasm for PrEP as a potentially valuable new HIV prevention strategy.

The trial is being implemented in 9 sites- Thika, Nairobi, Kisumu, and Eldoret in Kenya and Kampala, Kabwohe, Mbale, Tororo and Jinja in Uganda. 4700 HIV-1 uninfected individuals with in HIV-1 discordant relationships were estimated to be needed for this endpoint driven trial. Jinja site was expected to enroll between 300 and 500 couples. Of the 9 sites, Jinja was the last to be activated and enrolled her first couple on 1st June 2009. However, overall, the study began enrollment in 2008 and reached enrollment accrual on 5th November 2010.

The study is testing two types of antiretroviral drugs; tenofovir disproxil fumarate (TDF) and truvada, which is a co-formulation of emitricitabine/tenofovir disproxil fumarate (FTC/TDF), for safety and efficacy in pre-exposure prophylaxis. These are given to the HIV negative person in a discordant relationship who can either be male or female. The Negative person can randomly be assigned by a computer system to the TDF arm, the TDF/FTC arm or the Placebo arm. A placebo is an inactive substance (often a sugar pill) given to a patient in place of a medication. In this trial, neither the researchers nor the participants know who is on active arm (TDF or TDF/FTC) or on placebo and across the arms risk reduction counseling and condoms are given. The participants are enrolled and followed up for 24 - 36 months.

Because HIV-1 uninfected individuals within HIV-1 discordant relationships are at a very high risk of HIV-1 acquisition, new strategies that can prevent HIV-1 transmission among HIV-1 discordant couples, while allowing pregnancy to occur safely, are required. Epidemiological studies indicate that in subSaharan Africa one in two HIV infected persons is in a stable relationship with an HIV uninfected partner. The UNAIDS 2008 global

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epidemic report suggests that in Uganda, adults were more likely to contract HIV-1 if they are married and over 30 years than if they are single and in their twenties. Further more, modeling in Uganda revealed that 43% of all new infections in adults (15-49 years) in 2008 were among persons in discordant relations. Studies have also shown that due to cultural norms and traditions, the desire to have children among HIV infected people is high, especially in the young age group, and HIV discordance creates a serious dilemma for fertility decision-making in couples. Research done by Jolly Beyeza-Kashesya et al among HIV discordant couples in Kampala showed that only 56% of all HIV discordant couples consistently used condoms and that consistent use of condoms was less likely to occur among respondents who desired to have children.

Pre-exposure chemoprophylaxis, in which an HIV uninfected person in a discordant relationship is given an antiretroviral medication to maintain blood and genital drug levels sufficient enough to prevent HIV-1 acquisition, has been proposed as a potential HIV-1 prevention strategy.

The rationale for this approach is supported in part by the fact that studies have shown that in an HIV infected pregnant woman, a single dose of an antiretroviral called Nevirapine can prevent transmission of the virus to their babies, and by studies in non human primates show that daily antiretroviral use can protect against infection. While the concept has yet to be proved for HIV prevention, PrEP works to prevent against other infections, like malaria.

Both TDF and FTC/TDF have been proposed as possible safe and effective medications to serve as pre-exposure chemoprophylaxis. Scientists have focused on TDF and FTC/TDF in oral PrEP studies because they require only a single daily dose, have relatively low rates of side effects and because there is significant data on their long-term safety and resistance profiles in HIV positive people.

The potential for efficacy, safety, and cost for these two medications justifies evaluating both against a placebo, in a single clinical trial. This trial will answer whether PrEP decreases HIV-1 acquisition among HIV-1 uninfected individuals within a discordant relationship, and will benefit a very large heterosexual population who are at a very high risk of HIV-1 acquisition, if found effective and safe.

