



## Epidemiology of tuberculosis and HIV

The Tuberculosis-HIV co-pandemic has ravaged regions of Africa and Asia accounting for the majority of AIDS-related deaths<sup>1</sup>. Globally the continued tuberculosis (TB) epidemic is fueled by transmission of infection to susceptible hosts or reactivation of latent TB disease. An estimated one-third of the world's population is latently infected with TB.

### Latent TB infection

Following inhalation of the mycobacterium tuberculosis (MTB) infectious agent, a proportion of immune-competent individuals control the infection and remains free of TB disease for prolonged periods. These persons have a positive tuberculin skin test (TST) or positive Interferon Gamma Release Assay (IGRA) test which signifies immunological sensitization to the TB organism and are said to have latent TB infection. This state



of "latency" is thought to represent a dynamic balance between the TB organism and variations in host immune control<sup>2</sup>. From this reservoir of latently infected individuals, 5-8% of immunocompetent people develop TB disease in a life time. In patients with HIV infection these rates of progression from TB infection to disease are much higher<sup>3</sup>.

### Isoniazid preventive therapy (IPT)

Isonicotinic acid hydrazide (INH commonly known as Isoniazid) is a first-line drug used in the treatment of MTB

## ISONIAZID PREVENTIVE THERAPY (IPT) IN PERSONS INFECTED WITH HIV

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infection. It is bactericidal (i.e., kills actively replicating mycobacteria) by inhibiting the synthesis of mycolic acid, a critical component of the mycobacterial cell wall. It was manufactured in 1912 but its antimycobacterial effects were discovered in 1951. Together with streptomycin this drug at the time offered better chances of cure of MTB infection than monotherapy with streptomycin alone.

INH was also shown to be beneficial in preventing TB disease initially in animal models but also in humans from large randomized trials in the pre-HIV era<sup>4</sup>. This prevention was more effective in TST positive individuals. Adverse effects due to INH, especially liver toxicity, are reported for patients on IPT. Patients that take a longer course of IPT experience more protection than those who use shorter durations of INH<sup>5</sup>.

### Effect of antiretroviral therapy on TB incidence

Several studies provide evidence that increased access to antiretroviral therapy (ART) is associated with declining rates of TB in Persons Living With HIV (PLWHIV)<sup>6,7</sup>. This decline would be further augmented if IPT is efficacious in PLWHIV.

IPT has been shown to be useful in PLWHIV who are TST positive<sup>8</sup>. No benefit of IPT has been shown in individuals who are TST negative. Recent findings also demonstrate that the benefit of IPT continues as long as the therapy lasts<sup>9</sup>. To identify individuals who will benefit from

INH prophylaxis mechanisms to provide TST for all PLWHIV should be considered. This involves ensuring appropriate skills for administering the test and ensuring a return visit for reading of the TST. However a proportion of PLWHIV are allergic to TST<sup>10</sup> and this allergy may only be reversed after immune restoration by antiretroviral therapy. If we rely on TST results to initiate IPT among patients on ART, we might need to repeat TST after six months of antiretroviral therapy in previously allergic patients to identify additional persons that may benefit from



IPT. The excitement over the Interferon Gamma Release Assays (IGRAs), a series of immunological tests that depend on the detection of the body response to the TB antigen, has waned since they have demonstrated limited advantage over TST<sup>11</sup>. The higher costs and complexity of testing with IGRAs that needs specialized facilities preclude their use in routine public health care.

### World Health Organization recommendation

Against this background, World Health Organization (WHO) has recommended

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Dear Reader,

This edition of the ATIC newsletter has a theme that is close to many health care workers' hearts: HIV Prevention and Preventive Interventions critical to HIV/AIDS Care. The current local and global concerns in the HIV/AIDS arena are why the HIV prevalence rates are rising in countries like Uganda, and which preventive interventions can be used to reduce them.

A common advert on television says **"An AIDS Free Generation begins with you!"** and this phrase has now become the resounding message in the HIV and infectious diseases world as solutions are sought for the new HIV infection rates that continue to rise. In the 2012 UNAIDS publication "Together we will end AIDS." Michel Sidibe, the Executive Director UNAIDS speaks of the *AIDS-Plus Agenda*

## EDITORIAL

– *Shaping the future we want* where innovations are emphasized to promote a sustainable approach to an AIDS free generation. On 26<sup>th</sup> September 2012, the US Secretary of State, Hillary Rodham Clinton also spoke on the same issue while at UNAIDS Shared Responsibilities Event held in New York, USA. She made remarks on the possibility of an AIDS Free Generation saying nations need to take responsibility for the care of their own people, and if those hardest hit by AIDS lead the fight against the disease, the fight would ultimately be won.

The articles presented in this newsletter echo the global call towards an AIDS free generation. Please read on as we present you information, statistics and innovative interventions you can emulate in your community as we all work towards ending the AIDS scourge.

If you would like to access references used in this issue please contact us at:  
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### Isoniazid Preventive Therapy (IPT) in persons Infected with HIV

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universal IPT in PLWHIV, regardless of their TST status. This has enabled initiation of therapy among many PLWHIV<sup>12</sup>, but this means that a proportion of patients who are TST negative are needlessly exposed to side effects of IPT. This approach may be justifiable because of the difficulty in implementing widespread TST before IPT and also the high risk of TB infection in HIV infected persons. This strategy may lead to the rapid scale up of IPT but benefits of this approach have been challenged not only because of the need to target TST positive PLWHIV but also the brevity of the suggested duration of IPT which may not lead to durable benefits<sup>13</sup>. Another limitation to IPT in this population is a possible risk of treatment of active TB disease with INH monotherapy. This may occur when subclinical TB is missed during screening of PLWHIV for IPT. This may predispose individuals treated to

development of INH monoresistance and ultimately multi drug-resistant TB.

There have been successful reports of IPT in our setting after excluding active TB disease by smear microscopy. Sputum microscopy detects a small proportion of the patients with active TB disease. Culture of sputum in asymptomatic individuals with HIV infection has detected TB in up to 20% PLWHIV starting ART, implying that better diagnostic tests need to be employed to exclude active TB disease. The Xpert TB/RIF test offers new opportunity for ruling out TB disease before administering IPT<sup>14</sup>.

