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M O N T H L Y

**State of AIDS
Care 2004:
One world,
multiple
standards**

FEATURE: State of AIDS Care 2004

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State of AIDS Care 2004: One world, multiple standards

Scott A. Wolfe

What are the realities of HIV treatment access in developing countries? The reasons for hope and causes for concern were both on display at an IAPAC satellite symposium to the XV International AIDS Conference, which offered detailed updates from six countries at various stages of scaling up access to antiretroviral therapy.

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AIDS out of focus?

José M. Zuniga

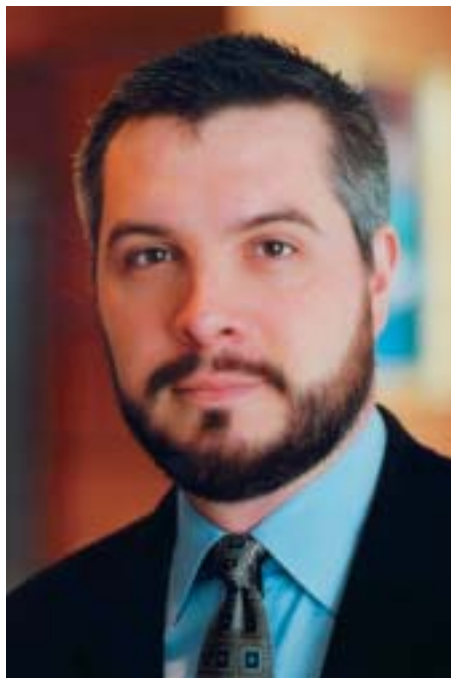
What does it take to focus attention these days? Events come and go, an endless barrage of images in the media. There has hardly been time to digest and comprehend what we have just seen before something new comes along, and everything that seemed important is all but forgotten, or at the very least placed on the back burner.

I should beware, of course, of over-generalization. For an African mother who is dying of AIDS-related complications, who has barely enough food to offer her children, let alone antiretroviral medication for herself or them, the “problem” of information overload does not exist. The distinction between the important and the trivial is a clear one for her, desperation having the effect of focusing one’s mind.

It is, instead, those of us living in the wealthy countries of the global North who are easily driven to distraction. In the United States, as I write this, we are in the middle of a presidential election campaign, and among the items dominating the broadcast media is discussion of which candidate’s campaign team is doing a better job convincing the citizens of “middle America” that their man is of the people.

At the same time, we are gearing up for holiday shopping and reading economic uncertainty in the toy industry’s re-evaluation of their expected sales. There are interesting new television shows to watch. There is a new sex scandal to follow.

And we cannot help but be drawn in when we witness the Boston Red Sox defeat the New York Yankees, finally, after nearly a century, overcoming their “curse” on the way to the (so-called) World Series. You have no interest in baseball? Relax. In another week, there will be an entirely different set of news stories.



Meanwhile, AIDS continues its march around the globe, steadily traversing the path that has been predicted for years. In another sign that the epicenter of the pandemic is moving east, into the densely populated countries of Asia, epidemiological experts are now estimating that India has overtaken South Africa as the nation with the most people living with HIV/AIDS.

From one perspective, this is all happening very quickly. At the current rate, AIDS may well take 70 million lives in just the next 15 years—cementing it as the worst pandemic in recorded history. However, from the perspective of many of the people whose political will is required to launch an effective, long-term response to HIV/AIDS—those, that is, who are living amidst the media saturation of the world’s wealthiest nations—it is all happening in near slow motion. In another example of the inequality that contributes to the spread and lethality of HIV disease, those who

have the power to act are the least likely to see, and remain focused upon, what must be done. By contrast, those whose very lives are in the balance have, by accident of a geographic and sociopolitical lottery, almost no power to effect change.

Lest this entire Report from the President be devoted to pessimism and challenges, however, I think that last fact can help point the best way forward. In a word, we need to find ways to put power in the hands of individuals and countries who are most affected by HIV/AIDS. Relying on the altruism of others is necessary in the short term, but it will ultimately be untenable.

In practice, this means governments should be encouraged to guarantee health-care as a human right, giving citizens the power to demand it and hold politicians accountable when it is denied them. It means that every initiative meant to scale up antiretroviral therapy must be self-sustaining. It means that even as we are working to reduce the price of antiretroviral drugs we should be plugging the brain drain and making plans to alleviate unsustainable physician:patient ratios in developing world countries. It means empowering local physicians and allied healthcare professionals with the knowledge they need to treat HIV/AIDS themselves.