The study has two main research objectives which include:

1. To determine if once daily oral PrEP with TDF or FTC/TDF provides additional protective benefit in preventing HIV-1 acquisition among HIV-1 uninfected persons within a heterosexual HIV-1 discordant relationship who are also receiving standard prevention interventions.
2. To assess the safety of daily PrEP using TDF or FTC/TDF by comparing rates of adverse events (AEs) among HIV-1 uninfected individuals randomized to TDF or FTC/TDF PrEP to placebo.

Data analysis by the University of Washington International Clinical Research Center (ICRC) is expected to start in the last half of 2012, followed by dissemination of study findings.
Results of the main protocol questions have not been analyzed yet. However, we have had four Data Safety Monitoring Board (DSMB) reviews to date. The DSMB is a body responsible for reviewing of the overall study progress and advising on its protocol implementation. In reviewing the unblinded data for this study, the DSMB did not find any significant concerns to warrant modification of the study protocol.

Although results of the main protocol questions from this study have not been analyzed yet, results from a similar trial carried out in the United States and 10 other countries, called The Pre-Exposure Prophylaxis Initiative, or iPrEx study were recently released.

In this trial 2499 healthy men, who have sex with men, were randomly assigned to take either one tablet of TDF/FTC or a placebo once a day.

At the end of the trial, there were 36 infections in participants who received Truvada and 64 in recipients who took the placebo. Researchers calculated that the use of Truvada reduced new HIV infections by an estimated 43.8% overall when compared to placebo.

The iPrEx results were heralded by international organizations as a first step toward other effective and potentially more feasible options for HIV prevention.

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CIRCUMCISION AS A MEANS OF HIV PREVENTION: FACT OR MYTH?

Dr. Stella Zawedde- Muyanja
MBChB, Medical Officer- ATIC

The decision by authorities in South Africa's KwaZulu-Natal province to circumcise prisoners as a way of combating the spread of HIV and AIDS in South Africa's prisons recently made world news headlines on the BBC.
Although some people from outside South Africa were skeptical of the move, most within South Africa welcomed it. The South Africa's Prisoners Human Rights Organization said that circumcision might be of best interest to the inmates and welcomed the move as long as inmates were properly informed.
This story was followed about a week later by Rwanda's announcement to circumcise two million men over the next two years in a major initiative to tackle AIDS. Work on the Rwandan project began in 2008 after studies indicated that circumcised males are 50 -60% more likely to be protected against HIV during sexual intercourse. Rwanda then went ahead to train health workers to carry out the procedure and has now come to the roll out phase. Rwanda's authorities are first targeting men in the armed forces (soldiers and police), as well as university students. They are also campaigning for all male infants to be circumcised.

Male circumcision is a minor surgical procedure done by the removal of foreskin from the penis.
It is an ancient practise that dates way back to biblical times, when Jewish boys, according to tradition, were circumcised on the 8th day after birth. This practise continues among Jews to this day and is practised by Moslems the world over.

Apart from being done for religious purposes, circumcision may be done as part of tradition. In some African tribes e.g. the Luo in Kenya, the Bagishu in Uganda and the Xhosa in South Africa, circumcision is a ritual rite of passage into manhood.

Circumcission may also be practised as medical procedure to cure ailments like phimosis, and paraphimosis.

The protective effect of circumcision against medical ailments was observed as far back as the 1930s when it was proposed that neonatal circumcision may protect against cancer of the penis. This claim was first made by an American, Dr. Wolbarst who reviewed 1,103 cases of penile cancer in the US and found that non of them occurred among Jews although 33 cases would have been expected since 3% of the American population was Jewish then.

His claims have since been validated. In the 55 years following this finding, there have been 750-10,000 cases of penile cancer in the US with 200 deaths annually. Of these cases, only 10% of the affected men have been circumcised.
In the field of HIV prevention, one of the first paper suggesting a protective effect of MC against HIV infection was published in 1986. Since then, many, observational studies have suggested a protective effect of male circumcision on HIV acquisition in heterosexual men.

