

The amfAR Treatment Insider

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Gotta Have HAART? Durban Debates the Global Standard of Care

by Emily Bass

“Rigor is not the issue of the day, reality is.” So spoke Oxford researcher Roy Anderson at a plenary session on “Living with HIV” at this summer’s International AIDS Conference. More often than not, neither rigor nor reality won out at the Durban, South Africa gathering. Instead, the two exerted an opposed, almost magnetic pull on a parade of speakers struggling to find solutions to glaring global inequities in access to anti-HIV drugs. Hovering somewhere above the plane determined by these two poles was a third principle: reducing prices of anti-HIV drugs through any means necessary so that poor countries facing catastrophic losses from the epidemic could have access to effective antiretroviral therapy.

Parallel importing, compulsory licensing, generic production, tiered pricing, bulk buying were the most commonly mentioned means to reach goal. Yet another tantalizing, albeit elusive possibility is novel treatment strategies to simplify, improve and decrease the cost of the existing standard of care. Simplification is vitally needed in industrialized countries, too, as healthcare systems strain to support the cost of lifelong HAART (highly active antiretroviral therapy), and their HIV-positive

inhabitants strain to support lifelong antiretroviral drug side effects.

At the end of the International Conference, researchers were still frustrated in their attempts to navigate between these conflicting poles of attraction. They could not chart a definitive course, but perhaps they had begun to trace out an emerging global effort to treat persons with HIV.

HAART in Africa

When it comes to using HAART in Africa, there’s good news and bad. The good news: Data from small pilot programs in the Ivory Coast and Senegal suggest that combination therapy will be no less effective in Africa than it is in the United States. In the Ivory Coast study, for example, 51% of those on antiretroviral therapy had undetectable viral loads after 10 months.

This Ivory Coast UNAIDS Initiative enrolled 2,144 individuals and provided anti-HIV therapy to those who could pay or qualify for subsidies. Even with subsidies and UNAIDS involvement, most Africans still not afford antiretroviral drugs. Only 422 of the 2144 participants received treatment. Of these, almost two-thirds took AZT/ddI dual therapy. A mere 36% had a protease inhibitor (indinavir) in their regimen.

In an overlooked presentation, Ivory Coast researcher A. Juillet analyzed the extent to which UNAIDS had improved drug access and concluded that, “the Initiative had a small impact on the prices of ARV [antiretroviral therapy] in the short-term.” In contrast,

generic availability of such drugs as AZT and d4T brought a 16% price reduction.

Making Do with Two Drugs

Dual therapy is undeniably a poor substitute for HAART. But when a UNAIDS-funded program treats two-thirds of patients with two nucleoside analogs, the question looms: Is some treatment better than none at all? This debate played out in various sessions and was officially tackled by Julio Montaner of the British Columbia Centre for Excellence in HIV/AIDS and Praphan Phanuphak, director of the Thai Red Cross AIDS Research Centre in Bangkok. Phanuphak, an outspoken advocate of maximizing limited resources, posed the question this way: Is dual nucleoside therapy worth providing if it can in the short run reduce disease progression, increase CD4 counts and possibly drop viral load enough to significantly reduce chances of transmission? His answer was an emphatic yes.

Little research has been done on how best to use limited therapeutic resources. Phanuphak cited HIV NAT 002, a trial of d4T plus ddI in which 58% of patients on the two-drug regimen for two years had undetectable viral loads. (This trial used the bDNA assay, which measures viral load down to what the more standard PCR test would consider 1,500 copies/mL.) Phanuphak argued that even if two nucleoside analogs do not fully suppress viral load, they may buy patients valuable time. Delaying treatment until CD4 cell counts approach 200 is a cost-saving measure, but other considerations can prevail. If a patient wants to secure a window of time to earn money, attend a wedding, or await the birth of a child, it may be better to intervene earlier.

One of the NAT 002 co-investigators, well known Australian AIDS researcher David Cooper, agreed. He commented, "We are encouraged by the persistent good responses. I think that on balance dual nukes are OK in the developing world as a hold measure for persons who can't afford triple [combination therapy]."

The Thai trial participants may also have benefited from improved treatment of concurrent infections after they began receiving special attention from the trial staff. Treating such infections is much easier than treating HIV and may significantly diminish HIV replication. In Durban, Zvi Bentwich of Hebrew University of Rehovot, Israel related such an experience when treating HIV-positive Ethiopians for intestinal worms. Bentwich observed that eliminating these helminthic worms reduced chronic immune system activation. Activated CD4 cells are

particularly prone to invasion by HIV infection and are the main site for viral replication.