So, what does it take to focus attention these days? Perhaps that is the wrong question. The millions who are living with and dying of HIV/AIDS in the developing world have already had their attention focused. It is rather our job to give them the power to do something about their own destinies. ■

José M. Zuniga is President/CEO of the International Association of Physicians in AIDS Care (IAPAC), and Editor-in-Chief of the IAPAC Monthly.



Is PEPFAR tackling HIV drug supply in wrong way?

Keith Alcorn

An organization representing front-line mission hospitals in 22 developing countries claims that the US President's Emergency Plan for AIDS Relief (PEPFAR) threatens to create unsustainable and wasteful two-tier treatment systems because of the insistence on using brand-name US Food and Drug Administration (FDA)-approved antiretroviral drugs.

The Ecumenical Pharmaceutical Network represents Christian hospitals, drug supply organizations, and development agencies from 22 countries, including many of the countries named as recipients of PEPFAR support.

In a statement issued in mid-October 2004 after the network's annual conference in Tanzania, members highlighted a number of concerns they have about the way in which PEPFAR is being imposed on healthcare systems.

They say that PEPFAR's insistence on FDA-approved brand-name drugs is creating confusion and extra work for overstretched healthcare staff in settings where generics are also available. This criticism was first raised at a meeting earlier this year hosted by the United States government, the World Health Organization (WHO), and southern African governments to review drug approval standards for fixed-dose combinations. Eric Goemaere of Médecins Sans Frontières told the audience of international regulatory officials, "If each partner comes to us only wanting to treat women or children, or only wanting to use a certain drug combination or branded products, it

will be chaos. If we have different supplies and different combinations coming in, it will create confusion both for the clinic and for patients who have already started with a particular fixed-dose combination."

Jennifer Patterson of Catholic Relief Services, one of the agencies funded by PEPFAR to deliver antiretroviral therapy through mission hospitals, explained why the program's requirement on brand-name drugs was creating extra work. "Our programs fear that they will suffer the burden of administration of multiple supply lines, that community workers will face the extra burden of explaining different regimens to patients within the same family, and that the use of loose tablets rather than fixed-dose combinations will create the danger of pill-sharing between family members because of the prevailing sense of community."

The US government has repeatedly stressed that it will not use drugs in its PEPFAR program that US regulators would not pass for use by American citizens, and

has invited generic manufacturers to submit their products to the FDA for approval. If the products receive approval, US Global AIDS Coordinator Randall Tobias has said they will be eligible for purchase with PEPFAR funds.

However, there are also concerns about the way in which drugs will be supplied to the field. Ecumenical Pharmaceutical Network coordinator Eva Ombaka says that PEPFAR's insistence on a vertical drug supply chain separate from existing systems could undermine efforts to improve national drug distribution systems.

The Ecumenical Pharmaceutical Network has also raised doubts about what will happen when the current funding for PEPFAR runs out in 2008. If the same level of funding is not forthcoming after 2008, levels of treatment achieved may not be sustainable, especially if brand-name drugs remain more expensive than generics and if the program has prevented the development of local drug production. ■

Clinton, WHO partner around ART scale-up

The Clinton HIV/AIDS Initiative (CHAI) and the World Health Organization (WHO) announced October 22, 2004, that they have agreed to jointly provide technical assistance on scaling up national HIV/AIDS care and treatment programs in developing countries that are member states of the WHO.

Under the partnership, CHAI and WHO will collaborate to assist countries with developing comprehensive care and treatment plans and strengthening existing country systems for procurement and supply management. By working together on the provision of technical assistance, CHAI and WHO will help harmonize treatment guidelines, monitoring and evaluation standards, and safe, reliable and efficient procurement processes across countries.

"We welcome the collaboration as it increases the options WHO can offer to its member states to secure access to much needed diagnostics and antiretrovirals

for [HIV-positive] patients," said Jim Kim, Director of the WHO's Department of HIV/AIDS.

