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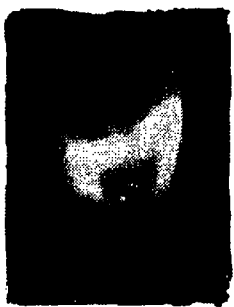
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In a World of Darkness, *Nourishing the Light*

IAPAC healthcare resource conference attracts 250 delegates from 14 countries to discuss new innovations to improve healthcare access for tens of millions who lack access to healthcare.

Members of Mexico's Frente Nacional de Personas Afectadas por el VIH/SIDA (National Front of People Affected by HIV/AIDS) demand access to AIDS drugs for all Mexicans with AIDS and exhort the Mexican government to respect the human right to healthcare. Photo: Tony Povedano © Por Esto! de Quintana Roo



Rebecca Voelker

In remote Nepal some 15 years ago, Nils Daulaire, MD, MPH, set out to stop a killer. His target, pneumonia, claimed more children's lives there than any other illness, yet local health professionals showed little concern.

Daulaire, now president and chief executive officer of the Global Health Council in Washington, DC, was told he would need a medical arsenal of well-trained physicians, x-rays, antibiotics, and laboratory tests to stop pneumonia. But the poor community could not afford such expensive tools. So the solution was simple: pneumonia would be treated when the community became more affluent.

Impatient, Daulaire located data indicating that pneumonia could be

diagnosed, albeit imperfectly, by assessing a child's respiratory rate and other simple signs. Effective treatment with an inexpensive antibiotic could be accomplished in five days, often for as little as seven cents per case. So he launched a diagnosis and treatment program that produced two notable results: a substantial decline in mortality and enormous opposition from the medical establishment.

Why the opposition? Daulaire said he believes it was rooted in the program's simplicity. It relied on community-based health workers and evaluation methods that were not exactly state-of-the-art. "This sometimes is termed second-rate medicine despite the fact that it's vastly better than no program at all," he said.

Daulaire's anecdote, offered last November during his keynote address at the International Association of Physicians in



AIDS Care's (IAPAC) Second International Conference on Healthcare Resource Allocation for HIV/AIDS and Other Life-Threatening Illnesses in Cancún, Mexico, aptly illustrates complex implications for HIV care.

Since governments and health systems worldwide simply cannot afford to give sophisticated antiretroviral combinations to everyone with HIV disease, the conference brought international experts together to discuss new ways to distribute existing health resources in ways that will benefit as many people as possible. Over four days, 250 delegates from 14 countries dissected resource allocation issues from perspectives that were not purely clinical.

They debated dilemmas of ethics, economics, human rights, and access to information that are inherent in a world where 16,000 people become HIV-infected each

day. If there was a consensus, it simply may have been that solutions will require a global response. Patricia Uribe, MD, coordinator general of CONASIDA (Mexico's National Council for the Prevention and Control of AIDS) and the conference chair, emphasized that point in her opening remarks to the conference.

"In a global society, the problems of one nation are the problems of us all," she said. "...[T]he participation of the various sectors of society and coordination among institutions and countries are clearly and urgently needed."

The problem of access to treatment centers on combination antiretroviral drug therapy, now considered the standard of care in the US and some other industrialized nations. These drug regimens have turned HIV infection into a more manageable disease. Yet at least 90 percent of the

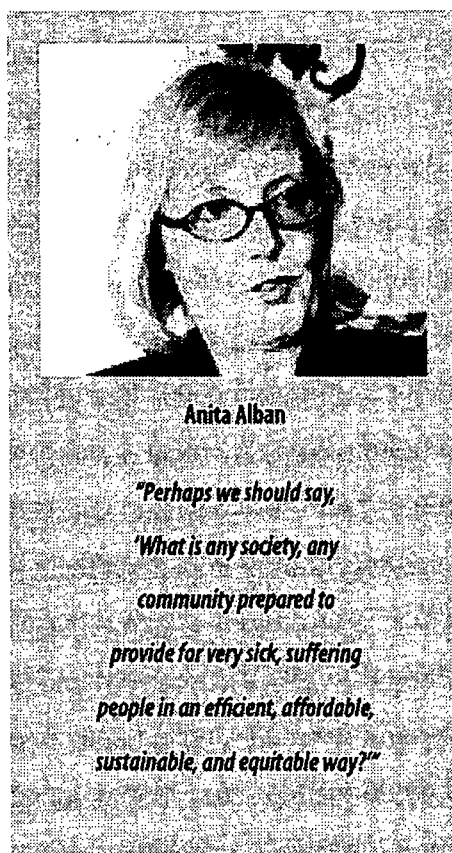
world's more than 30 million HIV-infected adults live in developing countries where combination therapies with protease inhibitors are, for the most part, a pipe dream of medical care.

