GMHC treatment ISSUES

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Treatment ISSUES

Treatment for women and prevention for infants: Can't we do both?

By Wendy Johnson, MD, MPH

The rate of new infections among women is growing at alarming rates. Although women make up about half of those living with HIV in the world, in Sub-Saharan Africa, the proportion of people living with HIV who are women is nearly 60% of adults and an astonishing 75% of young people between the ages of 15 and 24.[1] The numbers are reflective of gender inequality and the particular vulnerability of women in all societies. Women have less access to education and economic opportunity, which makes them more dependent on their families and on male partners. As a result of these power differentials, women and are less able to negotiate the terms of sex and safer sex practices, like condom use with their male partners. In many cases, women resort to engaging in survival sex for food and material support for themselves and their children.

In addition to a high burden of infection, women bear the brunt of the epidemic in other ways. Biologically, women are twice as likely as men to contract HIV from an episode of unprotected intercourse, and in discordant couples men are more likely to have introduced HIV into the relationship.[2] Socially and culturally, women are caregivers for the infirm and orphans and they suffer great financial hardships when their partners become sick or die. Despite the disproportionate burden of HIV on women in Africa, care and treatment programs have largely failed to respond to their specific needs or consider the special challenges women face when accessing care.

Nowhere is this phenomenon more evident than in the conception and implementation of "Prevention-of-Mother-to-Child-Transmission" (PMTCT) programs in the developing world. The PMTCT concept has its roots in a 1994 study, which showed that taking AZT during pregnancy dramatically reduced the chances of an HIV positive mother passing on the virus to her newborn.[3] While a short course was shown to be effective, AZT was then still prohibitively expensive for residents of poor countries. The AZT regimen quickly became standard for HIV positive pregnant women in wealthier countries. Since then, the PMTCT regimens for HIV-positive pregnant women in rich and poor countries have continued to sharply diverge. If women are provided with a complete package of care and treatment during pregnancy, the chances that they will pass the virus on to their children can be decreased to less than 2%. Without these interventions, about 20–45% of HIV-exposed infants will contract the virus.[4]

About 4 years after the 1994 AZT study, another study showed that a single dose of Nevirapine given during labor reduced intra-uterine and peri-partum transmission rates by 50%.[5] Because of its ease of delivery and relatively low cost, single-dose Nevirapine was quickly promoted as the prime PMTCT strategy in low-income, high-HIV-prevalence countries and was at the center of the World Health Organization's (WHO) first PMTCT recommendations in 2000.

Somewhere in this myopic focus on transmission rates, we lost sight of one simple fact: the survival of infants depends heavily on the well-being of their mothers. In 1999, Berer noted, "Short course AZT treatment is an intervention that uses women's bodies to deliver preventive treatment to infants. Although the anti-HIV benefit to infants is clear, there is no benefit to the women."[6] Nevirapine proved even worse. Studies subsequently demonstrated that mothers face an increased risk of developing resistance when they eventually must take anti-retrovirals for their own treatment if they had previously taken Nevirapine during pregnancy to protect their infants.[7]

Following the WHO guidelines, PMTCT programs were implemented in a number of pilot sites in Africa starting as early as 1999. For the most part, the PMTCT pro-

grams were instituted by international organizations, not primarily by public sector health services, so they tended to be fragmented and rely on intensive international support. Implementation was also "vertical" in nature. PMTCT clinics were often stand alone sites—separated from prenatal care and disconnected from treatment programs. One could find heavily-funded PMTCT programs in the same places where there was poor access to prenatal care and no c-sections, where institutional delivery rates were less than 50%, and where referral for treatment for pregnant women was a low priority.

As early as 2001, advocates argued for a reemphasis on care and treatment for women in PMTCT programs, but only recently did their arguments have a significant impact on implementation strategies.[8] The shift came largely due to widespread acknowledgement that PMTCT is not working as a vertically implemented, stand-alone program. The results of the 2007 PMTCT report card were damning. Over 500,000 children were infected with HIV in 2006, nearly all through mother-to-child transmission—a number that has not budged since the late 1990s. Only 16% of women in middle and low income countries were even tested for HIV during their prenatal visits, and only 27% of prenatal clinics in sub-Saharan African offered PMTCT services. Finally, of the estimated total number of pregnant women with HIV in countries with generalized epidemics, only about 20% received anti-retrovirals as prophylaxis to prevent transmission of the virus to their children. The vast majority of those received only single dose Nevirapine. Although more effective regimens have now been tested and proven, regimens which also have less risk of inducing resistance for the mother, they are more complicated, requiring longer courses, and have been difficult to implement. There is no mention of how many women were able to access anti-retroviral treatment (ART), but only two years after the widespread initiation of pediatric treatment, the report estimates that nearly a quarter of children who need ART received it in 2006.[9]