The next question Phanuphak tackled was, "Will double nukes engender resistance and complicate future treatment options?" His answer: not necessarily. HIV NAT 001 was a Thai study of AZT plus ddC in which 95 participants were able to switch after 66 weeks on dual therapy to a three-drug regimen that contained AZT/3TC or d4T/ddI plus the protease inhibitor Fortovase (soft-gel saquinavir). After 84 weeks of the new regimen, 78% of the volunteers had HIV levels below 50 copies/mL.

For his part, Montaner argued that it is both medically and morally unfeasible to settle for anything less than HAART. "HAART is defined by full [HIV] suppression; not by the number of drugs," Montaner noted. He pointed out that mortality rates are significantly lower among those on triple combination therapy, and that individuals on double nucleoside analog regimens switch drugs more frequently than those on HAART regimens.

Playing the Cycle Game

As with last winter's 7th Conference on Retroviruses and Opportunistic Infections in San Francisco, much attention was paid at the International Conference to structured treatment interruptions (STIs). STIs promise to cut the costs of therapy first because patients need not continually take drugs and second because they may permit patients eventually to stop therapy altogether.

The original theory behind STIs was that periodically going off therapy allows HIV levels to rebound temporarily, enabling the immune system to learn how to control HIV through repeated controlled exposures to the virus. STIs would function much like a vaccine and eventually permit patients to stop treatment permanently.

Data presented in Durban suggested that this approach was unlikely to be successful. The first long-term results from the 122-person Spanish Swiss Intermittent Therapy Trial, which is the largest STI trial to date, revealed no trend toward decreased viral loads after successive STIs. The SSITT participants begin the study with viral loads below 50 copies/mL while on HAART. They are supposed to stop HAART four times for two-week intervals separated by eight weeks on treatment. At week 40, they go off therapy until their viral loads rise above 5,000 copies/mL. Of the 14 now beyond week 40, only two had viral loads that stabilized below the 5,000-copy threshold.

"I think that on balance dual nukes are OK in the developing world as a hold measure for persons who can't afford triple [combination therapy]."

There were some indications that anti-HIV immune responses improved in SSITT participants, but cell culture tests measuring such responses might not reflect the situation within the human body, warned Andrew McNeil of the National Institute of Allergy and Infectious Diseases (NIAID) in the U.S. In his study of seven persons taking a break in treatment, immune responses to HIV actually decreased, not because the necessary CD4 cells disappeared, but because they lost the ability to proliferate as HIV levels increased. McNeil warned that some as yet undiscovered property of HIV infection suppresses immune activity beyond the virus's cell-killing effects.

If STIs now seem unlikely to lead to drugless control of HIV, at least they still could reduce the burden of drug side effects and costs. They also could make patients' lives easier by reducing the amount of medication they must take. Anthony Fauci, chief of the NIAID, was excited enough about these prospects to conclude his Durban lecture by showcasing his lab's treatment interruption research.

Fauci later commented, "[HIV] remission or eradication – that's not feasible for people in chronic infection. We're trying to create a situation in which people could be off drug for a fixed period and HIV doesn't rebound or impair CD4 count."

Fauci and his NIAID group are now focusing on what they call "SITs" – structured or short-cycle intermittent therapy. They are testing three different schedules: two

months on therapy with one month off; seven days on with seven days off; and two days on with five days off. In Durban, Fauci and his associate Mark Dybul presented the preliminary results of two pilot studies testing the SIT technique. The trials enrolled persons whose HIV had subsided on HAART to less than 50 copies/mL.

All nine volunteers following the one-month off schedule did experience a rebound in their HIV, but all returned to undetectable levels when back on therapy. So far, they have gone through two on-and-off cycles. There has not yet been any sign of drug-resistant HIV. This is everyone's main concern when allowing periodic high-level HIV replication. As in the SSITT, there also was no evident tendency for reduced peak viral levels during successive interruptions.

Four volunteers spending seven days on and seven days off drug have maintained viral loads below 50 copies/mL for two months so far. Three volunteers following the two-day on/five-day off schedule have not fared so well. By week eight, two of the three were

dubbed failures because their viral loads had rebounded to above 500 copies/mL. CD4 counts remained stable on both schedules.