Not only are the drugs prohibitively expensive in developing countries, health professionals sometimes do not have access to viral load and CD4⁺ cell tests that guide the use of antiretroviral drugs. In place of the gold standard, will healthcare professionals be willing to adopt "protease-sparing" regimens that rely on fewer, less costly agents? Or, will pharmaceutical companies be able to quickly develop an agent potent enough to be used as monotherapy? As new HIV drugs are developed, how can the ever-increasing number of combinations be tested in clinical trials and rapidly translated into clinical practice?

These questions of resource allocation become critical in terms of the devastation HIV will continue to inflict upon developing countries. Martha Ainsworth, PhD, an economics researcher with The World Bank, said HIV will claim 37 percent of adults who die of infectious diseases in developing nations by 2020; up from 8.6 percent in 1990. Latin America and the Caribbean will feel the burden acutely: HIV will account for 73.5 percent of the region's adult deaths from infectious disease by 2020. The proportion will be 32 percent in sub-Saharan Africa and 38 percent in Asia, Ainsworth noted.

The impact of AIDS as a thief of society's basic needs is becoming apparent. In such developing nations as Tanzania and Kenya, the annual cost of treating one AIDS case exceeds the cost of educating 10 primary school students, Ainsworth said. In Zimbabwe, AIDS has reduced life expectancy by 22 percent. And in the poorest half of households in Kagera, Tanzania, the death of an adult translates into a 32 percent reduction in food expenditures and a 15 percent decrease in food consumption for the household, she added.

Given some of these stark realities, how do nations set spending priorities? Any assumption that spending is based on people's needs and available resources may be an illusion, said Anita Alban, an economist with the Joint United Nations Programme on HIV/AIDS (UNAIDS).



Anita Alban

*"Perhaps we should say,
'What is any society, any
community prepared to
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sustainable, and equitable way?'"*

She presented data on AIDS spending patterns in five nations: Tanzania, Côte d'Ivoire, Thailand, Mexico, and the state of São Paulo, Brazil. In each nation, she said, spending is not necessarily based on the country's wealth or its HIV prevalence, but on priorities set by the sources of funding.

For example, Thailand, with one of the highest HIV prevalence rates in Asia,

devotes about two-thirds of AIDS spending to prevention and one-third for treatment. But Alban noted that nearly three-fourths of the money spent on HIV and AIDS in Thailand is from public coffers, reflecting the government's focus on prevention.

But even as UNAIDS tries to assist developing countries in choosing cost-effective strategies in prevention and care, Alban said it may be time to re-phrase questions about what constitutes cost-effective programs. "Perhaps we should say, 'What is any society, any community prepared to provide for very sick, suffering people in an efficient, affordable, sustainable, and equitable way?'"

Access to Drugs Through UNAIDS

A recent UNAIDS survey of drug availability at university hospitals in 20 developing nations found that such inexpensive drugs as haloperidol and diazepam are readily available, as are tuberculosis drugs, Alban noted. Six had AZT, two had some supplies of indinavir and saquinavir; none had nelfinavir or nevirapine.

No magic answer exists to the question of how access to life-prolonging drugs can be expanded. But in the past year, UNAIDS officials have launched pilot projects aimed at improving access to HIV drugs in developing nations. The pilot programs are projected to help 3,000 people gain access to drugs they probably could not otherwise obtain.

Since announcing its pilot programs,

Anita Alban photo: Tony Powe/Photo © For Estol de Quintana Roo



A conference delegate questions Joseph Saba, MD, of UNAIDS (fourth from left) and representatives from the four countries participating in the UNAIDS Drug Access Initiative. Photo: Smiley Pool © Houston Chronicle

Mexico's FONSIDA

In Mexico, limited resources have led the country's HIV/AIDS drug access program to be dubbed the "Titanic."