This contrasts starkly to the estimated number of pregnant women able to access treatment for themselves. At least 20% of pregnant women with HIV in Africa would be eligible for ART, but in a recent review of PMTCT programs implemented in Africa by a major US-based organization, only about 1% of women who tested HIV positive during pregnancy received treatment.[10]

Protection of the right to health for HIV positive women in Africa clearly requires a new framework for services which include integrating PMTCT programs into routine prenatal care for women and finding innovative ways to deliver ART treatment to HIV positive pregnant women before labor and delivery. The new models must consider the social, economic and political context of women's lives.

In Mozambique, the Ministry of Health shifted to an opt-out testing strategy for PMTCT programs in 2006. This shift in pre-test counseling meant that the test would be presented as a routine part of the prenatal care labs, much as it is in the U.S., giving women the opportunity to "opt-out" instead of requiring them to "opt-in" and affirmatively request the test. With this change, Manica and Sofala Provinces in central Mozambique began to integrate PMTCT services seamlessly into routine prenatal care. Innovative aspects of this model include: 1) one nurse taking care of the entire prenatal visit including routing prenatal care, syphilis testing, provision of preventive treatment for malaria, and HIV testing 2) combined HIV and syphilis testing 3) pre-and post-test counseling delivered in a confidential setting as part of the routine visit 4) on-site CD4 testing and triage for HIV positive women and 5) decentralized treatment programs with HAART available in the same health centers where prenatal care is offered.

Integrating HIV care of pregnant women and PMTCT into routine prenatal care reduces the burden on scarce human resources by streamlining the patient visit. This intervention also improves uptake of HIV testing. Since integrated opt-out testing was implemented, the percent of women accepting HIV tests rose to 90% from the pre-integration acceptance rate of 60%. Perhaps most importantly, integrating both PMTCT services and treatment as closely as possible into prenatal care means that more pregnant women get treatment for themselves; which is ultimately the best strategy to prevent HIV transmission to their children and also ensures that children will have a mother to care for them into the future.

Only 16% of women in middle and low income countries were even tested for HIV during prenatal visits.

Where decentralized, on-site care and HIV treatment was offered, a higher proportion of HIV positive women referred from prenatal care enrolled for care than those referred to off-site, nearby clinics. In places where women could get both prenatal care and HIV treatment at the same health clinic, 77% enrolled for care, versus only 28% who enrolled when they had to be referred to another site for their HIV treatment—even if the HIV clinic was nearby in the same town.[11] Mozambique now integrates even more services into the prenatal care visit itself. In many places, pregnant women can get their CD4 test done in the prenatal visit, the same day they receive their positive HIV test. A few sites now train prenatal care nurses to assess the HIV disease stage of patients using clinical guidelines combined with CD4 results and, if they are eligible under treatment guidelines, to prescribe the initial month of anti-retroviral

treatment until women can become enrolled in the HIV clinic. As result of these innovations, the percent of pregnant women receiving treatment has gone up from about 2% to around 10% in just a couple of years.[12]

While these results are encouraging, more must be done to shift the focus back onto the well-being of both mothers and children. In light of the great gains in HIV treatment access in Africa celebrated over the past several years, the lack of attention for pregnant women is all the more appalling. A new paradigm would focus not just on the infections prevented in children but equally importantly on the numbers of HIV positive mothers and children receiving treatment. By ignoring the mothers, we risk defining success by lowering infection rates in children[13], but increasing the number of HIV orphans.

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Interview with Myron Cohen, MD

Myron Cohen, MD, is Associate Vice Chancellor for Global Health and Director of the Institute of Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill.

Conducted by Robert E. Bank, Esq., Chief Operating Officer, GMHC

Robert Bank: Based on your research, Dr. Cohen, what role should Anti- Retroviral Therapy (ART) treatment of HIV infected people play in prevention efforts?

Dr. Cohen: Currently there are three important uses for ART: one is for post-exposure prophylaxis; we already have guidelines for use of ART in that arena. Second, there are a large number of trials going on exploring the possibility of pre-exposure prophylaxis using ART either orally or topically before exposure. The most important issue is the possibility that treatment also serves as prevention. When a person goes on treatment and the viral concentration in both the blood and genital secretions is suppressed, a person might be rendered much less contagious. We are currently trying to prove this.