### The South African experience

South Africa has one of the largest prevalences of TB and HIV. In the recently concluded XIX<sup>19</sup> International AIDS Conference in Washington, Rangaka and

colleagues presented findings of a study in which 1369 participants with HIV infection were randomized to twelve months of ART with INH prophylaxis or placebo<sup>15</sup>. Patients with TB were screened out using a symptom questionnaire and sputum smear and/or culture. TST results were not a requirement for randomization. IPT reduced the incidence of all TB diagnoses in the INH treatment group by 37%. Importantly the risk of stopping INH or placebo due to grade 3 or higher ALT elevation was twice as high on IPT (19 out of 662) as in the placebo group (9 out of 667) (P=0.05). There was however no difference in mortality between the two arms of the study.

### Practical concerns

The recent developments present an important move towards the control of TB in PLWHIV. However a few considerations

preclude widespread implementation of the WHO recommendations:

**1. TB diagnosis:** Screening for TB needs a very sensitive diagnostic test that is affordable and widely available for use in primary health care settings. Considering the multitude of challenges in health care provision it is unlikely that the limited resources in resource-constrained settings can be devoted to TB screening alone. Another option is to perform targeted screening for TB among symptomatic persons in HIV care clinics. Sputum smear plus the Xpert/RIF or MTB culture should be the basic minimum examinations for



excluding active TB disease in TB suspects prior to IPT.

**2. Monitoring for side effects:** If universal IPT is given to all patients with HIV, provision is needed to monitor

for liver toxicity using clinical and biochemical indices. The health providers should be on alert to detect any signs and symptoms of liver toxicity (nausea, right hypochondrial pain/tenderness, yellowing of the eyes, etc). The biochemical tests would also be vital to assess the extent of liver injury and also to determine the resolution of toxicity.

**3. Adherence to IPT:** Most reports on IPT have been from studies in which patients have been followed up (in routine or study clinics). The patients have been counseled and monitored closely for side effects. Addition of IPT to cotrimoxazole prophylaxis and ART needed by PLWHIV might present additional therapeutic burden to these people. A recent study by Namuwenge et al in Uganda indicates that only 33% of patients starting IPT in a programmatic setting completed the six months of treatment. The reasons for non completion need to be addressed for successful implementation of an IPT programme<sup>16</sup>.

The decision of what approach to adopt for IPT depends on the resources available to specific TB programmes. There is no doubt about the benefit of antiretroviral therapy

and IPT in reduction of TB cases but this comes at a cost (need of diagnostics to exclude active TB disease and monitoring of side effects due to INH).

The difficulty arising from the lack of a gold standard for TB infection may partially be overcome by using the programmatic approach for IPT as suggested by WHO. This however is still beset by technical and logistic challenges.

### Conclusion

Much as preventive treatment for TB is desirable, there are practical concerns so IPT should occur in tandem with other measures of control like early identification and treatment of patients with active TB disease. In programmatic settings, administration of IPT in PLWHIV without considering TST results would needlessly treat up to one-third of patients who are TST negative. IPT without TST could be reserved for populations in congregate settings with a high risk of TB transmission. And for IPT to be beneficial in PLWHIV it should be given for a long time. Finally, in case of any TB-related symptoms, a diagnosis of active TB should be excluded before considering IPT.

For close to three decades, Uganda has experienced the effects of a generalized HIV/AIDS epidemic. Through the national response and sexual behavioral change campaign guided by the ABC strategy (Abstinence and delay of sexual debut, Being faithful to one's sexual partner and appropriate and consistent condom use) the country saw a significant decline in the largely heterosexual epidemic with HIV prevalence falling from as high as 30% in the 1990s to 6.4% in 2005. However, according to the survey released by Uganda Bureau of Statistics (UBOS) the Ugandan



HIV prevalence has increased from 6.4% to 7.4% in 7 years. New HIV infections in the year 2011 alone were 130,000- a 1.5% increase from the previous year, translating into more than 350 daily HIV infections. 80% of these new infections are through heterosexual transmission, 20% are

## BACK TO THE BASICS, COMBINATION PREVENTION IN HIV PREVENTION

*By Christine Kihembo, ATIC Team Leader*

vertical infections, and less than 1% is blood borne. Uganda is the only country among high HIV burden countries documenting a rising HIV incidence in sub-Saharan Africa. UBOS's revelation has since then triggered many public discussions in the media with key HIV experts and stakeholders deliberating on what could have gone wrong to turn around the HIV control success the country has previously been heralded for.

Many factors have been cited to explain the HIV epidemiological trend in Uganda. Some of these factors include; inadequate HIV prevention, care and treatment coverage rates, sexual behavioral disinhibition, complacency within the population and HIV fatigue.

In this article, we go back to the basics and revisit HIV combination prevention interventions that so far have been documented and those adopted in the Uganda's current HIV prevention strategy

### Combination Prevention

Thirty years into the global HIV pandemic, in the absence of an effective and safe vaccine, no single preventive intervention/strategy has been proven sufficient to control and thus eradicate HIV/AIDS. However certain interventions have been shown to be efficacious in offering significant protection against HIV transmission and acquisition when applied in combination with other interventions for synergy or additive effects while adequately and sufficiently addressing the epidemiological HIV profile. This is commonly referred to as "Combination HIV Prevention."

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UNAIDS defines combination HIV prevention as the “strategic, simultaneous use of different classes of prevention activities (biomedical, behavioral, social/structural) that operate on multiple levels (individual, relationship, community, societal), to respond to the specific needs of particular audiences and modes of HIV transmission, and to make efficient use of resources through prioritizing, partnership, and engagement of affected communities.” Therefore as we envision zero new HIV infections, zero AIDS-related deaths and zero discrimination in a world where people living with HIV are able to live long, healthy lives, we are reminded to know our epidemic so as to know the right response.

### Combination HIV Prevention Packages

Mathematic models have been devised whereby the individual host’s biological and behavioral factors are related to the epidemiological pattern and structural factors such as gender equality and public health infrastructure to come up with HIV transmission probabilities and thus tailored preventive combination strategy. The guiding principle is that strategies should aim at reducing the infectiousness of the HIV infected people and reducing HIV susceptibility of those not yet infected.