In 2002, three randomised controlled trials to assess the efficacy of male circumcision for preventing HIV acquisition in men commenced in Africa. The trials were carried out in Kisumu, Kenya , in Rakai , Uganda and on Orange Farm, South Africa.

In Uganda, 4996 uncircumcised, HIV-negative men aged 15-49 years who agreed to HIV testing and counselling were enrolled. Men were randomly assigned to receive immediate circumcision (n=2474) or circumcision delayed for 24 months (2522). HIV testing, physical examination, and interviews were repeated at 6, 12, and 24 month follow-up visits. The primary outcome was HIV incidence. Analyses were done on a modified intention-to-treat basis

In South Africa, a total of 3,274 uncircumcised men, aged 18–24 years, were randomized to a control or an intervention group with follow-up visits at months 3, 12, and 21. Male circumcision was offered to the intervention group immediately after randomization and to the control group at the end of the follow-up. The data was analyzed in intention-to-treat, univariate and multivariate analyses.

In Kisumu, a total of 2,784 uncircumcised men were randomized (1,391 in the intervention group and 1,393 in the control group). The median age of randomized participants was 20 years. Male circumcision was offered to the intervention group immediately after randomization and to the control group at the end of the follow-up . The primary end point was HIV acquisition.

All three trials were stopped early due to significant findings at interim analyses.

Combined results from all the trials showed as a relative risk reduction of acquiring HIV of 50% at 12 months and 54% at 21 or 24 months following circumcision.
A meta-analysis of the secondary outcomes measuring sexual behaviour for the Kenyan and Ugandan trials and found no significant differences between circumcised and uncircumcised men and the incidence of adverse events following the surgical

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circumcision procedure was low in all three trials.
Following these trials, the World Health Organization (WHO)/Joint United Nations Program on AIDS (UNAIDS) recommended adult male circumcision for the prevention of heterosexually acquired HIV infection in men

However WHO cautions that Male Circumcision should not replace other known methods of HIV prevention and should always be considered as part of a comprehensive HIV prevention package, which includes the existing ABCs of prevention.

Studies on acceptability of circumcision in traditionally non circumcising communities across sub Saharan Africa have shown that circumcision is acceptable in Africa.
A metanalysis of 13 studies from nine countries showed that an average of 65% (range 29–87%) of uncircumcised men were willing to become circumcised. 69% (47–79%) of women favored circumcision for their partners, and 71% (50–90%) of men and 81% (70–90%) of women were willing to circumcise their sons.

Studies to detect the feasibility and cost effectiveness of circumcision roll out in communities in Sub Saharan Africa have found the practice to be both feasible and cost effective. A mathematically modeled cost effectiveness analysis of circumcision that was done in South Africa showed that for every 1000 men circumcised, the procedure cost 180 dollars for every HIV infection averted (a total of 55,000 dollars). but saved a total over 2 million dollars in life time costs of HIV treatment

At about 900,000 new infections every year, SubSaharan Africa needs more prevention methods that work . So we may ask ourselves, despite the available evidence, why does controversy still surround medical male circumcision as a means of HIV prevention?

Part of the reason may be that in the past, circumcision practices were largely culturally or religiously determined and as a result there are strong beliefs and opinions surrounding its practice. People coming from communities that practice it are more likely to have opinions in favor of it while those coming form communities that don't practice it are likely to have opinions against it. Most of the opposition to circumcision as a means of HIV prevention comes from developed countries where circumcision may be largely unpracticed.

A statement by US Doctors Opposing Circumcision states that results from the 3 randomized trials should be interpreted cautiously since all the trials were stopped early and this may have exaggerated the benefits of medical male circumcision.

In the same statement, the doctors state that since medical male circumcision was only seen to reduce the incidence of female to male transmission of HIV and does not have an impact on any other mode of transmission of HIV, e.g. male to female heterosexual transmission and homosexual transmission; it is unlikely to have an impact on the overall HIV epidemic in Sub Saharan Africa.