The agreement will also help accelerate the pace at which countries receiving funds from the World Bank and the Global Fund to Fight AIDS, Tuberculosis, and Malaria can access CHAI-brokered agreements for reduced prices. The prices, which CHAI negotiated in October 2003 and January 2004, cover medicines that are critical components of the four WHO-recommended first-line antiretroviral regimens that are the foundation for its "3 x 5" initiative. The initiative aims to work with countries and partners to provide antiretroviral therapy to 3 million people by 2005.

"Because CHAI is a leader in negotiating breakthrough pricing for HIV/AIDS medicines and diagnostics, and WHO is the leading global authority in public health, our collaboration will significantly advance the goal of providing antiretroviral treatment to 3 million people by 2005," said CHAI Chairman Ira Magaziner.

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State of AIDS Care 2004: One world, multiple standards



Thailand

Brazil

Botswana

Haiti

Russia

Uganda

Scott A. Wolfe

Over the past two years we have witnessed tremendous developments in the effort to extend necessary care and treatment for HIV/AIDS to the world's most affected regions. Although access to life-saving antiretroviral (ART) therapy remains extremely limited—some 440,000 out of 6 million persons in immediate need have been reached thus far¹—the foundation for rapid ART scale-up has been laid through successful harnessing of political and financial commitments, antiretroviral (ARV) drug price reductions, and establishment of important legal and trade frameworks. One may believe, therefore, that while the ambitious goals of the World Health Organization (WHO) “3 x 5” initiative, for example, may ultimately prove out of reach, the spirited movement that they signify is meeting with some success.

Although HIV infection has been a veritable death sentence for most people living in resource-poor countries, the possibility of ARV access promises to revitalize families, communities, and nations reeling from the effects of the global AIDS pandemic. The hope that this inspires is quite palpable. However, the introduction of these sophisticated medicines into settings hamstrung by conditions of poverty and limited infrastructure raises new questions about how best to ensure the health and increased welfare of the populations for which they are destined.


Among the questions we face are ones such as how best to ensure that ARVs are complemented by development of infrastructure, including increased access to necessary care services and the rapid training of healthcare professionals; how to ensure patient adherence and a sustainable flow of antiviral and complementary drugs; how to address the inevitable metabolic and morphologic complications of highly complex multidrug ART; and how to cope with the inevitable failure of first-line ARV regimens in many patients when second, third, and salvage regimens remain

prohibitively expensive and/or unavailable in many settings.

Below this rapidly growing numerator of questions and challenges lies a common denominator of realities that renders our shared interest in expanding access to these life-saving medicines a potentially untenable journey. Awaiting these shipments of drugs are skeletal healthcare systems that often define scarcity in nearly every sense; governments which are often obligated to pay greater annual service on foreign financial debt than they spend on all social services combined; doctors, nurses, and allied health professionals who are and will be asked to prescribe and monitor drug treatment modalities that in wealthier nations are not top choices and are often of constricted efficacy; and nations which are grateful for assistance, but have no certain way to guarantee the sustainability of services that are being expanded, should foreign assistance dollars suddenly evaporate. Indeed, our hope is tempered by the serious challenges that lay ahead.

Against this backdrop, the International Association of Physicians in AIDS Care (IAPAC) recently accelerated its advocacy and technical assistance efforts aimed at ensuring that the fight against HIV/AIDS is everywhere undertaken in full view of these challenges and with the human right to health as the centerpiece of mounting global activity. The XV International AIDS Conference in Bangkok served as the catalyzing event at which this program was launched.

Entitled “State of AIDS Care 2004: One World, Multiple Standards,” IAPAC’s July 15, 2004, satellite symposium was designed to reveal—via the experiences and insights of hand-picked experts—snapshots of the quality of care available to people living with HIV in regionally diverse areas, and to elaborate the dichotomy between state-of-the-art care available to a few, and the status quo of care available to most. Presentations focusing on Botswana, Brazil, Haiti, Russia, Uganda, and Thailand



IAPAC's satellite symposium was designed to reveal snapshots of the quality of care available to people living with HIV in regionally-diverse areas, and to elaborate the dichotomy between state-of-the-art care available to a few, and the status quo of care available to most. Presentations focusing on Botswana, Brazil, Haiti, Russia, Uganda, and Thailand explored broad global care and treatment issues.

were nestled between opening and closing remarks which, respectively, explored broad global care and treatment issues, and the WHO's efforts to grapple with the matters at hand.