#### Reducing HIV Infectiousness:

HIV Infectiousness refers to the potential or ability to transmit the HIV virus, therefore interventions in this category mainly consider those who are already infected



with the virus. These include; prevention of mother to child transmission (PMTCT), sexual and parenteral transmission risk reduction through HIV testing, behavioral risk reduction through correct consistent use of condoms, treatment of STIs, antiretroviral therapy, blood screening for transfusion, opportunistic infection management (resulting in reduced plasma and genital viral loads) and needle exchange among intravenous drug users.

Not only does HIV testing precede the above biomedical interventions and for creating linkages between services but also it has been shown to significantly result in less risky behavior among those who test positive as they are more likely to engage

in opportunistic infection prevention practices and seek lifesaving services. Unfortunately there is no evidence indicating that those who test negative reduce risky behaviors.

The use of antiretroviral drugs (ART) in prevention is also an important tool to reduce HIV transmission. PMTCT trials have reported success rates reducing maternal transmission to as low as 5% and below. It is well documented that effective ART reduces viral load thereby reducing one’s infectiousness. This has been further indicated by the pre-exposure prophylaxis (PrEP) studies that illustrated reduced HIV transmission with use of prophylactic antiretroviral drug use among HIV discordant heterosexual couples. This has strengthened the advocates for ART use for HIV prevention as well as treatment.

#### Reducing HIV Susceptibility:

Interventions that reduce one’s susceptibility to HIV acquisition include; male medical circumcision (MMC), use of ART containing microbicides, treatment of STIs, effective vaccines and behavioral risk reduction interventions.

Behavioral risk reduction interventions involve a cycle of information, education and communication strategies, coping/adjustment alternative bearing the socioeconomic environments in mind that is all geared at achieving behavioral change towards decreasing high risk behaviors. Not only have behavioral risk reduction interventions been shown to be effective for HIV prevention at a population level but has also been proved effective among the most at risk populations.

MMC has been proved to be effective in reducing heterosexual HIV acquisition by up to 60% among men in 3 clinical trials. MMC also provides an opportunity for linking men to other reproductive health services. Though not directly protective for women, the benefit can be realized after large scale MMC population effect.

#### Structural Considerations

Additionally, there are cross cutting issues that would need to be considered in order come up in order to come up with effective HIV prevention strategies. These range from gender equality issues, socio-cultural issues and legal issues that can impact HIV prevention strategies for a given community.

#### Considerations for HIV combination strategy

Earlier prevention strategies were mainly focused on HIV negative persons and emphasized behavioral risk reduction and behavioral change strategies like Uganda’s “ABC strategy”. As more biomedical

interventions have been devised they have been adopted along the way.

The current Ugandan HIV prevention strategy aims are based on combination prevention. The strategy is “expanding and doing prevention better....” as its slogan goes. It highlights behavioral, biomedical and structural interventions with the priority targets being the adults and youth involved in multiple sexual partnerships; youth engaged in cross-generational sex relationships and their partners; men and women who engage in transactional sex and their clients; and adults working away from home such as transport, migrant workers and uniformed men.

For any prevention program, coming up with which interventions to adopt relies on the scientific evidence supporting efficacy and effectiveness of the package of intervention as tailored to the epidemiological needs. Like in other many other undertakings, affordability and sustainability should be considered. Given the scientific evidence and the strategies in place to curb the epidemic one wonders what Uganda is doing wrong. However, it is important to note that a commitment to HIV Combination Prevention programs must be in place to truly reduce the prevalence and incidence of HIV in the nation.



The current Minimum Package of HIV Prevention Services for Adults in Uganda Core Components:

1. PMTCT
2. Male circumcision
3. HIV counseling and testing
4. Antiretroviral Therapy
5. Condom promotion Complimentary Components:
6. BCC integrated into existing structures (religious institutions, work places, school, etc)
7. IEC Messages and social norms reinforced through mass media
8. STI screening and treatment
9. Blood Transfusion Safety and Infection Control
10. Supporting policy and advocacy

# MALARIA PREVENTION IN MALARIA/HIV COINFECTION

By Dr Mumpe Mwanje, SMP Field Manager

## Introduction

There is a large geographic overlap between high risk areas of malaria transmission and HIV prevalence rates in sub-Saharan Africa, which increases the likelihood of dual infection in an individual. The immunology of malaria is not well understood; however there is a tendency to develop partial immunity to malaria among people living in malaria endemic areas. This immunity is characterized by an age-related reduction in the level of parasitaemia, clinical symptoms, and severity of clinical disease in such individuals. However this immunity is reduced or lost when one spends time away from the endemic region, during pregnancy, or when immunosuppression is present as occurs in HIV/AIDS.

Growing evidence shows that HIV and malaria fuel and exacerbate each other. An HIV infected individual living in a malaria endemic area is more likely to suffer malaria disease compared to a non HIV infected one living in the same area. Malaria infection rates are increased in those with low CD4 counts and /or high viral loads; such individuals tend to have more severe malaria disease with higher malaria related deaths. Anti-malarial therapy is less effective in HIV infected patients due to drug-drug interactions. Pregnant mothers, particularly first time mothers living in malaria endemic areas lose the partial immunity against malaria, becoming more vulnerable to malaria infection. In pregnancy, HIV infection is associated with even more episodes of malaria, higher grades of fever, more severe disease and more adverse birth outcomes. Similarly, HIV infected children experience increased rates of malaria infections and higher parasite densities with advanced immunosuppression compared to HIV negative children in malaria endemic areas.

On the other hand, a malaria episode in an HIV infected person is associated with a transient increase in HIV replication. Not only does this accelerate progression to AIDS, especially with repeated infections, but it also increases ones infectiousness and thus the risk of HIV transmission.

Given this interaction it is therefore important that malaria prevention be integrated into routine HIV care. In this article, malaria preventive measures focusing on an HIV infected person are reviewed.

## Malaria: Parasite, Vector, and Transmission

In designing malaria control strategies, understanding the causes of malaria, the vector and malaria transmission is important.

### The malaria parasite vector and transmission

Malaria is an infectious illness caused by the Plasmodium parasites. Five species exist that can infect humans: *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and *P. knowlesi*. *P. falciparum* species cause most of the severe malaria disease episodes worldwide.

