The 2004 International AIDS Conference and How to Globally Counter HIV/AIDS

Vincent Idemyor, PharmD

Advocate Bethany Hospital and Department of Medicine, University of Illinois College of Medicine, Chicago, Illinois, USA

This article reports noteworthy HIV/AIDS clinical trials presented at the XVth International AIDS Conference, Bangkok, July 2004, and also outlines goals of comprehensive prevention, care, treatment, and monitoring plans. The Bangkok conference theme was "Access for All." Outlined are goals of comprehensive prevention, care, and treatment programs: increased education and prevention efforts, greater involvement of national health authorities, reduction of new HIV infections, increased use of voluntary counseling and testing, increased acceptance and use of condoms, acceptance of an individual's right to be protected against HIV infection during sexual activity, increased support of NGOs, reduction of sexual partners, increased sexual fidelity, availability of antiretroviral medication, prevention of mother-to-child transmission, reduction of AIDS deaths, improved surveillance of sexually transmitted infections, improved blood supply security, increased coordination with tuberculosis and malaria treatment, equity for urban and rural persons, increased orphan services, reduction of orphan rate, greater involvement of local leaders, increased media involvement, reducing HIV/AIDS discussion taboo, reduced injecting drug user needle sharing, and continuing education for health care professionals. Monitoring parameters include incidence and prevalence of HIV infections, use of voluntary counseling and testing, condom use and attitudes to right of protection, AIDS deaths, orphan rate, public advertisements, leadership participation, antiretroviral use and availability, public awareness of services, blood supply security, and professional education. **Key words:** *Access for All, comprehensive programs, HIV/AIDS*

Approximately 40 million people worldwide live with human immunodeficiency virus (HIV) infection, the viral infection that causes acquired immune deficiency syndrome (AIDS). To review what has been learned about this global problem and to discuss what can be done to control this pandemic, physicians, scientists, public health officials, and community organizers, including this author, met and exchanged ideas from July 11 through July 15, 2004, in the Southeast Asian city of Bangkok at the 15th International AIDS Conference.

A conference that began in 1985 as a much smaller annual gathering of scientists sharing information on HIV has become a biennial gathering of more than 15,000 delegates from 160 countries and turned Bangkok into a global village for one week.

The Bangkok conference included very little medical science compared with past conferences that were marked by major breakthroughs in understanding the pathogenesis of HIV and in antiretroviral drug discoveries; however, extensive material was presented in the areas of social science, economics, policy, and implementation.

Major scientific breakthroughs in the field of HIV/AIDS normally require that extraordinarily complex immunological riddles be overcome to try to outsmart the virus. There were few noteworthy clinical trials presented that looked at the efficacy and safety of antiretroviral drugs. In the protease inhibitor (PI) class, Gathe[1] reported the 48-week final analysis of the IMANI–1 TC3WP study involving the use of lopinavir/ritonavir as a single

For correspondence or reprints contact: Dr. Vincent Idemyor, 5305 South Drexel Avenue, Chicago, Illinios 60615 USA.
Email: Idemyor@juno.com

HIV Clin Trials 2005;6(1):43–49

www.thomasland.com

agent in 30 antiretroviral-naïve patients in an oral presentation. The number of patients reaching viral loads <50 copies/mL was 60% in an intent-to-treat analysis and 90% in the as-treated analysis. There was a mean 317-cell rise in CD4 lymphocyte count. However, there was concern about the long-term outcomes of those who were successful on this regimen, because single-agent therapy is not currently recommended as best practice in the therapeutic management of HIV disease.

Ruane et al.[2] described how maintenance with lopinavir/ritonavir alone in 19 patients who were well-controlled on highly active antiretroviral therapy (HAART) regimen with no underlying protease resistance effectively maintained virologic suppression (viral load < 75 copies/mL) in 73% of the HIV-infected individuals. The 27% failure rate in this patient population with prior treatment success is of great concern to HIV/AIDS treating clinicians.

Typical HAART includes a PI or nonnucleoside reverse transcriptase inhibitor (NNRTI) with a combination of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs). PIs seem to offer the opportunity to be used sequentially in many situations. Some of the PIs appear to have a greater capacity to overcome viral genetic barriers that can lead to development of resistance, thus there is a greater resurgence of interest in the proper role of PIs in the therapeutic management of HIV disease.