Robert Bank: Where are we with respect to number three as far as clinical trials are concerned?

Dr. Cohen: That's a good question. Treatment as prevention has captured worldwide attention. The New York Times did an editorial calling treatment as prevention "a breathtaking aspiration for AIDS." Two big assumptions are currently being tested in clinical trials. One assumption is that early treatment serves to benefit the individual. We are trying to prove that the benefit of much earlier treatment actually outweighs the cost. I don't just mean the cost in dollars; I mean also unexpected toxicities as well. The second assumption being tested is, whether in fact, by using anti-virals we suppress virus in genital secretions so much that a person is actually rendered less contagious to their partner. The National Institutes of Health (NIH) is sponsoring a trial that is testing both these assumptions. The trial has enrolled more than 700 couples, but it won't be done for several years.

In addition population-based studies can determine whether, if enough people in a population are treated with ART, HIV incidence in the population would go down. I think Dr.Julio Montaner is trying to organize such a trial in British Columbia.

Robert Bank: What are the difficulties of such a trial?

Dr. Cohen: First, a trial to prove that ART prevents transmission requires the use of serodiscordant couples. Such couples can be difficult to enroll and manage. Second, we are obligated to use every possible counseling

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mechanism to prevent HIV transmission. So with really good counseling you might make transmission so improbable that you need a very large number of subjects enrolled in the trial. Third, couples don't always sustain their relationship. If they break up the trial becomes more difficult. Fourth, we anticipate early benefits from ART but we are not sure they can be sustained; for example, you might see that anti-viral therapy reduced transmission dramatically in the first year or two, with benefit lost because of lack of adherence or development of resistance, or other unanticipated problems. So such a trial has to go on for a very long period of time.

The big problem with a population based trial is the challenge in treating an entire population.

Robert Bank: Is there some way that you can explain to our readers the importance of other STDs in the acquisition and transmission of HIV?

Dr. Cohen: There is a lot of confusion around this issue. At the end of the day HIV is an STD; most of the people who acquire HIV acquire it sexually.

The classical STD pathogens that cause ulcers and inflammation are transmitted, generally speaking, much more readily than HIV. Someone who is co-infected with HIV and an STD becomes more contagious for two reasons. They can first infect their sexual partner with another pathogen that increases the probability of a transmission event. Second, the inflammation associated with an STD causes the person who has both HIV and an STD to become more contagious. There is at least one study that suggests that you can break through your anti-viral therapy when you get a superimposed STD. STDs are really important players in increasing the efficiency of transmission of HIV.

However, several studies that treat STDs in a community have failed to reduce incident infections of HIV. This has caused great consternation and lack of confidence. But the problem is not that STDs are not important. The problem is that to effectively change the community level of HIV through treatment of STDs requires something incredibly special—treating the right STD with the right drugs at just the right time for the right duration of time. This has been very difficult to accomplish.

Robert Bank: I have heard you speak at numerous conferences over the years and you are one of the leaders in thinking about HIV treatment and prevention and connecting them. With respect to the trials and the work that you have done in your career, what is it that keeps you going?

Dr. Cohen: I have been inspired by visible progress. In 1985 we started an infectious disease ward committed to the care of HIV patients but all we could do was treat opportunistic infections. At that time about 10% of all the beds at University of North Carolina (UNC) hospital were occupied by patients with HIV infections, and we had a high mortality rate. Fast forward 20 years and we rarely have to admit patients with HIV to the hospital because of the massive advances in treatment. As we work more internationally, our challenge is to bring the same benefit to people who live outside the United States.

Robert Bank: I want to end by saying that it is extremely inspiring to hear your passion and it is helpful because it gives people a lot of perspective around how far we've come. You once stated that with respect to the HIV Vaccine, its discovery is analogous to the builders who built the beautiful cathedrals in England—that they never actually got to see them completed in their lifetimes. Do you still believe that to be the case for us?

Dr. Cohen: We have not yet succeeded in making a vaccine. We have two key possibilities: to develop a strategy where exposure evokes neutralizing antibodies or cell mediated protection so great that the exposed person will not acquire HIV.

As an alternative, cell mediated immunity might not prevent infection, but would lower HIV in blood and genital secretions to such a great extent that the disease cannot progress and the person is rendered less contagious.

The bottom line is we have no choice but to make an HIV vaccine no matter how long it takes.

This interview was conducted in December, 2008.