The program, launched formally in December 1997, targeted children and pregnant women as the first groups to receive free medications for HIV disease and AIDS under its auspices. But unlike the oceanliner that took hundreds to their graves, FONSIDA is aimed at expanding the availability of life-prolonging therapy beyond its first 250 recipients.

"Because of the focus on the children and the women, we have been called a Titanic syndrome... but we don't have enough money to cover everyone," said Alejandro Cravioto, MD, PhD, director of the program and head of the medical faculty at the National Autonomous University of Mexico in Mexico City.

As his country hosted IAPAC's Second International Conference on Healthcare Resource Allocation for HIV/AIDS and Other Life-Threatening Illnesses, Cravioto explained how FONSIDA was created and its objectives for the future.

The program grew from discussions between Cravioto and a colleague, hematologist Anthony Caso, MD, about establishing a re-insurance program for asymptomatic HIV-infected people. After two insurance companies expressed interest, they took the idea to the Mexican minister of

health, a former medical school dean. With the health minister's cooperation, Cravioto said, "this grew into a trust fund in which people in the private, public, and the academic sector would come together and chip in money to be able to supply drugs to people who were HIV-positive or had AIDS."

The Mexican government provided an initial \$3 million (US), which has grown to about \$35 million through interest and additional donations. Cravioto explained that a large Mexican bank administers the money in a trust fund at no cost. FONSIDA's operational needs—office space, computers, fax machines, and salaries for its employees—are supplied by outside sources. The money in the trust is used solely to purchase drugs, he emphasized.

Those eligible for drugs through FONSIDA must be on their state registry of HIV-infected people and unable to qualify for drug coverage through the governmental social security system. But because FONSIDA's funds are limited, Cravioto said decisions had to be made as to who the first beneficiaries would be. "The only complete group we could supply drugs for were all the children registered at that time with HIV and AIDS in Mexico City," he said.

About 30 children outside of Mexico City later were added to the program, bringing the number of young recipients by late 1998 to 190. "We also started a program with 60 pregnant women with the position that once the baby is born, we would continue the treatment of each one of these women because we do not consider it ethical, the idea that once the baby is born the mother is not attended," Cravioto noted.

He said several pharmaceutical companies have become

involved with donations of money, drug supplies, or assistance in training healthcare professionals. In fact, a pilot Mexico-US program supported in part with \$4.4 million over three years from Bristol-Myers Squibb Company was scheduled to be announced in Mexico City on Dec. 1, 1998.

The program will include a number of collaborators that will focus on community outreach and education, training for healthcare professionals to increase institutional capacity for care, and product donations. Bristol-Myers Squibb's role in the program primarily entails professional education, said Jim Sapirstein, RPh, director of infectious diseases and franchise management for the company's Intercontinental Pharmaceutical Group.

As collaborations increase and more influential individuals within Mexico become involved in his program's work, Cravioto said eventually FONSIDA may "become, in a certain way, a regulator for the price of these drugs." To increase its buying power, he said FONSIDA is exploring the possibility of agreements with other Latin American countries through the Pan American Health Organization to buy drugs cooperatively and negotiate lower prices.

FONSIDA also is working with the National Actors Guild in Mexico and some individuals in the country's television industry to promote awareness of HIV/AIDS. "We feel we have an obligation as physicians and interested people to make others realize that there is no single group of people who might not be affected," by HIV infection, Cravioto said.

UNAIDS has weathered stinging criticism from activists who contend the drug initiative does not provide drugs for enough of the people who need them. Even so, said IAPAC Deputy Director José Zuniga, such beneficent programs beg an overwhelming ethical question: "Is it better to extend life-prolonging care for a few who probably would die without the UNAIDS intervention, or deny the care to all because it cannot be offered universally?"