A number of presentations alerted the attendees to the pharmacokinetics of boosted PIs. Atazanavir, an azapeptide aspartyl PI approved in 2003 by the Food and Drug Administration (FDA), was shown to have double boosting effect on saquinavir when combined with ritonavir. Saquinavir drug concentrations increased significantly as compared to boosting with ritonavir alone.[3]

An update at 96 weeks on the fusion inhibitor enfurvitide, studies known as TORO, was presented.[4] The TORO studies compared enfurvitide plus an optimized background regimen to optimized background alone in heavily treatment-experienced HIV-infected individuals. At 96 weeks, 55% of the (N = 368) patients remained on treatment with enfurvitide plus optimized background. Twenty-three percent of patients on enfurvitide plus an optimized background had viral loads <50 copies/mL versus 8% in the optimized background arm.

The Perinatal HIV Prevention Trial (Thailand) investigators reported and published their data dealing with the compelling problem of nevirapine resistance when a single dose of the medication is used for preventing perinatal transmission.[5,6] In the developing world, single-dose nevirapine regimen for preventing perinatal transmission is the most widely available form of treatment because it is relatively inexpensive. In their studies,[5,6] more than 600 pregnant women who received zidovudine at week 28 of gestation were randomized to no additional therapy or to a single intrapartum dose of nevirapine. The infants in the group receiving a single intrapartum dose of nevirapine were further randomized to an additional single dose of nevirapine or no nevirapine within the first week of life. The addition of nevirapine was more effective at preventing perinatal transmission, however women with resistance mutations who were subsequently started on nevirapine-based regimen for treatment had a poorer response to treatment than those who had not received a single intrapartum dose of nevirapine.

An intensive investigation in the area of metabolic complications of HIV disease continues, and some data did emerge at the conference. However, we are still waiting for long-term results from randomized trials in the developing world where the primary endpoint is the evaluation of currently available antiretroviral regimens, and objective assessments of body composition, markers of insulin resistance, and measures of glucose and lipid blood concentrations are secondary endpoints.

In the area of HIV pathogenesis, Dr. Anthony Fauci of the United States National Institutes of Health lectured on the role of HIV-associated immune activation in an unabstracted lecture. He narrated how HIV directly activates the immune system, leading to increased T-cell turnover, increased activation-induced death of T cells, a decrease in the size of the CD4 T lymphocyte pool, and a state of activation-induced immune deficiency. So far, only HAART has been shown to reverse the immune activation successfully. However, HAART cannot eliminate the reservoir of latently infected T cells.

Papers on adherence were presented that showed high levels of medication compliance in the continent of Africa.[7,8] This is important because a few years ago there were concerns about adequate adherence and sustainability in the developing world.

However, research on interventions to improve adherence is still in its early development.

Although some scientific and medical advances were reported, the main thought on almost everyone's mind seemed to be the issue of access and the severe lag between what is available to a few people and what is needed by many more.

THE BANGKOK CONFERENCE AND ACHIEVING "ACCESS FOR ALL"

The theme of the Bangkok conference was "Access for All," which highlighted the importance of cooperation among various disciplines, ranging from science to community organizers. At the conference, scientists, policy makers, activists, and HIV-infected individuals gathered to discuss the state of HIV pandemic and how to stop its progression. In 1994, about US $200 million was available for resource-limited countries for HIV treatment and prevention, whereas by 2004 about $5 billion was available for resource-limited countries from the Global Fund for AIDS, Tuberculosis and Malaria; the World Bank; Bill and Melinda Gates Foundation; the European Union; and the President's Emergency Plan for HIV/AIDS Relief (PEPFAR).

In 2003, the World Health Organization (WHO) adopted a plan called the 3 by 5 Initiative, or simply, 3 by 5, which is setting a target of getting three million people in resource-limited settings on antiretroviral therapy by 2005. The aim is to mobilize the many stakeholders globally, regionally, and locally who will play a part in rapidly expanded access programs of antiretroviral therapy in the developing countries. Currently, between 100,000 and 150,000 individuals in the developing world have access to antiretroviral therapy, many through nongovernmental organizations. If it is estimated that approximately 3 million people currently are at a stage of HIV infection at which antiretroviral therapy would be medically indicated, then, at this rate, the goals of the 3 by 5 program cannot be met. Additionally, there are numerous other aspects of the pandemic that will not be addressed solely by providing the urgently needed antiretroviral therapy to those for whom it is indicated. It is clear that comprehensive plans to counter HIV/AIDS must be put in place in countries in the developing world. What should be the goals of such plans?

WHAT ARE THE GOALS OF A COMPREHENSIVE PLAN TO COUNTER HIV AND AIDS?