Vertical transmission of malaria occurs when Plasmodium is carried from one infected host (usually man, but can be other vertebrates) to another by the Anopheles mosquito vector. Anopheles mosquitoes breed in clean fresh stagnant water and thrive well in warm humid temperatures with a lifespan of 2-3 weeks on average. An adult female Anopheles mosquito lays about 50-150 eggs every 2-3 days; these take on average about 7-14

days to develop into mature mosquitoes. Anopheles mosquitoes are nocturnal (active at night), endophagic (feed indoors) and endophilic (rest indoors) and can fly up to 1.5 km.



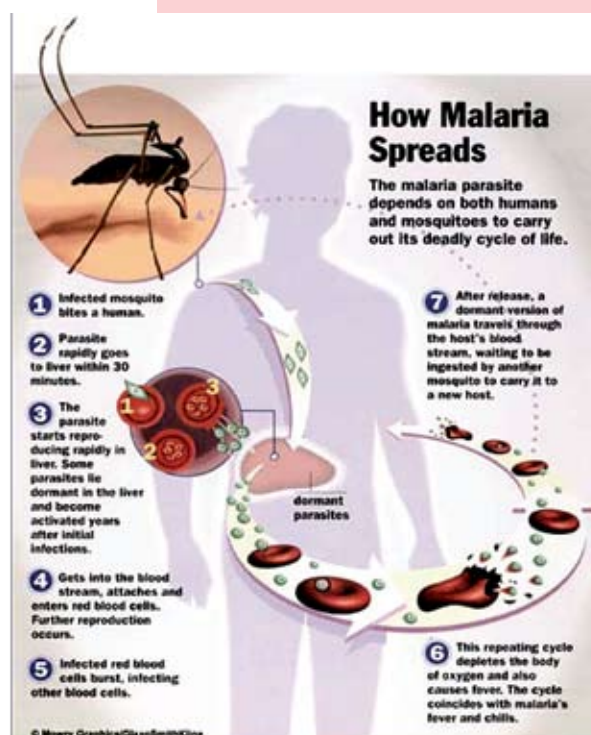
### The malaria lifecycle.

The malaria parasite lifecycle is generally divided into 3 parts: the mosquito stage, the human liver stage and the human blood stage as illustrated below:

### Malaria prevention strategies

Though proven effective malaria prevention interventions exist, none of them are 100% effective on its own. The current prevention strategies aim at interrupting the lifecycle in one way or the other.

Vector-specific prevention strategies include preventing mosquito bites by use of insecticide treated nets (ITNs) and mosquito repellants, and reducing the mosquito population in the environment through indoor residual spraying and having proper sanitation infrastructure.



# UGANDA ADOPTS PMTCT OPTION B PLUS

By Christine Kihembo, ATIC



## Introduction

Mother-to-child transmission (MTCT) is the transmission of HIV from an HIV-positive mother to her child during either pregnancy, labour, delivery or breastfeeding. MTCT rates range from 15-45% in the absence of any intervention. However this can be significantly reduced to as low as 5% and below with effective prevention of mother to child transmission (PMTCT) interventions. PMTCT has evolved over the last 10 years with scientific evidence of new approaches with better prevention outcomes. The World Health Organisation released PMTCT guidance in 2010 based on equally effective PMTCT option A and B options as covered in our June 2012 newsletter edition and later provided guidance on PMTCT option B+.

Uganda has been implementing the WHO PMTCT Option A with some few sites implementing option B. However, in line with the global commitment and effort to eliminate MTCT by the year 2015, Uganda adopted option B+ in September 2012 to combat MTCT that accounts for 20% of the new HIV infections.

## What is PMTCT Option B+?

PMTCT Option B+ is a treatment program that includes initiating as soon as possible and maintaining all identified HIV positive pregnant or breastfeeding mothers on Antiretroviral therapy (ART) for life regardless of the mother's clinical stage or CD4 cell count. Additionally all HIV exposed babies (i.e babies born to HIV positive mothers) receive daily Nevirapine prophylaxis from birth till 6 weeks irrespective of the infant feeding option.

Uganda's option B+

ART regimen of choice is Tenofovir/Lamivudine and Efavirenz (TDF/T3C/EFV) which currently is available as a fixed drug combination in one pill taken once daily.

## Why Option B+?

As mentioned earlier, Uganda has adopted PMTCT option B+ in effort to achieve virtual elimination of MTCT. National PMTCT data analysis in 2010 revealed implementation challenges with option A. More specifically that very few mothers (8%) previously on option A, continued HIV care after delivery with only a fifth of HIV-positive infants surviving and on treatment. Worse still a good proportion of these mothers are still in their reproductive ages putting subsequent pregnancies at risk of HIV transmission with previous interventions.

As we may all be aware, Antiretroviral Therapy (ART) is only a piece in the overall

PMTCT package. For Uganda to maximally benefit from Option B+ roll out and scale up, it requires that other PMTCT prongs are not overlooked. Therefore Option B+ should go hand in hand with preventing primary HIV infections among women of reproductive/child bearing age, preventing unwanted pregnancies among women living with HIV/AIDS and providing appropriate treatment, care and support to mothers living with HIV, their children and families to achieve virtual elimination of MTCT.

Specifically for Uganda, virtual elimination of HIV MTCT is comprised of all of the following;

- Reduced MTCT rates at population level to <5% in breast-feeding populations
- Reduce MTCT rates at population level to <2% in non-breast-feeding populations
- Reduced number of exposed babies infected with HIV by 90% in 2015
- Reduction of unmet need for family planning among HIV positive women to zero and
- Reduced new HIV infections among women of childbearing age to less than 50%

## Advantages of Option B+

**PMTCT option B+ intervention presents several advantages to the mother/baby, the health worker and the health care system.**

Option B+ Advantages	
Mother & Baby	<ul style="list-style-type: none"> <li>• Reduced lifetime HIV transmission risk(earlier ART initiation and continuation)</li> <li>• Simpler and easier dosing schedule</li> <li>• Reduced stigma associated with syrups: Nevirapine syrup (for bay) used for only six (6) weeks</li> <li>• Reduced risk of developing HIV drug resistance</li> </ul>
Health workers & Health care system	<ul style="list-style-type: none"> <li>• Better linkage to chronic care system as mother has to continue ART</li> <li>• Reduced losses to follow up</li> <li>• Simplified drug provision and better adherence</li> </ul>

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Like in many other new interventions, there are anticipated challenges. PMTCT option B+ will ultimately put more pressure on the already limited resources (infrastructure, human resource and logistics) as a significantly big proportion of the population will require life long ART

### **National Roll out Plan**

With the anticipated challenges in mind, the Ministry of health has planned roll out and scale up of Option B+ in a phased manner. Geographical and HIV epidemiological patterns have been considered with option B + pilot starting off in the central region

with plans to have nation-wide coverage by the end of 2013.