The unfortunate fact is that rationing of HIV care exists worldwide. Even in industrialized nations, triple-drug regimens are not available to all who could benefit from them. But the UNAIDS program is intended to go beyond drug distribution. Program officials hope to help build a healthcare infrastructure in the participating developing countries. Without a system for appropriate drug delivery, healthcare for people with HIV will continue to suffer, said Joseph Saba, MD, a UNAIDS clinical research specialist who has overseen negotiations between pharmaceutical companies

and governments involved in the initiative.

Two of the programs were launched last summer in Uganda and Côte d'Ivoire; two others in Vietnam and Chile were expected to be up and running by the end of 1998. Saba and representatives from the individual countries have worked with seven pharmaceutical companies to negotiate discounts on antiretroviral drugs and drugs for opportunistic infections, palliative care, and sexually transmitted diseases.

IAPAC is scheduled to begin monitoring the programs in March with a site visit to Uganda, Zuniga said. Monitoring procedures will record how the programs are meeting eligibility criteria and following standards for training healthcare professionals.

Negotiating Discounts

Dorothy Ochola, MD, coordinator of Uganda's drug access initiative, said her program has been able to negotiate discounts of 15 percent to 45 percent; she said the largest discounts have been arranged with Glaxo Wellcome. Lassine Ouattara,

first secretary of the Ministry of Health in Côte d'Ivoire, said his country's program has negotiated discounts of 50 percent to 70 percent.

The discounts are negotiated jointly by UNAIDS officials and representatives from the individual countries. Saba said discounts generally are offered as a subsidy or an immediate price reduction. In Uganda and Côte d'Ivoire, non-profit companies have been established to procure drugs, distribute them, and manage inventories. Each country also has set up a multidisciplinary advisory board to determine criteria for participation by medical centers and patients.

Saba made it clear during his presentation that UNAIDS' role in the access initiative is not to buy the drugs. In Uganda, for example, the government subsidizes the less expensive drugs used for palliative care or to treat opportunistic infections. Currently, patients who want antiretroviral drugs must pay for them themselves.

In Côte d'Ivoire, the government will

Pediatric AIDS

Everyone loves children, don't they? Hoosen Coovadia, MD, professor of pediatrics at the University of Natal in Durban, South Africa, is not so sure.

"It is 15 years into the AIDS epidemic, and we have not even begun to do something meaningful for children," Coovadia stated during a dialogue on children's healthcare at IAPAC's Second International Conference on Healthcare Resource Allocation for HIV/AIDS and Other Life-Threatening Illnesses.



Hoosen Coovadia, MD

"It is 15 years into the AIDS epidemic, and we have not even begun to do something meaningful for children," said Coovadia. With nearly 600,000 children becoming HIV-positive every year, he called upon the world AIDS community to consolidate efforts in preventing and treating HIV infection in children.

With nearly 600,000 children becoming HIV-positive every year, he called upon the world AIDS community to consolidate efforts in preventing and treating HIV infection in children. With forceful eloquence, Coovadia urged such groups as the Joint United Nations Programme on HIV/AIDS (UNAIDS), The World Bank, non-governmental organizations (NGOs), academic scientists, and medical researchers to develop a comprehensive global program covering a spectrum of issues, from preventing vertical transmission to caring for children orphaned by AIDS.

What is needed, Coovadia said, is "nothing short of a massive international effort, sweeping through and galvanizing the far corners of Africa, Asia, and Latin America.

"This effort must serve to move governments

from their straitjacket of pleading poverty and indulging in excess, to shake the giant pharmaceutical companies out of their post-Reagan, post-Thatcher complacency, to pursue a gentler economics which gives more attention to social responsibility and a little less to corporate profits... and to stem the wastage of funds on inefficient and ineffective NGOs, even community-based organizations, [that] exist because of the uniqueness of their relationship to communities but argue for funds on the generalizability of the resource of their program."

Mark Kline, MD, professor of pediatrics at Baylor College of Medicine and Texas Children's Hospital in Houston, shared Coovadia's concern, noting that two particular clinical research findings have revolutionized HIV therapy for children: results from AIDS Clinical Trials Group 076 that demonstrated AZT's ability to reduce the risk of vertical transmission by two-thirds, and the use of combination antiretroviral therapy to slow disease progression.