They also express their fears that circumcision may create a false sense of security among circumcised men that may make men more reluctant to use condoms. Condoms when used consistently and effectively have been shown to reduce the risk of HIV transmission.

Other concerns against the roll out of medical male circumcision in Sub-Saharan Africa are

- Lack of adequate funds and / or adequately trained health care workers to be able to safely roll out this procedure
- Increased patient burden on an already over stretched health care system.

These concerns aside, practitioners in SubSaharan Africa where HIV is hyperendemic, where traditional prevention methods have failed to curtail the epidemic and where access to lifesaving ARV medicines are available to only 36% of people who need them, would do well to examine the evidence and look at the possible benefits of medical male circumcision.

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TASK SHIFTING

By Brenda Mitchell
Pfizer Global Health Fellow 2010
Nurse Trainer Fellow

FROM THE EDITORIAL TEAM:

When IDI opened its doors in 2004, there were around 50 patients (called "friends" here at IDI) attending each day. As we write, this number has since increased to around 300 per day. In order to cope with these large numbers IDI has turned to Task Shifting. Task Shifting is the name now given to a process of delegation whereby tasks are moved, where appropriate, downstream to less specialised health workers. By reorganizing the workforce in this way, task shifting can make more efficient use of the human resources currently available. For example, when doctors are in short supply, a qualified clinical officer or nurse could prescribe and dispense antiretroviral therapy. Further, community workers can potentially deliver a wide range of HIV services, thus freeing the time of qualified nurses. Training a new community health worker takes between one week and one year depending on the competencies required. This compares with three or four years of training required for a nurse to fully qualify. (*ref* WHO Task Shifting booklet).

Our readers from upcountry settings will be more familiar with Task Shifting and will be pleasantly surprised that we are applying it here in a setting that could be passed off as "well resourced".

Wherever the task shifting model is applied, it is important to equip the personnel who will be taking on new roles with the skills and knowledge that are essential for them to take on their new role.

Brenda Mitchell, a Pfizer Global Health Fellow, was seconded for 6 months as a Nurse Trainer Fellow. Her scope of work has been to survey the training needs of the nurses; develop and implement an orientation and training programme; annual development plan and to build nursing school relationships. The overarching goal is to have a sustainable training programme which equips nurses to meet the needs of this dynamic environment.

She shares with our ATIC readers her experience and how she has been able to work with and motivate our nurses here at IDI. We hope all of us can draw from her experience and replicate these in our health facilities…….

…….. As an outsider, "Muzungu", coming into the department, I needed to learn about the Nursing Team and to gain trust before starting on my work here.

We did a "3 Things" exercise at our first meeting. Each nurse had to write down 3 things they like about their job and 3 things that frustrate them. I collated the positives and we have A3 printouts in the Nurse Visit area as a reminder of what makes their work rewarding. Positive reinforcement and affirmation statements can be really impactful.

Some of the positive findings were,

- All nurses agreed that IDI is a great place to work and they feel part of an important team environment
- Senior management has been extremely supportive in driving change in areas like the Nurse Visit room. (The Nurse visit room is currently being expanded to include areas where nurses can conduct private clinical exams.) This change will be a huge step forward in allowing confidential and respectful Nurse Visits which has a positive impact on the care of our "friends" and the job satisfaction of the nurses.

I then set out to address the negative concerns because I knew that trying to implement a training programme without first addressing concerns and giving support would be folly.
Health workers and Health managers in other settings should be aware of the need to maintain self-esteem and continue to look at ways to maintain a highly motivated team.
Unfortunately it only takes one or two de-motivated team members to affect many around them, so working on motivation for the team is important. To have a motivated and driven team is vital to the team's success. Re-igniting the spark to get the best out of a team takes time and effort but it is all well worth it because motivated teams are much easier to train and to retain. The three main areas I worked on with the nurses are :

Self Esteem

- Positive reinforcement – catching your team doing something well and recognising it can have a major effect. Telling staff at appraisal time they have done well is not enough. Praise good work, effort and ethics when you observe it. We all know how it feels to have recognition for a good job done we need to recognise each other and share it at that time.