HIV prevention including PMTCT remains high on Uganda's agenda. As we all strive towards virtual elimination of maternal to child HIV transmission, let us all health workers do everything possible in our means to avert MTCT.

## NEW AND CURRENT GUIDELINES & REPORT DOCUMENTS

1. WHO June 2012 Antiretroviral Treatment as Prevention (Ta sP) of HIV and TB programmatic update. Available at [http://whqlibdoc.who.int/hq/2012/WHO\\_HIV\\_2012.12\\_eng.pdf](http://whqlibdoc.who.int/hq/2012/WHO_HIV_2012.12_eng.pdf)
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8. WHO November 2012. WHO global strategy for the surveillance and monitoring of HIV drug resistance 2012.. Available at [http://apps.who.int/iris/bitstream/10665/77349/1/9789241504768\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77349/1/9789241504768_eng.pdf)
9. WHO Dec 2012 Prevention and treatment of HIV and other sexually transmitted infections for sex workers in low- and middle-income countries. Available at [http://apps.who.int/iris/bitstream/10665/77744/1/WHO\\_HIV\\_2012.19\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77744/1/WHO_HIV_2012.19_eng.pdf)
10. WHO 2012 update Who Manual For Hiv Drug Resistance Testing Blood Spot Specimens. Available at [http://apps.who.int/iris/bitstream/10665/75829/1/WHO\\_HIV\\_2012.30\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/75829/1/WHO_HIV_2012.30_eng.pdf)

Interrupting parasite cycle in the human host and reducing malaria related illness can be done through case management and chemoprophylaxis. Early diagnosis and effective prompt treatment of malaria eliminates the parasites in the blood, reducing chances of malaria. Treatment aims at killing the sexual forms which otherwise are infective for mosquitoes. Effective Malaria treatment therefore reduces the length of morbidity and the risk of mortality.

Intermittent preventive treatment (IPT) describes the administration of a full

high risk groups to malaria infection. All strategies therefore are essential in PLWHAs living in malaria endemic areas.

#### **Cotrimaxazole prophylaxis**

Preventive treatment with cotrimaxazole (septrin) has been shown to reduce morbidity and mortality among children and adults living with HIV/AIDS by preventing opportunistic infections. Septrin has also been shown to be 99.5% effective in preventing malaria in PLWHA. Septrin is 99.5% effective against Malaria compared to 95% for Fansidar (sulfadoxine/pyrimethamine) with both drugs having an 80% therapeutic efficacy for malaria treatment.

#### **Malaria in pregnancy**

As mentioned earlier, pregnant mothers in stable malaria areas lose the partial immunity, implying that an HIV positive pregnant mother is at greater malaria risk. In areas of stable malaria transmission, WHO

recommends a package of IPT, use of ITNs, and effective case management of illness and anaemia for malaria prevention and control during pregnancy. Insecticide-treated nets and prompt effective case management are recommended for all pregnant women living in malarious areas.

Fansidar is the drug of choice for IPT during Pregnancy. IPT is the recommended approach to the prevention of malaria in pregnancy in mothers living in high malaria burden areas; it is often administered during antenatal visits during the second and third trimesters. IPT not only prevents clinical disease among pregnant women but also prevents vertical malaria transmission. It is important to note that cross Septrin / Fansidar malaria resistance development is scientifically plausible though its occurrence has not yet been documented. IPT is also being considered for potential malaria prevention among infants in high malarious children. Therefore since HIV positive pregnant mothers will already be on septrin prophylaxis: which is effective for malaria chemoprophylaxis, they do not require the Fansidar IPT.

Lastly, insecticide-treated nets should be provided as early in pregnancy as possible to all pregnant women living in malarious areas and should be used at all times through the post-partum period

#### **Effective Malaria case management**

Effective malaria management is essential for all cases and for pregnant women in malarious areas. Iron supplementation for the prevention and treatment of anaemia should routinely done during antenatal care.

Artemisinin-based Combination Therapy (ACTs) remains the drug of choice for non-complicated malaria for general cases and in the second and third trimesters. For infections during the first trimester, quinine is preferred to ACTs. However, there is need to take care when treating HIV infected individuals on ART for malaria due to potential drug interactions especially with artemisinin derivatives.

#### **The Uganda Basic Care Package (BCP)**

*In Uganda, a country with high malaria and HIV burdens, a Basic Care Package (BCP) was developed to help prevent HIV transmission and reduce morbidity and mortality particularly from malaria and diarrhea diseases. BCPs are provided to health care institutions in Uganda for free distribution to people with HIV. The BCP incorporates five interventions: Cotrimoxazole prophylaxis, Insecticide-treated bed nets (ITNs), the household-based Safe Water System, HIV voluntary counseling and testing (VCT) among family members of people with HIV (family VCT) and condoms. Studies have shown high BCP uptake and usage.*

#### **Conclusion**

Malaria and HIV remain the leading causes of morbidity and mortality in high prevalence areas with dual infections commonly occurring. Interaction between the two diseases occurs, with each disease fuelling the progress of the other. Given the complexities that arise due to the HIV/ Malaria co-infection and treatment it is only logical that their preventive strategies are emphasized and integrated.



therapeutic course of an anti-malarial to at risk subjects at specified times regardless of whether they are infected or not. IPT is now the recommended approach to the prevention of malaria in malaria high risk people especially pregnant women in endemic areas. Chemoprophylaxis is very crucial in individuals with no malaria immunity.

The choice of combination of strategies depends on the malaria endemicity with mosquito avoidance and reduction and case management being applicable for high endemic areas in addition to IPT being necessary for high risk groups in endemic areas.