As the box titled "Goals of a Comprehensive Plan to Counter HIV and AIDS" shows, there are many features needed to create an effective program to combat HIV/AIDS. Each component addresses a distinct issue. All of the components are logical steps, and so it may be best to view this approach as a comprehensive effort rather than a complex one. The complexity that does exist comes from the necessary coordination of efforts to achieve efficient service delivery to individuals, their families, and sexual partners.

The Importance of Education and Prevention

The most effective strategy available at this time to stop the pandemic is prevention of new infections, largely through public education about condom use, increased fidelity, and high-risk behaviors. Many activities are part of an effective prevention strategy, including public advertising, voluntary counseling and testing, community outreach, condom distribution, antiretrovirals for pregnant women, and antiretrovirals for those for whom medically indicated. A major part of the education effort must be through public advertising.

Public Advertising

Public advertising must raise topics that previously have been taboo in a culture, for example, open mention of sexual activity and the need for condom use. However, public advertising is no guarantee that infection rates will magically be lowered. High profile national leaders must step into view, along with local community leaders, educators, and clergy. National celebrities pitching safe sex on television can help. Promotion of fidelity and the reduction of sexual partners are ticklish issues, but there is a correlation between reduced numbers of sexual partners and a reduction in HIV transmission rates.

Advertising must also address condom use and emphasize that condom use will save the lives of many people. The emphasis on the importance of getting tested for HIV infection status is also a crucial component of an advertising campaign.

Goals of a Comprehensive Plan to Counter HIV and AIDS

- More effort on education and prevention
- Greater involvement of national health authorities to prioritize HIV control and AIDS treatment
- Reduction in rate of new HIV infections
- Widespread availability and use of voluntary counseling and testing
- Greatly increased acceptance and use of condoms
- Greater acceptance of condom use by those frequenting sex workers
- A public awareness campaign leading to widespread acceptance of an individual's right to be protected against HIV infection during sexual activity
- Increased support of nongovernmental organizations (NGOs)
- Reduction of the number of sexual partners per sexually active person
- Increased rates of sexual fidelity
- Greatly increased coordination with tuberculosis and malaria treatment
- Availability of antiretroviral medication to all persons for whom medically indicated
- Widespread use of prevention of mother-to-child transmission ART protocols
- Reduction of deaths from AIDS
- Improved surveillance of sexually transmitted infections
- Improved security of blood supply
- Equity of service availability for urban and rural persons
- Increased orphan placement in homes and reduction of orphan rate
- Greater involvement of local leaders, including elected officials, clergy, and schools
- Greater involvement of media
- Greater openness in society to discussion of the HIV epidemic and available solutions
- Less sharing of needles by injecting drug users
- Continuing education for all personnel working on HIV/AIDS epidemic

A major challenge of a comprehensive plan is to confront centuries of male domination and sexual exploitation of women and all the ingrained attitudes accompanying this frequent societal dynamic. The comprehensive plan has the enormous task of addressing the anger that men feel when their partner wants them to get tested or to wear a condom.

With the correct choice of words, almost any issue can be addressed publicly. Explicit messages that cannot be placed on billboards can be placed on late-night television and radio. In addition to promoting the benefits of fidelity, a comprehensive plan will establish as a community value the right of a person to protect himself or herself against possible HIV infection during sexual activity. However, the foregoing steps will not be effective by themselves without voluntary counseling and testing.

Voluntary Counseling and Testing (VCT)

VCT is crucial to the success of a comprehensive program. The ultimate goal is to have every person aware of his or her HIV status and to guide his or her behavior accordingly. Those who test negative receive counseling on how to stay negative. Those who test positive receive counseling on how to protect others and how to monitor their viral load and CD4 status and are educated about the potential benefits and risks of antiretroviral therapy. Those who are counseled and/or tested are encouraged to refer friends, relatives, and sexual partners to the VCT Project. It needs to be an accepted civic virtue to get VCT and know one's HIV status.

VCT services provide a portal through which a person can be permanently engaged into the prevention and treatment system. People are encouraged to refer their friends. The public must associ-

ate VCT with the availability of antiretroviral therapy (ART) and must have an awareness of the potential benefits of ART. If people do not know the way in which ART can improve quality of life and extend life and if ART is not available, they may conclude there is little point in being tested.

Antiretroviral Therapy

A comprehensive approach needs to obtain medication at bulk purchasing prices and to make people aware that medication is available. Staff must be capable of monitoring CD4 counts in large numbers of people and of starting ART when medically indicated. The extensive challenges posed by resistant strains of the virus need to be met by skilled practitioners who, in many countries, have limited choices of pharmaceutical alternatives. Risks must be presented as part of informed consent before starting with ART.