Of course, such provisional data should not encourage community use of SITs. The long-term success of this approach remains an open question. Patients may not be able to keep their HIV suppressed over long periods because of the emergence of drug resistance. The interval between treatment cycles that best precludes this danger is still not known.

The precise steps required when interrupting therapy are also undetermined: Current knowledge of the speed with which the body eliminates drugs is insufficient to decide exactly when each drug should be stopped. If all drugs in a combination regimen are stopped at once, some will disappear from the body very quickly while low levels of other drugs persist. A patient's HIV will in effect be exposed to suboptimal treatment for up to several days. As the virus again begins to replicate under these conditions, mutated drug-resistant HIV may out-compete normal, "wild-type" virus and become widespread in the patient's body. Only further experience will define the extent of that risk of developing drug resistance.

"We're trying to create a situation in which people could be off drug for a fixed period and HIV doesn't rebound or impair CD4 count."

In the NIAID study, patients on efavirenz stopped the drug a day before their other medications because of its particularly long half-life in the blood. Giving the drug a 24-hour head start to clear out of the body appears to have worked – at least so far.

A major worry is the nucleoside analogs. Their intracellular half-lives vary immensely, making it nearly impossible to know exactly when to stop each drug.

The number of open questions surrounding SITs led some community advocates to question whether NIAID should have brought its data to the conference. Doubts do remain about SITs' ultimate impact on HIV suppression, drug side effects and patient quality of life, the economic benefit is self-evident.

That economic benefit last year led Bombay AIDS specialist Shashank Joshi on his own to try month-long on-off cycles of AZT or d4T, 3TC and saquinavir. He tested this schedule in 26 newly diagnosed patients with HIV viral loads above 20,000. Joshi reported that after a year, all had undetectable viral loads and remained clinically asymptomatic.

The Rush to Cut Corners

The economic benefit of treatment interruptions may be most compelling in resource-poor regions. It also

has great attraction in developed countries as these nations struggle to cope with HAART's pharmaceutical and patient management costs.

Western models of HIV care may in any case be too aggressive. British AIDS specialists in particular take this position, as does Dr. I. S. Gilada, Secretary General of People's Health Organization in India. He said, "I don't even think what the Western world is doing is right. On more than 60 to 70% of occasions, they are over-treating their patients, treating when it is not required, often treating with higher doses than what is optimal, and with more drugs." The argument over "rigor versus reality" may have an unanticipated resolution if it turns out that simplified therapies are preferable even in industrialized lands.

There is a difference between conservative treatment and blindly cutting corners, however. Techniques like treatment interruptions, dual nucleoside analog therapy and delayed therapy have yet to be vetted by extensive, long-term study. For that reason, they are not ready for acceptance as standard practice.

Preventing Mother-to-Child Transmission Highlights Durban Conference

by Emily Bass

At the 13th International AIDS Conference in Durban, updates on mother-to-child-transmission (MTCT) strategies told a tale of two worlds. In one world, the race to prevent transmission has been almost won; in the other, the most effective regimens still leave women and newborns at loggerheads with a virus that uses every misstep to its advantage. Where there is access to HAART, more and more pregnant women are starting or remaining on combination therapy with good results. The most pressing concerns are the unknown long-term effects to children exposed to these drugs *in utero* and the risks of developing drug-resistant virus. In the developing world, studies of simple drug regimens have reported dramatic effects on rates of transmission at the time of delivery. They hardly eliminate all transmission, though, and there is troubling evidence that their benefits may be eroded when women breast-feed their infants.

The Promise of Short Regimens

Daya Moodley, of the University of Natal Medical School, presented the much-anticipated results of the 617-infant South African Intrapartum Nevirapine Trial (SAINT). This trial compared giving AZT and 3TC to

the mother during labor and to the baby for the following seven days to a very short course of nevirapine – one dose to the mother during labor plus one dose to both newborn and mother one to two days after birth. In line with last year's Ugandan study, HIVNET 012, SAINT found that simple nevirapine regimens resulted in reduced MTCT rates of 12% to 14%, as measured six to 12 weeks after birth.