#### **Malaria prevention strategies among HIV infected patients**

Given the Malaria/HIV interaction mentioned above, it is imperative that malaria prevention be emphasized among people living with HIV/AIDS (PLWHAs). Prevention strategies for HIV infected individuals are not very different from prevention strategies in the general population only that adult non pregnant PLWHAs in malaria endemic areas are





## INFORMATION COMMUNICATION TECHNOLOGIES (ICTs) FOR HIV PREVENTION

*By Devy Emperador, GHC Distance Learning Fellow*

Current literature in disease prevention such as diabetes has shown the utility of information and communication technology (ICT) in changing behavior. When we look at HIV/AIDS, despite the arsenal of effective biomedical interventions to prevent HIV transmission, these strategies all have an underlying behavioral component that must be addressed. At this year's International AIDS Conference 2012 in Washington, D.C, a panel discussion was held on the use of information and communication technology (ICT) in the care, prevention, and treatment of HIV/AIDS. With increasing telecommunication capacity in many countries and the growing number of individuals with access to mobile phones and computers, using ICTs for HIV prevention could help address the behavioral component of prevention, thus improving access to services and resources regardless of location.

ICTs include internet and mobile-phone based interventions; these can be used in a variety of ways to promote health prevention strategies. Examples include: interactive informational websites that help reinforce and introduce information about HIV prevention counseling to help build capacity among health care workers; text message sexual health appointment reminders, enabling client and health worker interactions; and social media

websites such as Facebook allowing HIV positive individuals a space to share their stories and experiences with each other. These are only examples of the kinds of programs that can be achieved when ICTs are integrated.

Recent reviews conclude that ICT-based interventions are effective in promoting positive behavior change to prevent disease. ICTs were shown to increase rates of HIV testing among users. A recent systematic review meta-analysis looking at 12 studies that used computer and internet-based HIV prevention interventions concluded that ICTs were effective in increasing condom use and reducing risky sexual activity, number of sexual partners, and incident sexually transmitted infections (STIs). The review also found that ICT-based interventions were as effective as face-to-face interventions. While not specific to HIV prevention another review looking at 14 studies of non-HIV text-message interventions also shows short-term positive behavioral outcomes.

Despite positive outcomes on the use of ICTs for HIV prevention there are challenges that must be addressed to maximize the effect of ICT interventions, especially in developing countries such as Uganda. These challenges include the high initial costs of developing and strengthening ICT infrastructure, the

necessity to increase internet and mobile reach, and the need to enhance computer literacy among the population. Use of ICTs by the population can vary as well—results from a pilot study conducted in northwestern Uganda looking at the effectiveness of a text message HIV/AIDS campaign to the general public showed that not all participants engaged in the text messages. That study concluded that targeted interventions, especially among at-risk individuals, are best when trying to change knowledge and behavior. Despite these challenges, developing the infrastructure for ICT-based interventions will be less costly in the future and has shown to be feasible, acceptable, and possibly as effective as face-to-face interventions.

Although the rates of HIV worldwide are steadily decreasing, we have yet to eradicate this disease in the world. In Uganda the rate of HIV infection is even increasing. Focusing on HIV prevention is a high priority in slowing and reversing that trend in Uganda. In this technological age, it seems only fitting to integrate ICTs with proven HIV prevention strategies. This could be useful especially with the younger generation as they are more likely to embrace new technology. Using ICTs in a targeted way and combining them with proven HIV prevention strategies will be a helpful addition to the HIV prevention toolkit.

## THE EMERGING ROLE OF TENOFOVIR IN TREATMENT AS PREVENTION

*By Joseph Walter Arinaitwe, ATIC*

### **The driving concept of treatment as prevention**

Antiretroviral therapy (ART/HAART-highly active antiretroviral therapy) for treatment of HIV has been a very successful strategy in curtailing progression of HIV to AIDS. This has significantly increased the quality of life of those already infected with HIV. The recent advances in treatment have lent new perspectives to the possibilities that ART has to offer. HAART utilizes a combination of 3 drugs with different mechanisms of action to stop viral replication thereby suppressing the levels of HIV viraemia (viral load) to undetectable levels, not just in the bloodstream but also in the genital secretions. Viral load is indeed the single greatest risk factor for all modes of HIV transmission therefore proper ART reduces the risk of transmission of HIV from one person to another. This is the driving concept of treatment as prevention. This strategy has already been adopted for prevention of mother to child transmission (PMTCT) with good levels of success and



research has demonstrated that this strategy can be expanded to cover other risk groups like serodiscordant couples.

Several studies have been conducted to ascertain the extent of the effectiveness of the treatment as prevention strategy. One such study; Prevention of HIV-1 infection with early initiation of antiretroviral therapy, carried out in 9 countries (Botswana, Malawi, Kenya, South Africa, Zimbabwe, Brazil, India, Thailand and

*Continues on pg 10*



USA) enrolled HIV-1 serodiscordant couples randomized in a 1:1 ratio. Another such study; treatment as prevention for HIV in China, conducted by the China CDC enrolled approximately 39,000 heterosexual serodiscordant couples. These 2 studies along with several others have all come to a similar conclusion, that antiretroviral therapy can reduce the rates of sexual transmission of HIV. The treatment as prevention strategy therefore bears potential for significant public health benefits in the fight against HIV, along with the expected personal benefits.

### Current practice

In Uganda, treatment as prevention is already in play in the form of PMTCT. Uganda has adopted the WHO recommended PMTCT Option B+ which the Ministry of Health is rolling out nationally in a phased approach. This PMTCT plan recommends the use of Tenofovir (TDF) in combination with Lamivudine (3TC) and Efavirenz (EFV) as the preferred regimen for HIV-infected pregnant women as well as breastfeeding mothers, for prevention of vertical transmission. TDF is preferred because it presents a significantly lower risk of anaemia in pregnant women, a condition that can seriously complicate pregnancy.

Post exposure prophylaxis is also another application of treatment as prevention, as will be discussed later on.

Interestingly, Tenofovir is the drug at the centre of treatment as prevention, not just in practice but in research as well, as we shall see later on. But first, what is tenofovir?

### About Tenofovir

Tenofovir belongs to the class of NRTIs; nucleoside (nucleotide) reverse transcriptase inhibitors. Tenofovir is an acyclic nucleotide reverse transcriptase inhibitor and is currently the only nucleotide analog approved by the FDA for use against HIV (the nucleoside analogs include zidovudine (AZT), lamivudine (3TC) and abacavir (ABC) among others).