"But this really is of little help or consolation to the 1600 children born with HIV every day worldwide or the 1200 who die daily from HIV infection worldwide," Kline said, since availability of therapy is primarily in the US, Canada, and Western Europe. "We can't do a study like [ACTG] 076 in the US and expect it to be applied universally," he added.

In collaboration with IAPAC and other partner organizations, Kline is working to establish a new, state-of-the-art clinical center in Constanta, Romania. With a capacity to care for 1400 HIV-infected children, it would be the world's largest pediatric HIV facility, Kline said.

Pulling together resources for the center is a monumental task. After 40 years of communist rule in Romania, Kline said the country's clinical research infrastructure is nearly non-existent. "Expertise is lacking, and sponsors in Eastern Europe are not willing to collaborate," he noted.

In marshaling a global response to pediatric HIV/AIDS, Coovadia referred to programs called GOMBFF — growth monitoring, oral rehydration, breast feeding, immunization, female education, fertility regulation, and food supplements — that have had an immense impact on the lives and health of children around the world.

Though still necessary, they are insufficient against HIV, he said. For example, growth monitoring does little good when high proportions of HIV-infected infants in developing nations die before their first birthday. And breast feeding is not universally recommended because of transmission risks.

"The existing global programs are almost inappropriate for this modern age of the HIV pandemic," Coovadia said. "We require something new."

provide subsidies, but patients will pay varying amounts. Pregnant women, for example, will be expected to pay for one-fourth the cost of drugs, and poor people, half.

Ochola said her country's access program had 515 patients on antiretroviral therapy, as of November 1998. Even though minimal supplies of antiretrovirals have been available in Uganda for two years, she said the drugs were not properly prescribed. "People were accessing these drugs through relatives who had been living abroad, or through their own arrangements." Therefore, an important part of the program in Uganda is establishing a clinic system with trained healthcare professionals who can properly prescribe the drugs.

In Vietnam, Nguyen The Dung, MD, of that country's Centre for Tropical Diseases explained critical resource shortages. Combination therapy is not offered because AZT is the only antiretroviral drug available. And it is in such short supply that there is not enough for the approximately 2000 HIV-positive women who become pregnant in Vietnam each year. CD4⁺ cell count tests are very expensive and viral load testing is not available. But the center has had some good results in treating opportunistic infections, according to The Dung.

"Many of our patients recover after the treatment of opportunistic diseases," he said. "They are still alive and look well."

Officials in Chile projected that about 100 patients would receive therapy through the access initiative by the end of 1998. Raquel Child, MD, coordinator of Chile's National Commission on AIDS, said 25 percent discounts from three drug companies enabled a 20 percent increase in the number of patients who could be covered by the program.

Conference participants, seemingly amazed by some of the large discounts mentioned, questioned how price reductions for different countries are determined.

"What's a fair price?" Peter Young, vice president of Glaxo Wellcome's HIV/Opportunistic Infections Area, asked rhetorically. He noted that speakers from UNAIDS and The World Bank had indicated a pattern exists in some developing nations: those with the higher seroprevalence rates have a lower per capita gross national product. Therefore, Young noted, appropriate pricing depends on characteristics of the market where the drugs will be sold.

Providing access to life-saving drugs, Young said, is a multifaceted process

that should include private industry, governments, non-governmental organizations, and international agencies. "It's not [pharmaceutical companies'] sole responsibility, but we can collaborate," he said.

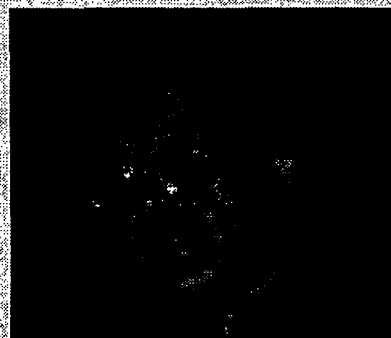
"The reality of how much it costs to produce different agents is very important," added Mike Youle, MD, director of HIV clinical research at the Royal Free Hospital in London, England. "It is highly unlikely that we'll ever get a protease inhibitor for pennies because of the cost of production."

IAPAC Executive Director Gordon Nary pointed out that increasing numbers of drugs in development in the United States "fractionalize" the US market each time a new one is approved: "By 2004, the profit-center for new AIDS drugs—some already approved and some still in the pipeline—may not be the industrialized nations of the North, but the less industrialized countries of the South," he said.