One-year data from HIVNET 012 showed that seven out of 30 (23%) women who received a single dose of nevirapine acquired resistance mutations, including K103N, the point mutation that renders HIV essentially unsusceptible to all approved non-nucleoside reverse transcriptase inhibitors (NNRTIs). These mutations become undetectable 13 to 18 months after delivery. Both the short duration of dosing and the relative fitness of wild-type HIV compared to K103N-mutated strains probably contribute to the virtual elimination of the NNRTI-resistant HIV. Minor undetectable populations of NNRTI-resistant HIV may still be present, but the prevailing opinion at the conference was that the very short nevirapine courses would still be safe for use in repeated pregnancies.

It remains to be seen how nevirapine will affect the treatment options of women in developing countries should antiretroviral drugs become available through the standard health-care system or clinical trials. During ongoing treatment with nevirapine or other non-nukes, even a small subpopulation of resistant virus could re-emerge and pose problems over time. Although potent anti-HIV combination regimens remain a distant, hypothetical prospect for most women in the developing world, widespread nevirapine MTCT programs are possible, and their effects deserve close monitoring.

One option, where the resources are available, is to offer both AZT and nevirapine, reserving nevirapine for women diagnosed late in pregnancy. Another, suggested by University of Alabama at Birmingham researcher Sten Vermund, is to reserve NNRTIs for pregnancy and to move forward with adult therapy solely in the form of protease inhibitors and nucleoside analogs (also known as NRTIs). "If nevirapine is used in the wider community for HIV care, then community resistance could be a sizable problem," stated Vermund. "This is why I believe that policy makers at UNAIDS and in ministries of health should consider NRTI/PI combinations as the standard for care where affordable and reserve NNRTIs for MTCT." Ruling out an entire class for adult treatment may not be an option, considering cost, toxicities, underlying resistance profiles, and the fact that the NNRTI efavirenz (Sustiva), which offers once-daily dosing, is an attractive option for simplified regimens.

News on NRTI-based regimens came from BMS 094, a study presented by McIntyre's colleague, Glenda Gray. BMS 094 looked at the efficacy of four different regimens for prevention of MTCT, including a previously untested dual NRTI combination: d4T, ddI, ddI/d4T, and AZT. All four regimens were given from weeks 34 to 36 of pregnancy through week 6 of the infants' life. At six weeks postpartum, the rates of transmission in the four arms were 4.2%, 1.9%, 2.0% and 6.3%, respectively. All four regimens cost between \$60 and \$100 per mother-child pair. The study has not yet yielded data on resistance patterns or long-term rates of transmission.

There was an average -1.2 log (94%) reduction in mother's viral load during the 094 trial's relatively extended course of therapy. One-third of the women studied had less than 400 copies/mL at the time of delivery. The reduction in viral load may have led to the superior results in this trial. BMS 094 and similar studies could be useful in designing innovative treatment strategies. One widely discussed option proposed using short-course antiretroviral therapy to reduce viral load, followed by a therapeutic vaccine to stimulate immune-based viral control.

Breast-Feeding Controversy

Data on the efficacy of antiretroviral therapy given during pregnancy and at the time of delivery tells only part of the story about transmission risk. One Kenyan study by Ruth Nduati estimated that 44% of all HIV infection in breast-fed children is acquired through mother's milk. The clearest example of this came from the southern African PETRA study, which looked at rates of transmission in 1802 infants. The trial measured the efficacy of AZT/3TC when administered to mother and baby in three different schedules: from week 36 of pregnancy through the first week after delivery; during labor and the week afterward; or during labor only. A control arm received only placebo. At six weeks, rates of transmission varied from 9.2% in women who started therapy at week 36 to 19.2% in the placebo arm. By 18 months, this spread had narrowed considerably. Although a trend favoring treatment persisted, there was no significant difference in rates of transmission among the four arms, including the placebo one. Some 70% of infants in the study were breast-fed, and researchers concluded that this factor alone accounted for "the loss of efficacy in all regimens."

The simplest way to reduce the risk of transmission through breast milk is through formula feeding. This

strategy eliminates exposure to HIV, but it also means that infants do not receive the nutritional and immunological benefits of breast milk. Kenyan researcher Ruth Nduati and her colleagues presented data on rates of mortality in 401 breast- and bottle-fed infants born to HIV-infected women. At 12 months and again at two years, there was no significant difference in rates of mortality between these infants. At three months, infants randomized to the formula-feeding arm had higher rates of diarrhea and dehydration. Although the added diarrhea did not translate into higher mortality rates, it did underscore the need for access to adequate supplies of formula and clean water, as well as continued monitoring and support of mother and child.