Although some professionals believe that widespread availability of ART will make people more careless about safe sex, effective ART lowers viral load dramatically and makes people less infective and less likely to transmit an HIV infection. In this sense, highly active antiretroviral therapy (HAART) may be seen as a preventive measure from a public health point of view.

A comprehensive plan is very involved in prenatal programs and with the utilization of appropriate medications and labor and delivery interventions to lower the rates of mother-to-child transmission (MTCT). HIV-positive mothers also need education to make an informed choice about breastfeeding, because breastfeeding by an infected mother can increase the potential for MTCT of HIV infection. Many of the above plan elements require numbers of well-trained people far in excess of the current staff levels.

Monitoring of drug resistance should be performed on defined groups to evaluate the adequacy of interventions.

Staff Training for Scaling Up

Capacity building will be a central mission of any comprehensive approach. Programs need to partner with educational institutions to develop and provide accelerated courses that graduate skilled personnel for positions such as counselors for VCT, nursing assistants, staff for prenatal clinics, phlebotomists, laboratory technicians, and pharmacy technicians. Modest scholarships need to be provided for qualified persons to attend these courses. A number of physicians, nurses, pharmacists, social workers, and laboratory technicians will have already received their professional training, and a comprehensive approach will update them on advances and provide training in specific areas. Once staff members are trained, they will need to reach out to the communities.

Community Outreach

A comprehensive program has staff members who knock on doors; visit communities; distribute material in cities, towns, and villages; and talk with business owners to ensure their employees are informed. This approach spreads the message of the significant community benefits that can be realized by having everyone confront the HIV epidemic. Outreach efforts engage local leadership, religious groups, and the media.

Outreach meets with school administrators, teachers, and parent groups to pave the way for helpful information to be given to adolescents and those about to enter adolescence.

Community outreach maintains excellent relations with the press. All media outlets, big and small, are engaged. High-level staff from comprehensive programs meet with publishers of newspapers and owners and directors of television and radio stations to support and educate them and help them understand the necessity of cooperation. The media needs to understand that it is in their economic self-interest to cooperate with getting out the message and in giving low, or free, public service rates for advertising.

Laboratory Services

There is an extreme shortage of capacity to test for HIV status and CD4 counts throughout much of the developing world. Even if the capacity existed, the issue of funding for testing has not been adequately addressed. Bulk purchase of HIV status test kits can lower the cost of the test materials to less than US $2, and significant advances are being made in lowering the cost of CD4 counts when performed in relatively large runs. However, in

countries with large numbers of infections, the CD4 monitoring costs can be quite significant. A number of projects are developing protocols for evaluating readiness for ART based on parameters that are less expensive than CD4 counts. It is expensive to monitor viremia levels, and alternative approaches or cheaper procedures should be developed.

The fact that a large percentage of the population in the developing world lives in rural areas needs to be taken into consideration; service delivery will need to occur outside of the highly centralized urban centers.

Community-Based Care

A comprehensive plan must be able to offer services in a wide variety of urban and rural communities. In urban centers with larger facilities such as hospitals, it will be possible to offer many services with specialists already on site. At the other end of the service-delivery spectrum, there is a need for staff to go to villages on a regular basis to deliver services. Many people cannot afford fee-for-service nor afford to travel to where services might be available.

A comprehensive plan provides medical guidance, assistance, and continuing education to health care professionals in clinics and hospitals in all areas relating to HIV infection and AIDS, including the complications caused in persons with HIV/AIDS who also have tuberculosis and/or malaria.

In some rural settings, traveling clinics need to be available on a regular schedule. A comprehensive plan makes a concerted effort to bring services close enough to every resident of a country so that it is practical for them to utilize the services. The need for social services runs parallel to the medical and organizational challenges.

Social Services

Social services need to be provided in the areas of counseling individuals and families; placing orphans; and talking with teachers, parents, and students as part of community outreach. When indicated, a social worker or intake worker needs to evaluate individuals and families and make referrals to the appropriate components of a comprehensive plan or to outside providers when such services exist. But after all is said and done, millions of people will succumb to a painful death from AIDS.

Care of the Dying

A comprehensive approach will provide expert hospice advice and guidance to families that have a person dying in the home and will include home visits on a regular basis. Assistance for caregivers is also provided, including specific guidance for persons caring for people with advanced HIV or AIDS. Many of these dying people will leave orphaned children.

Orphan Placement

A comprehensive program will evaluate the circumstances of children who have been orphaned due to death of parents or caregivers from AIDS. Attempts will be made to place orphaned children with relatives or, when this is not possible, in a suitable home. Funds will be expended on supporting orphans. As effective antiretroviral medications are made available, the rate of new orphans will diminish.