Within the human body, HIV survives by infecting a cell and utilizing the cell's nucleosides and nucleotides to generate its own genetic material for replication. The NRTI class of drugs mimics the body's nucleosides/nucleotides and is thus taken up by the virus thereby blocking HIV's reverse transcriptase enzyme to prevent viral replication.

Tenofovir is currently formulated as the orally bioavailable prodrug Tenofovir Disoproxil Fumarate (TDF). TDF is traditionally used for the treatment of HIV in-

fection and the treatment of viral hepatitis, particularly Hepatitis B infection.

### Use in adults

The recommended adult dose is 300 mg taken orally once daily.

### Use in children (new recommendation)

Usage in children below the age of 14 has previously not been recommended because TDF is associated with decreases in bone density with increased susceptibility to fracture. However WHO recently reviewed currently available published and unpublished data on the safety, efficacy and dosing of TDF in children and adolescents and suggests that TDF seems to be efficacious in children and adolescents (2yrs to >18yrs). This review also suggests that TDF has not been identified to be solely culpable in the development of the undesirable effects of therapy.

In fact, the FDA has approved the use of TDF in children above the age of two years and adolescents. The recommended dose is 8 mg/kg body weight (up to a maximum of 300 mg), administered once daily.

### Drug Interactions

Interaction of tenofovir with other medicines is mainly at the elimination point, the kidney. TDF is eliminated mainly through active tubular secretion in the proximal tubules (active-meaning there are transporters that carry the TDF molecules across the tubular membranes). Therefore, drugs which interfere with the proximal tubular tenofovir transporters interact with TDF.

These medicines include but are not limited to;

1. Antiviral medications such as acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir; may increase concentrations of TDF
2. Nonsteroidal anti-inflammatory medications (NSAIDs); are associated with tenofovir nephrotoxicity
3. Didanosine (ddI); TDF increases DDI levels (note that ddI usage in ART has been phased out in Uganda due to the toxicities it presents)
4. Ritonavir; increases TDF concentrations and has been associated with TDF nephrotoxicity

Concomitant administration of the following medicines with tenofovir increases the chances of nephropathy developing as they are known for their association with nephrotoxicity, caution should therefore be exercised with; TMP-SMX (septrin), dapsone,  $\beta$ -lactams like penicillins, fluoroquinolones (like ciprofloxacin), amphotericin B, pentamidine, e.t.c

*(For more about TDF, refer to Vol. 4 Issue 3 September 2008 Newsletter: Pg 6)*

## TDF in treatment as prevention

### Post-exposure prophylaxis (PEP)

TDF combined with 3TC and NVP/EFV is currently recommended as the preferred regimen for PEP; this choice varies however, depending on the risk of exposure or the drug susceptibility of the source of the infection. Currently PEP is available in Uganda to health workers exposed through occupational hazards like needle-stick injuries, splashes and rape / defilement victims.

### Pre-exposure prophylaxis (PrEP)

Several trials involving the use of TDF either alone or in combination for PrEP have been carried out/are on-going. Most notable amongst the concluded studies are the TDF2, the partners study and the VOICE study.

**TDF2 study;** this was conducted in Botswana, 1,200 men and women (55% men) were enrolled and randomized to receive either Truvada (tenofovir+emtricitabine) or placebo. Overall, Truvada reduced the risk of infection by 63%.

**The Partners study;** this was conducted in Uganda and Kenya. The partners study recruited 4,758 male-female couples in which one partner was HIV-positive. The uninfected partners were randomized to receive either tenofovir, tenofovir+emtricitabine (Truvada) or a placebo. The results of this study indicated that the risk of infection was reduced by 67% in those who received tenofovir alone and by 75% in those who received Truvada. Among people randomized to take TDF alone, having a detectable plasma drug level cut the risk of HIV infection by 86% compared with those having an undetectable level, cementing the value of adherence. The study was quite successful, to the extent of being halted more than 18 months early after an interim review of the data found a highly significant effect of PrEP.

**The VOICE study;** this is an on-going study being conducted in Uganda, South Africa and Zimbabwe. The VOICE trial (Vaginal and Oral Interventions to Control the Epidemic) is a major HIV prevention trial comparing tenofovir microbicide gel with oral pre-exposure prophylaxis using the tenofovir / emtricitabine combination pill Truvada. This trial aims to verify the effectiveness of PrEP in women.

With all the research, scientific advent and novel applications of the treatment as prevention, we can most certainly expect much more from tenofovir in the fight against HIV.



# ASK ATIC....



## RAPID TESTING FOR HIV DIAGNOSIS

By Geoffrey Oguma, SMP Lab Technologist

### Introduction

HIV rapid serology testing remains the cheapest and most common means of establishing HIV sero-status for individuals two years or more in age. Rapid HIV tests are immunological tests based on the principle of an HIV-specific antigen-antibody reaction. HIV is composed of several proteins and infection will trigger formation of specific antibodies; HIV antibodies will be found in all HIV-infected patients when chronic infection is established.

There are several rapid test kits/devices available. These include; Unigold recombigen, STAT PACK, MULTISPOT and Clear view Complete. Most of the rapid tests are able to detect both HIV1&2. Rapid HIV testing is widely used for point of care under provider initiated counseling and testing (PICT), routine counseling and testing (RCT) and voluntary counseling and testing (VCT) in static clinics and during outreaches. The rapid test kits can be used on different specimen such as whole blood, serum saliva and urine. The fact that rapid tests are generally highly sensitive, provide quick results and do not require highly technical expertise testing has made them the tests of choice in high HIV prevalence and resource limited settings like Uganda.