An estimated 44% of all HIV infection in breast-fed children is acquired through mother's milk.

Nduati also presented the first study to examine the impact of breast-feeding on maternal, rather than infant, mortality, reminding the audience, "Replacement feeding is an important option for women as well as children." Women who breast-fed lost more weight than those who formula fed and were three times more likely to die. Controlling for other factors, the Kenyan team concluded that 86% of the deaths was attributable to breast-feeding. Their ongoing research will attempt to confirm these results and identify underlying metabolic and nutritional causes.

South African researcher Anna Coutsooudis highlighted the complicated issues involved in feeding choices. In follow-up data to her 1999 report in *The Lancet*, Coutsooudis again found that infants who received a mixture of bottle- and breast-feeding were at a higher risk of mortality than those who were exclusively breast- or bottle-fed. Infants who were exclusively breast-fed for up to six months had no more risk of contracting HIV than those who were never breast-fed.

This unexpected, controversial result came from a retrospective analysis of a 536-infant study of the effect of vitamin A supplements in reducing MTCT (no protective benefit was observed). Since the trial was not a breast-feeding study, its results may be flawed by confounding factors that remain unaccounted for. One major criticism of Coutsooudis' analysis is that the mothers who exclusively breast-fed may have been healthier in some way. Most importantly, their viral loads may have been lower. Coutsooudis maintains that viral loads were similar regardless of feeding method among the subset of mothers in whom she checked. Still, mastitis and other breast conditions may well have been greater in the mixed breast-feeders than the exclusive ones. Such inflammation can provide a route for HIV to enter breast milk in greater quantities.

Coutsoudis argued that the apparent protection conferred by exclusive breast-feeding could be explained by reduced digestive tract inflammation in the infants. They were not exposed to the allergens and contaminants present in reconstituted formula and other liquids given the mixed-fed babies. Extra inflammation possibly present in these babies' digestive systems could make them more susceptible to the HIV even though their total intake of breast milk was less.

HAART Safety

Current U.S. guidelines recommend that pregnant women start or remain on whatever anti-HIV regimen is best for their own health. Not surprisingly, this translates into increasing numbers of women giving birth on highly active antiretroviral therapy (HAART) combinations. The overall experience has been good. Data from the U.S. observational study known as the Women and Infant Transmission Study (WITS) showed that rate of transmission was inversely correlated with the number of drugs a woman was taking. Rates of transmission for women on AZT monotherapy were roughly 7.7%. The figure dropped to 1.1% for women on HAART. The researchers concluded that HAART provided "an independent protective effect" regardless of viral load levels at delivery. In a Puerto Rican cohort presented by Carmen Zorrilla, there was no transmission – and no significant side effects – in women taking HAART or AZT/3TC during pregnancy.

One note of alarm came from Patrizio Lorenzi's Swiss Mother+Child HIV Cohort Study. Two years ago, Lorenzi and his colleagues set off alarms with initial reports of unusually high rates of adverse events in pregnant women and newborns on HAART. In the Durban update, Lorenzi's most striking finding was an increased risk of premature delivery in women taking HAART as compared to those on AZT or no HAART at all. Twenty-eight percent of women on combination therapy delivered prematurely, as opposed to 17% on AZT and 14% in the group that received no drugs at all. Lorenzi's first study prompted a National Institutes of Health review of women who gave birth on HAART. The report concluded that HIV itself may increase women's risk of delivering prematurely and that protease inhibitors did not increase that risk.

Findings presented at Durban again contradicted Lorenzi's observations. In Zorrilla's cohort, for example, there was an average prematurity rate of 20 percent across all the arms of the trial. However, the Swiss research is a useful reminder that careful ongoing study of HAART is needed to determine the extent of short- and long-term risks to mother and child.

Additional HAART further encourages the evolution of drug-resistant HIV. Several studies at the International AIDS Conference looked at the relationship between resistance-conferring mutations and rates of transmission. A U.S. study of that correlation found that 12 of 24 women who transmitted HIV to their babies had NRTI or NNRTI resistant virus. Eight out of 23 (35%) infected infants also had resistant virus, and all except one infant had HIV resistance patterns resembling that found in their mothers. Not surprisingly, there was a threefold increase in risk of transmission linked to AZT resistance. Additional risk factors for transmission included low CD4 counts, high viral load and having started on AZT prior to pregnancy.