Universal access to ARV's

Referring to activists' calls for universal access to antiretroviral drug therapies, Ainsworth of The World Bank urged governments and individuals in poor countries to "think-through whether subsidizing

complicated, expensive treatments with uncertain benefits is the most cost-effective use of limited resources."



Gordon Nary

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Ainsworth, who is co-author of The World Bank's policy research report, *Confronting AIDS: Public Priorities in a Global Epidemic*, ranked prevention and treatment-education, palliative care, and prevention and treatment of opportunistic illnesses, including tuberculosis, as crucial government investments. She ranked last the provision of antiretroviral therapies in resource-scarce settings especially given expense, regimen complexity, uncertainty about long-term benefits, and variability of efficacy from one patient to another.

Citing Thailand as an example, Ainsworth explained that a World Bank-UNAIDS study indicated provision of palliative care and effective treatments of opportunistic illnesses cost \$1,600 a year per patient. That annual expenditure per patient increases by \$10,000 when triple-drug antiretroviral therapies and supporting monitoring services are added to the mix. In industrialized nations, Ainsworth added, the cost of adding antiretroviral therapy is closer to \$20,000 a year per patient. The implied question: Is this the wisest use of scarce healthcare resources?

Eric van Praag, MD, of the World Health Organization's Initiative on HIV/AIDS and STIs, agreed that the cost and



More than 250 delegates from 14 countries participated in the Second International Conference on Healthcare Resource Allocation for HIV/AIDS and Other Life-Threatening Illnesses. Photo: Tony Povedano © Por Estol de Quintana Roo

Gordon Nary photo: Smiley Pool © Houston Chronicle

complexities of antiretroviral therapies are two equally important constraints. "Just adding the drugs into the existing care delivery by specialists or generalists, private or public, may be counterproductive," van Praag told conference delegates.

"Comprehensive care across a continuum could offer the prerequisites of safe and effective use of antiretroviral drugs whenever affordable and will ensure that the additional cost for patients on antiretroviral drugs are kept to a minimum," said van Praag. "It has, however, severe repercussions for equity as it will mean phasing stepwise" rather than universal access [to antiretroviral drugs] in sites able to provide quality comprehensive care. Optimally, said van Praag, training, monitoring, and operational studies should guide the step-by-step implementation of antiretroviral drug access, especially where healthcare resources are scarce.

Cost vs. Benefit

Wherever profitable markets emerge, new HIV drugs and new combinations will make cost-benefit analyses an important part of the healthcare equation. But even for economists, they are difficult calculations. "So much of the human benefit cannot and should not be measured in just monetary terms," said Charles Farthing, MD, medical director of the AIDS Healthcare Foundation in Los Angeles, Calif.

Even so, Farthing said new protease-sparing regimens or dual protease combinations could offer a lot of antiviral bang for less buck than a triple regimen with a protease inhibitor. He said that a triple combination of AZT, 3TC, and abacavir could be an effective regimen that may cost about \$200 less per month than a triple drug combination containing a protease inhibitor.

Farthing also maintained that triple therapy may not be necessary. Clinical studies, he said, are showing that therapy with two protease inhibitors is capable of complete HIV suppression at a lower cost than three drugs. The combination of ritonavir and saquinavir is about half the cost of a triple regimen; he noted, because ritonavir's ability to inhibit the hepatic metabolism of saquinavir means both drugs can be given at lower dosages.

Even though it is still under investigation, Farthing said an indinavir-ritonavir combination is promising. Even in different dosages—400 mg of each or 800 mg of



Charles Farthing, MD

"The need for a vaccine against HIV is perhaps the most important health issue facing our world today. Other approaches to date have shown such little promise, but the animal models of live-attenuated vaccines have shown solid protection."

indinavir and 100 mg of ritonavir—the dual combination maintains higher levels of indinavir than a regimen of AZT, 3TC, and indinavir, and with a lower pill burden. However, some physicians worry that an indinavir-ritonavir combination translates into monotherapy because the drugs have similar resistance profiles. Again, it has not been studied, but Farthing suggested that indinavir and ritonavir together may produce such a high blood level of drug that it actually will translate into potent monotherapy.