### HIV Testing algorithms

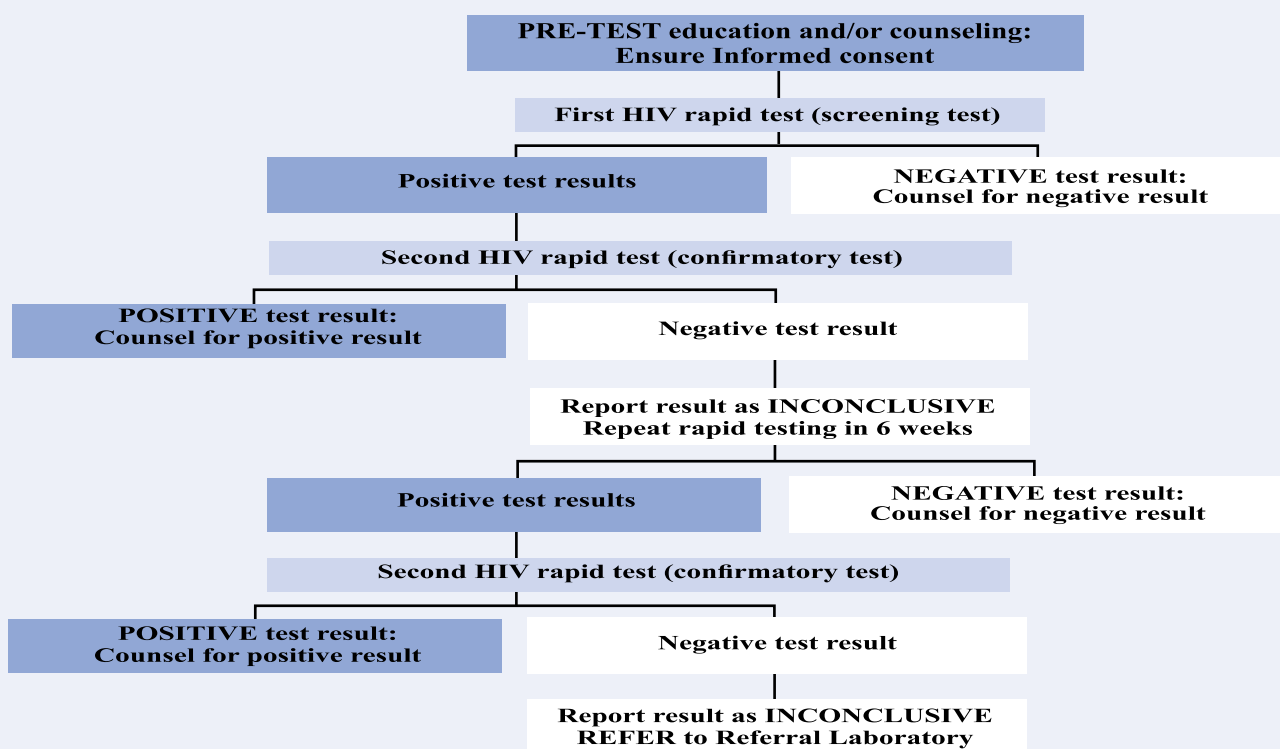
Although rapid tests generally have high sensitivity (capacity to correctly identify individuals infected with HIV), some may be more specific (specificity is the capacity to correctly identify individuals not infected with HIV) than others. With these considerations and knowledge of the prevalence levels in the population and other practical issues, the World Health Organization recommends use of several rapid tests simultaneously or serial testing.

The Ugandan Ministry of Health (MOH) recommends the use of at least two rapid tests as shown in the algorithm below:

In Uganda, the rapid tests of choice in the algorithm are as follows;

First Test (Screening)	Determine
Second Test (Confirmatory)	STAT PACK
Third Test (Tie breaker)	Unigold

It is important to understand the HIV rapid testing basic principles, interpretation of the test and to undertake necessary quality assurance measures in order to come up with a meaningful result that can be used to guide care and treatment intervention. A poorly carried out or interpreted HIV test not only causes confusion and





distress to the client tested but can also result in poor medical interventions.

### Case scenario below;

A pregnant woman took an HIV test in May 2011 at a health facility during antenatal visit and was reported HIV positive; she was enrolled into PMTCT (option A) services in higher health facility. She delivered in January 2012. DNA PCR and HIV serology for the baby were negative. The mother was retested and she was found to be HIV sero-negative.

### Question

*Is this woman HIV positive or negative? What could have gone wrong with the first test? What should the laboratory personnel always do to avoid such confusion? What should the clinician do for this client?*

As mentioned earlier, good understanding of the HIV testing protocol is critical to minimize errors in HIV diagnosis. In the case scenario above, a false positive result would mean that the mother received ART unnecessarily, while a false negative would mean that she would miss the PMTCT intervention, increasing the risk of HIV transmission to the baby.

### False HIV results.

There are several factors that lead to a false positive HIV test. Technical errors are the most common, which can be as a result of improper specimen collection, labeling, storage and preparation which may contaminate specimens, use of expired or defective testing devices, incorrect sample type or volume dispensed to the test devices, wrong reagents/buffers, wrong readings and wrong documentation of results.

However, there are some documented causes of false positive HIV test which include Epstein-Barr virus infection, pregnancy, receipt of HIV vaccine, high serum bilirubin levels and certain autoimmune diseases.

Similarly, false negative results can be caused by technical errors above. They can also be due to early HIV infection in the acute phase (window period) before antibodies are produced; this window period typically takes between 3-12 weeks.

### Scenario continued....

On retrospective review of records of this mother's medical records, it was found that actually only one HIV kit "determine" had been used as other kits had been out of stock and no follow up testing was advised or done.

Therefore this was inadequate testing in the first place with insufficient reporting of results. No checks were in place at the second health unit; no repeat testing or review of referral notes were observed. This mother received unnecessary ART with its potential side effects and possibly received negative psychosocial implications as well.

### Practical laboratory considerations when doing HIV rapid tests

#### Sample collection:

- Obtain the right specimens for the test kits used and observe safety and infection prevention of the rules of the testing area.
- Have SOPs in place for sample collection, packaging and transportation in relation to rapid testing, quality control (QC) and QA;

#### Test Kits:

- Use the right kits for the recommended and adopted testing a logarithm
- Keep the testing devices at the right temperature (2 – 8° C for ELISA reagents or room temperature for the rapid test kits).
- Check the expiry dates and integrity of the test kits to ensure they are not expired or damaged before use.

For indeterminate results: double check and rule out possible contamination and report results accordingly. Encourage repeat testing at 3 and 6 months respectively. If resources permit, do a confirmatory test that uses a different testing modality. Finally have a QA/QC system in place to ensure that all is well in the testing process.

### Conclusion

As rapid HIV testing has become widely available as the major HIV diagnostic tool, there is need to ensure that it is properly performed to give the right result to avoid the untoward implications of a false positive or false negative HIV result.

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