Caring for the Woman, Not Just the Mother

by Emily Bass

Eric Goemaere is a physician from Doctors without Borders who heads an HIV/AIDS clinic for infected mothers and community members in Khayelitsha, South Africa. Speaking in the aftermath of the encouraging reports on preventing mother-to-child transmission at the International AIDS Conference, he observed with satisfaction, "MTCT [programs] will now be seen as very politically correct and beyond that very feasible."

About 1,800 HIV-infected infants are born each day in South Africa. Universal, or even widespread, MTCT coverage would reduce this figure dramatically. Unlike the complicated, costly project of treating infected adults with antiretrovirals, MTCT programs appear to offer a straightforward solution to one of HIV's most devastating routes of transmission. At the most basic level, MTCT programs require little more than HIV testing kits and a small supply of nevirapine or AZT and 3TC. In many instances, the elements of pre- and post-test counseling, formula feeds and antenatal care are also included. Even so, the package of care involves far fewer laboratory and human resources than even the most bare-bones adult HIV clinic would offer.

Wait a Minute

Cost-effectiveness aside, MTCT programs have their drawbacks. Many parties – women, in particular – are left out of the equation. At Ubumbano IoMama, a women's satellite meeting in Durban, attendees told stories of MTCT interventions that boiled down to receiving a diagnosis and a drug with little or no counseling, support or follow-up care. Such intervention may cut

down on perinatal transmission but does nothing for women themselves. At a time when women make up more than half of the world's AIDS cases, this is a dangerous omission. Activists were quick to point out that the Boehringer-Ingelheim offer to developing countries of five years' free nevirapine for MTCT did not include treatment for the mothers. Nor did any of the numerous studies of MTCT in African countries include antiretroviral therapy for women participants.

At the official meeting, many speakers acknowledged the ethically uncomfortable, if not untenable, implications of offering treatment to the women solely to prevent transmission. "Short-course AZT uses women's bodies to deliver benefit to the infant," stated Dr. Allen Rosenfield in a keynote lecture titled "Where is the M in MTCT?". At the same session, South African pediatrician and MTCT advocate Glenda Gray observed that current evaluations of MTCT efficacy take women into account solely as "vectors of viral transmission."

Failure to manage women's disease with whatever treatments are available may well reduce the long-term efficacy of MTCT strategies. Many babies, both infected and uninfected, will die without their mothers. In Durban, Kenyan researcher Ruth Nduati showed data indicating that maternal death causes an eightfold increase in the risk of subsequent infant mortality. As the number of orphans increases, so do the economic and social costs to families and nations. "[The economic studies] have been most discouraging," said Sten Vermund of the University of Alabama at Birmingham, "It highlights the massive loss in productivity and the distortion of the 'dependency ratio' in Africa due to the death of mothers and fathers. Therapy for mothers, whether it's oriented toward opportunistic infections, HIV or both, would be a huge step forward in addressing this crisis."

A Foot in the Door

It is a step that many MTCT advocates are ready and willing to take. Instead of holding back MTCT offerings, they argue, it is time to use them as the cornerstone of a larger strategy for HIV management. "MTCT is the entry point for a broad range of things," said Goemaere. "As soon as you make an offer of MTCT, people go for testing. As soon as they go for testing, they're going to make support groups, which means action groups. You will have to attend these people, make clinics for them – it's a snowball effect."

Many MTCT programs are already being designed with this type of expansion in mind. In the Kenyan model, women will be referred to existing programs at hospitals and community programs for follow-up, coun-

seling and regular management of opportunistic infections. "While the mom is pregnant, you don't hear about her issues," said Dr. Mbori-Ngacha. "If you only see a woman in the antenatal clinic, you don't get a sense of her problems." In South Africa, Doctors Without Borders added an adult HIV clinic to the country's single publicly funded perinatal transmission prevention program. With this in place, infected men, women and children are now cared for using currently available drugs, including basic medications for STDs and opportunistic infections plus cotrimoxizole (Bactrim) prophylaxis for *pneumocystis carinii* pneumonia (PCP). A similar offering is in place at a University of Alabama-sponsored study site in Zambia. In each case, the results are promising. "While the impact is hard to document due to the lack of a control group [for ethical reasons], nonetheless the data suggest a substantial decline in mortality compared to what might be expected," said Vermund.