Transparency and Record Keeping

All of the forgoing depends on funding. Moreover, funding will need to be sustained. Funders will not continue to contribute unless there is rigorous accountability. A comprehensive plan needs to have total financial transparency, including a thorough and professional accounting component and independent audits. Careful medical record keeping is essential for patient care as well as for providing documentation to funding sources and for clinical studies dependent on patient records.

Monitoring the Degree of Success of a Comprehensive Approach

It is essential to monitor the populations in which a comprehensive plan is utilized, or there will be only inadequate and anecdotal information regarding the efficacy of the approach. Some of this data collection is costly. It is important that funding sources adequately plan for and finance the necessary monitoring. As shown in the box titled "Monitoring the Degree of Success of a Comprehensive Approach," there are many indicators of efficacy.

Monitoring the Degree of Success of a Comprehensive Approach

- Reduction in rate of new HIV infections
- Increased monitoring and data collection of infection rates
- Widespread use of VCT
- Greatly increased acceptance and use of condoms
- ART available for persons for whom medically indicated
- Reduced number of deaths from AIDS
- Increased public belief of right to protect self from infection during sexual activity
- Reduced rate of newly orphaned
- Greatly increased public advertising about HIV/AIDS
- Greatly increased participation by community leaders in confronting epidemic
- ART used for prevention of mother-to-child transmission when medically indicated
- Decreased birth rate, due to condom use
- Increased popular awareness of services available
- Improved data collection and reporting of sexually transmitted infection data
- Improved blood supply security
- Health care professionals' participation in continuing education

CONCLUSION

As the third decade of the AIDS epidemic unfolds, the HIV-related needs of tens of millions of individuals are threatening to overwhelm communities around the world. The forgoing discussion of a comprehensive plan provides an example of the type of effort that is needed if care in the developing world is to reach the minimum standard considered acceptable in the more developed countries. Some of the hardest hit nations in the developing world cannot offer basic health services to their populations.

Despite increased global concern in recent years, those who seek to provide HIV/AIDS services are aware that the needs of communities far exceed the currently available resources. The costs of providing these services are modest in the context of global wealth compared to the projected costs that will be incurred if the necessary assistance fails to materialize. The international community has a moral responsibility to interact with the developing world where most HIV infection is occurring as a full partner in ensuring the well-being of these populations.

ACKNOWLEDGMENTS

I appreciate the thoughtful contributions of Joe Grossman, MSW, for his valuable input in the preparation of this article.

REFERENCES

1. Gathe JC, Washington MY, Mayberry C, Piot D, Nemecek J. IMANI-1 TC3WP. Single drug HAART-proof of concept study. Pilot study of the safety and efficacy of Kaletra (LPV/r) as single drug HAART in HIV+ ARV-naïve patients-interim analysis of subjects completing final 48 week data. In: Program and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract MoOrB1057.
2. Ruane P, Luber A, Gaultier C, et al. Maintenance therapy using lopinavir/ritonavir (LPV/r) alone with well-controlled HIV Infection. In: Program and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract TuPeB4577.
3. von Hentig NH, Mueller A, Haberl A, et al. The ATSAQ-1 cohort study: pharmacokinetic interactions of atazanavir (AZV) and saquinavir (SQV) in a ritonavir (RTV) boosted protease inhibitor therapy regimen. In: Program and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract WeOrB1235.
4. Arasteh K, Lazzariri A, Clotet B, et al. TORO: 96 week virological and immunological response and safety evaluation of enfuvirtide with an optimized background regimen. In: Program and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract MoOrB1058.
5. Lallemant M, Jourdain G, Le Coeur S, et al. Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med.* 2004;351(3):217–218.
6. Jourdain G, Ngo-Giang-Huong N, Le Coeur S, et al. Intrapartum exposure to nevirapine and subsequent maternal responses to nevirapine-based antiretroviral therapy. *N Engl J Med.* 2004;351(3):229–240.
7. Ferris DC, Dawood H, Chiasson MA, et al. Self-reported adherence to antiretroviral therapy and virologic outcomes in HIV-infected persons in Durban, KwaZulu Natal, South Africa. In: Programs and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract WePeB5829.
8. Oyugi JH, Byakika JT, Raglang K, et al. Treatment outcomes and adherence to generic triomune and maxivir therapy in Kampala, Uganda. In: Program and abstracts of the XV International AIDS Conference; July 11–16, 2004; Bangkok, Thailand. Abstract WeOrB1323.