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- Peer recognition is the most powerful of all. Starting a "Nurse of the Month" award has been powerful in many ways. Writing down what someone did and how it made you feel also helps the person recognising good work.

Goal Setting

Setting work goals is important and is not just for those with high career aspirations. There are many areas in the clinic where expertise and development can occur.

Setting goals also leads well into performance and personal development plans. The following template that we used in goal setting can be replicated in other health facilities.

- What do I want from my career – stated in the positive
- Do I need help to achieve this (another person/course/resource) or do I need the actions of others first?
- What will it look like when I get there? – evidence.
- What will this outcome get for me? (What will motivate me towards this?)
- Are there any barriers where this outcome will not work for me? (What can stop me achieving this?)
- Context – where and when do I want this to happen What resources do I need to get there?
- What is the first action I must take to achieve this? (When will I start?)

Mentoring

The mentoring programme has commenced and we have 6 Nurses currently being formerly trained for this. We have worked through documentation to use to ensure both the mentee and the mentor gains from the experience. This will be used as a measurement tool for both Mentor and Mentee for effectiveness and skill set development.

Each new Nurse to the clinic will be assigned at Orientation to a Mentor and ongoing assessment will be part of the process. These Nurses will also share their expertise in different areas with others who are interested in learning more specific detail. The Mentor programme could easily be expanded in time to assist with upcountry clinics. The Mentors could visit and work side by side with Nurses in the clinic and the rural clinic Nurses could also gain experience with some time spent at IDI. Again, this can be replicated in other settings and gives senior Nurses recognition for their skill and experience whilst up skilling new or inexperienced Nurses to a high standard.

By focusing on personal development, continued medical education and cross-functional teamwork, we will ensure IDI nurses continue to play their new roles well and deliver the support required of a centre of excellence. This in turn will translate into improved service delivery as we better ourselves and better our service.

My 6 months at IDI have flown. There is so much more I would like to achieve with the Nurses and the clinic in general. The work at IDI is inspiring and although I am here to help with development and training, I truly believe that I am the one who will have learned the most from this experience.

Brenda Mitchel(4th right) with the IDI Nursing Team.

ask ATIC

Barbara Namirembe Muwonge ATIC – Pharmacist

I am a clinical officer with a private health care facility in Kampala. When I received HIV training we were told that when initiating ART, we should always use 3 drugs. We were told this was because the use of less than 3 drugs predisposed patients to drug resistance.

However in PMTCT, we use monotherapy and dual therapy to prevent vertical transmission in mothers who do not need ART for their own health.

Does that not expose these mothers and babies to ARV drug resistance?

Q

A

Your concern over the development of resistance when using mono or duo therapy in management of pregnant mothers who do not need ART for their own health is valid. The use of just one or two ARVs in pregnancy can induce ARV resistance that could compromise the efficacy of future HAART regimens for the mother (as well as for the infant, should the infant become infected despite the PMTCT intervention).

Despite concerns over resistance, we still use these regimens because several studies have confirmed the efficacy of short-term ART involving only one or two ARVs in significantly reducing the risk of vertical HIV transmission. The relative simplicity and low cost of these PMTCT strategies make them attractive options in resource-limited settings such as ours.

As noted before in this newsletter, because of resource constraints, Uganda is implementing Option A until resources become available for it to implement **Option B**. **Option A** consists of maternal zidovudine prophylaxis from 14 weeks with single dose Nevirapine during labour and AZT+ 3TC for a week after labour. The infant then receives daily NVP syrup from birth until 1 week after all exposure to breast milk has ceased.