"It's strength that counts, not the number of drugs," Youle noted.

Despite the paucity of cost-effectiveness data on HIV therapy and the need for more research into this area, Youle said inexpensive, effective diagnoses and treatment are possible. He suggested that lymphocyte counts can easily predict CD4⁺ cell counts to guide treatment. He also cited a study conducted in South Africa in 1995 that showed that adding 3TC or 3TC plus zalcitabine to an existing dual nucleoside combination could reduce hospitalizations by 47 percent.

Even though dual nucleoside therapy is not recommended in most industrialized nations because short-lived potency results in the development of drug-resistant virus, Youle said "the jury is still out on dual

nucleosides" in settings where triple drug regimens and protease inhibitors are not available. He also suggested that the addition of hydroxyurea to dual nucleoside therapy merits further study. "It's cheap and showing impressive results," he said.

Vaccine by 2000

Despite progress in drug development in recent years, the lack of an effective HIV vaccine remains a glaring deficiency in the scientific response to HIV. "The need for a vaccine against HIV is perhaps the most important health issue facing our world today," Farthing said.

In the belief that an effective vaccine can be developed, Farthing and colleagues at IAPAC launched a campaign in 1997 to further research into a live-attenuated HIV vaccine.

"Other approaches to date have shown such little promise, but the animal models of live-attenuated vaccines have shown solid protection," Farthing said.

The campaign's call for volunteers to be inoculated with the eventual vaccine in a clinical trial produced 300 responses from willing individuals, including scores of physicians, he noted. The virus that IAPAC has targeted for a live-attenuated vaccine has been prepared by Ronald Desrosiers, PhD, of the New England Primate Research Center at Harvard Medical School.

Based on Desrosiers' research into a live-attenuated vaccine against Simian immunodeficiency virus (SIV) with deletion of the nef gene, the virus proposed for human studies is HIV-1 Δ-kURNe. It lacks three of HIV's nine genes—vpr, vpu, and nef—as well as two regulatory elements. "Our current plans are to proceed with a human trial of HIV-1 Δ-kURNe in terminal cancer victim volunteers," Farthing said. If those results were promising, a trial employing the IAPAC healthy physician volunteers would be the next step.

But several hurdles still stand in the way. Farthing said officials from the National Institutes of Health and the International AIDS Vaccine Initiative (IAVI) are less than enthusiastic because disease progression has been reported in Asian macaque monkeys infected with nef-deleted SIV and another SIV strain lacking a second gene and regulatory elements. The data have had a chilling effect on research funding, Farthing said.

"This seems wholly unjustified when you consider that SIV in macaques is a

more vicious virus than HIV in humans," he added.

IAPAC remains committed to its goal of having the first clinical trial with a live-attenuated HIV vaccine up and running by 2000. But US Food and Drug Administration guidelines for safety testing with immortalized cell lines must be satisfied first, at an estimated cost of \$3 million. "We will keep the pressure up until funding is found," Farthing maintained.

Future success of an HIV vaccine depends on a number of additional issues, said UNAIDS's Alban. "We need to start examining who will get it, who will benefit, and who will get it later as opposed to first," she said, adding that people with the highest risk behaviors should be first.

Beneath an overhead projection of the outline of a massive snake, she likened the movement of the AIDS epidemic to "the skeleton of the serpent." In many developing nations, she noted, an inexpensive vaccine will be the only weapon against HIV. With planning and an eye on costs associated with vaccine development, she said, "We have to try to get the snake to move in the direction we would like."