The expanded concept of MTCT is a community-based model for HIV care. Like TB programs, MTCT assistance has the potential to identify and treat a large number of individuals already in contact with the health-care system. Defined in this way, the programs become more useful – and more expensive. "I think the resistance to MTCT in this country is partly due to the fact that they know very well when they start by putting their finger in [the AIDS epidemic], they will not be able to stop," said Goemaere.

The specter of the snowball effect may explain why some countries, notably South Africa, have yet to move forward with a national MTCT prevention initiative. In August, South Africa announced that it was holding back an "implementation phase" that would make nevirapine available to all pregnant women. Instead, health minister Manto Tshabalala-Msimang called for "continued research" on the drug in all five South African provinces. At press time, only women participating in approved research projects will be able to access the drug. South Africa's decision came in spite of a favorable cost-effectiveness report on nevirapine sponsored by its own Ministry of Health.

Although South Africa may be dragging its heels, it seems likely that MTCT initiatives will continue to take root around Africa and the developing world. Durban marked a point of no return in global recognition of the importance of access to treatment. MTCT programs have the ability to bridge the gap between prevention and treatment and to mobilize HIV-infected women and their families to demand treatment for themselves. As Zambian researcher Chewo Luo stated in her fiery plenary speech on MTCT, "It is up to women to say what the solution is."

Coping with the Husband

by Emily Bass

Nevirapine may be safe for newborns, but are MTCT programs safe for women? For those involved in tracking the alarming statistics of violence against HIV-positive women, the answer has less to do with drug toxicity than with gender inequity and the pervasive social stigma surrounding the virus. "If a woman fears violence, how can she tell her husband [that she is HIV-positive] or return to her community?" asked Nadine France, a World Health Organization researcher who studied the links between violence against women and HIV in Rwanda. "What happens if her husband or partner sees that she is taking the drugs?"

MTCT programs place women in the potentially dangerous position of being the first member of a household to be diagnosed with the virus. If women disclose their status, they run the risk of being blamed for bringing the disease home. Often this means violence and loss of financial and emotional resources. If they decide not to disclose, they must cope alone with the burden of shame, secrecy and isolation.

In South Africa, Kenya and Zambia, researchers are attempting to bridge this gender gap by reaching out to couples for HIV testing and counseling. A recent *Lancet* study of couples-focused voluntary counseling and training (VCT) in Kenya, Tanzania, and Trinidad found that this approach reduced rates of unprotected sex among both men and women. "Women fear blame, abandonment and adverse consequences," said Dr. Dorothy Mbori-Ngacha, a Kenyan pediatrician. "So we've opened the antenatal clinic door to men. They come because they have a common interest in the unborn child."

Reaching out to men will be all the more important if MTCT programs are expanded to include adult antiretroviral therapies. Although testing during pregnancy means that women are the first to be diagnosed, it is no guarantee that they will be the first to access treatment. "Obviously what will happen, given the

power balance is that as soon as [antiretroviral] treatments become more popular and more known, it will be impossible for the women not to share them with their partners," said Eric Goemaere of the Doctors Without Borders AIDS clinic in Khayelitsha, South Africa.

Several studies at the International Conference documented wide variation in women's willingness to learn their HIV status – from more than 90% in Thailand to less than 30% in several African studies. Understanding the social and cultural forces underlying these disparities will help in the design of programs that support, rather than stigmatize, women participants.

Many advocates hope that by increasing awareness and bringing women and their families in for voluntary testing, MTCT programs will indeed increase community access to information about HIV prevention and care. There may be no better place to start. As Geeta Rao Gupta of the International Council for Research on Women told a Durban crowd, "Empowering women empowers families, communities and entire nations."

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AIDS RESEARCH



Emily Bass Joins the *Insider*

The *Treatment Insider* is pleased to welcome Emily Bass on board as our new senior correspondent. We look forward to a long and fruitful collaboration.

Emily most recently hails from *HIV Plus*, where she was senior writer. While at *HIV Plus*, Emily concentrated on obstacles to care for women and children, development of antiretroviral drugs and the writing of federal standard-of-care guidelines. Her background is certainly reflected in this issue's coverage of the 13th International AIDS Conference.

Recent projects include a women's clinical trial handbook, a special issue of *Poz* for the newly diagnosed and an ACLU conference on HIV and hepatitis in prisons.

Her work has also appeared in *Ms.*, *MAMM*, *Out*, *Salon* and *aidsmeds.com*.