The different drugs contained in this regimen have different risks for development of resistance associated with them

ZIDOVUDINE

The choice of AZT monotherapy for PMTCT was made because of evidence from earlier studies which revealed that resistance emerged in patients receiving AZT monotherapy who had late-stage HIV disease, low CD4 cell counts and had been exposed for more than 9 months.

Clinical data document a low prevalence of AZT resistance following short-course AZT regimens to women who don't need ART for their own health, hence it is not likely that short-term administration of this agent during PMTCT will compromise the efficacy of this agent in future HAART regimens for the mother.

AZT prophylaxis (as a single drug) is therefore only recommended for women who do not require therapy for their own health (CD4 of >350 cells/mm3) and for a short duration (6 months or less).

LAMIVUDINE

Resistance to 3TC has only been noted when this drug has been used for more than one month. In studies where AZT with 3TC added after thirty-two weeks gestation, no 3TC resistance was reported with the use of this regimen for less than one month, whereas one to two months of prophylaxis was associated with a 20% risk of 3TC resistance. This resistance is beneficial because it decreases viral fitness.

NEVIRAPINE

Considering the NNRTI class used in PMTCT the story changes dramatically. A single mutation can confer resistance to NNRTI drugs such as NVP and EFV. These drugs have a long half-life; detectable drug levels persist for up to 2 weeks for NVP following a single dose. The persistence of sub therapeutic drug levels in the face of active viral replication is associated with the rapid development of NNRTI resistance among a significant proportion of women receiving single dose -NVP for PMTCT. It is for this reason that a dual NRTI regimen (e.g. AZT + 3TC) for at least 7 days is recommended to provide a suppressive tail of ARV coverage following single dose -NVP at labor. Much lower NNRTI resistance rates of 0% to 7% at 2 to 6 weeks postpartum have been reported with the use of NRTI tail regimens.

A recent study from South Africa found that although NVP resistance mutations were present in a high proportion of women who received single dose NVP at 6 weeks postpartum, the mutations rapidly faded to low levels over time and resistant variants were detected less frequently These data are consistent with recent clinical trials results suggesting that response to NVP-based HAART might not be compromised in women who initiate HAART more than six

months after their exposure to single dose NVP.

Recommendation

For women who require ART for their own health less than 12 months after receiving single dose NVP and for infants who do become infected despite single dose -NVP or extended infant NVP prophylaxis, WHO recommends a PI based regimen

The table below surmarises WHO ART recommendations for mothers exposed to various PMTCT regimens.

Table 9. Choice of ART regimen for HIV-positive women with prior exposure to PMTCT prophylaxis

CHARACTERISTICS OF PREVIOUS PMTCT ARV EXPOSURE	RECOMMENDATION
single dose -NVP (+/- short-course AZT) with no NRTI tail within the last 12 months	• Initiate a non-NNRTI regimen • 2 NRTIs + PI preferred over 3 NRTIs
single dose -NVP (+/- short-course AZT) with an NRTI tail within the last 12 months	• Initiate an NNRTI regimen • If available, check viral load at 6 months and if >5000 copies/ml, switch to second-line ART with PI
single dose -NVP (+/- short-course AZT) with or without an NRTI tail more than 12 months before	• Initiate an NNRTI regimen • If available, check viral load at 6 months and if >5000 copies/ml, switch to second-line ART with PI
All triple ARV regimens, irrespective of duration of exposure and time since exposure	• Initiate NNRTI regimen • If earlier triple ARV regimen was NNRTI-based and was stopped without administration of an NRTI tail, check viral load at 6 months, if available, and if >5000 copies/ml, switch to second-line ART with PI

CORRECTION:

Dear Health Care workers,

Please note that the ATIC Adult Drug Identification Charts that were sent to your health center in 2010 had an error in the formulation of the Aluvia tablet pictured.

The correct formulation should be 200/50 mg NOT 400/100mg .

(We have sent stickers marked 200/50mg with this newsletter which you can paste over the error)

We apologize for any inconveniences caused.

We at ATIC remain committed to serving you.