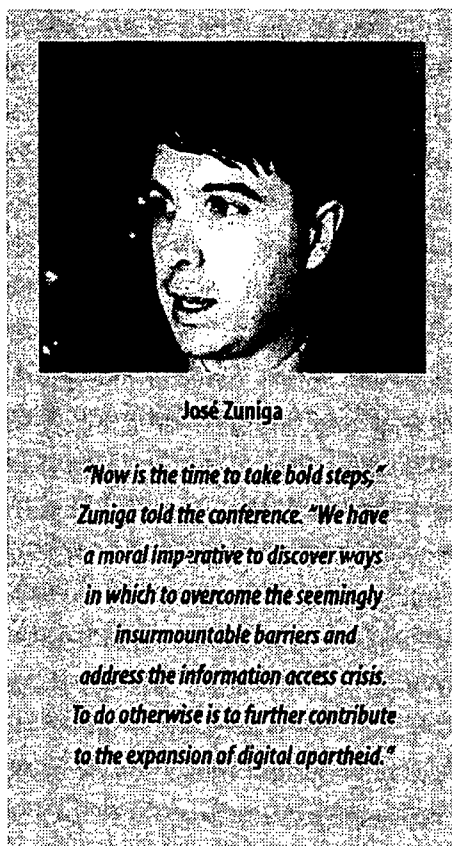
Complex Models

Even if the snake moves favorably, widespread use of an effective vaccine still is many years away. Studies to determine how less expensive drugs like hydroxyurea fit into combination therapy are progressing, but could take some time to complete.

In the meantime, Steve Mayer, MD, medical director of outcomes research and epidemiology at Abbott Laboratories, suggested that the same types of computer modeling that guide chemical plant design or aircraft construction could be applied to clinical trials of HIV drugs.

Mayer pointed out that 11 currently approved HIV drugs produce 616 possible combinations. "How can we do all the clinical trials?" he asked. "And if we don't look at [all the combinations], we are missing some opportunities to optimize therapies." He said that complex models—those that use large numbers of variables—can consider the interplay of drug pharmacokinetics, virus activity, immune response, and patient compliance in predicting the efficacy of hundreds of combinations.

"We already have important insights from simple models," Mayer noted. But he said complex interactions that take place among different types of immune cells



with different antigen specificities before opportunistic infections occur are a critical missing piece that is needed to develop highly predictive models.

In the future, Nary of IAPAC said research may also produce a model capable of immediately updating drug regimens as new data are reported. "People who would enter into a program in April may be on one regimen, and people who enter in August may well be on another regimen that is more cost-effective and improves their survival."

In fact, Nary said, computer modeling could be a key tool in developing clinical guidelines that can help determine how to use existing resources because they are based on cost. "If I have \$5 million a year to spend on drugs, I need to look at a variety of factors that will determine how many productive, quality months of life I will be able to provide to the people of my country for this investment in drugs," he explained.

"It may be various combinations, it may be new combinations we haven't even seen yet. We need to be flexible in setting up guidelines that can be adapted as new information comes along" and can be plugged into computer models capable of making immediate revisions.

In the dawn of a new millennium that promises unprecedented technology

advances, Nary focused on a central issue in computer modeling. "This is the Information Age, but we have to put the information into a model in a way we can all use, that is creative and that challenges this constant need to use limited resources for the maximum value on the largest number of people."

Universal Internet Access

Each day, creative uses of technology make the world a smaller place, Zuniga of IAPAC pointed out. In less than a decade, the Internet has knitted together all walks of society in nations throughout the world to share information on seemingly infinite numbers of topics. Yet he drew a harsh analogy between the consequences of poor access to both healthcare and information.

"Access to computers, the Internet and, as important, training to acquire the skills necessary to benefit from this technology, is dictating who can participate in the Information Age and who cannot," he said. "As with healthcare, the inequities in access to health information and support on the Internet has spawned a world of information 'haves' and 'have-nots.'"

Zuniga cited statistics from the Global Internet Project, a collaboration of high-level executives from 16 software and telecommunications industries: From 1993 to 1995, the number of Internet users worldwide tripled, to as many as 60 million. By 2000, analysts predict a quarter-billion Internet users worldwide.

In an effort to provide universal access to the Internet, Zuniga announced that IAPAC has launched a new initiative that will seek equipment donations and technical assistance to establish local public access points and skills training worldwide. "We hope to secure a commitment from the Global Internet Project and from other organizations and individual leaders in the high-tech world to develop a global program to address the access issue in as many countries as we can," he said.

"Now is the time to take bold steps," Zuniga told the conference. "We have a moral imperative to discover ways in which to overcome the seemingly insurmountable barriers and address the information access crisis. To do otherwise is to further contribute to the expansion of digital apartheid." ■

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