Opening the proceedings, IAPAC President/CEO José M. Zuniga set the mood for the evening by engaging the sensibilities of a kindred battle—the US civil rights movement—drawing an analogy between the predicament faced by civil rights leader Martin Luther King Jr., and that now confronting the global community at its latest crossroads in the fight against HIV/AIDS.

The passages, captured in King's famous "Letter from a Birmingham Jail,"² bear repeating. A white supporter of the cause, seeking to comfort King through a calmed acceptance of the slowness of change, wrote to King: "Christians know that the colored people will receive equal rights eventually, but it is possible that you are in too great a religious hurry. It has taken Christianity almost 2,000 years to accomplish what it has. The teachings of Christ take time to come to earth." To this letter, King responded in meditations penned on scraps of jailhouse paper:

Such an attitude stems from a tragic misconception of time, from the strangely rational notion that there is something in the very flow of time that will inevitably cure all ills... Time itself is neutral; it can be used either destructively or constructively. Human progress never rolls in on the wheels of inevitability; it comes through the tireless efforts of men willing to be

co-workers with God... Without this hard work, time itself becomes an ally of the forces of social stagnation.

Such tenacity in the face of great challenges, Zuniga noted, must infuse our collective efforts, and the challenges ahead should not discourage us from charging forward. "For our part," he declared, "IAPAC commits itself to acting as a full partner in the immediate effort to expand access to life-saving and -enhancing treatment, but we are gathered here to say that this must be done with a view of health as a human right, and a focus on not resting until we have eliminated the differences in standards of care for this disease that remain the unfortunate reality."

Moving on from guiding principles to practical issues, Zuniga proceeded to paint a quick picture of the epidemiological picture that is the global AIDS pandemic, and to elaborate the various challenges that are faced. Reminding the audience that ART expansion is but one among a series of necessary responses, Zuniga categorized the first-line challenges as the scale-up of prevention efforts; scale-up of treatment; the feminization of the epidemic (coping with deepening gender imbalances in infection rates and access to services); impact alleviation, with focus on the growing "orphan" generation; and the continued harnessing of political, financial, and technical resources.

Describing the slow pace of progress in the two-plus decades of the global pandemic, Zuniga related estimated figures regarding

the mounting need for financial resources for global prevention, care, and support efforts: US\$8 billion in 2004, doubling to US\$15 billion by 2007. Of course, the greatest single cause of increases in required funding will be for the ARVs needed to treat infections not prevented. It is troubling to add, Zuniga remarked, that as the funding need grows so too does the gap between need and actual commitments.

The greatest single portion of the opening presentation, informed by IAPAC's long-standing contributions to and experiences in this area of concern, was spent discussing the issue of gaps in the numbers of and HIV care knowledge among healthcare providers in resource-constrained settings. Citing a July 2004 report to provide an example of healthcare service gaps, Zuniga noted that among six high-burden Asian countries, the HIV-trained physician to HIV-positive patient ratio varies anywhere from a high of 1:3,140 in Cambodia to a low of 1:11,250 in Vietnam.³ Of course, these are numbers that would pale in comparison to the situation in the majority of high-burden African nations. Overall, many experts agree that mere access to HIV-trained personnel is the single greatest challenge to appropriate care and support. Asked to tell you how manageable are patient case-loads of these sizes, most physicians and allied care professionals working in the luxurious (by comparison) settings of affluent countries would surely opine that quality of care would have to be greatly sacrificed.

Country perspectives



Thailand



The symposium's country-specific presenters further defined the global landscape Zuniga surveyed. Each provided unique insights into the particular status quo and challenges faced in their respective settings. The first of these, Praphan Phanuphak (Thai Red Cross AIDS Research Centre, Bangkok) reiterated the pointed statement contained in the symposium's title "One World, Multiple Standards," noting that while the global community rarely speaks to these multiple standards, they exist everywhere, and the first order of business must be to address them openly, and with due candor.

Phanuphak's country presentation revealed that in Thailand—a country typically cited as a success story—almost 25 percent (150,000) of the 604,000⁴ people living with HIV/AIDS are in immediate need of treatment; however, only 33,000 are on ART. To those 33,000 (13,000 treated through government-funded programs and 20,000 through third-party sources) will be added another 50,000 throughout 2004, all treated with the country's fixed-dose generic drug combination GPO-Vir [nevirapine (NVP)/lamivudine (3TC)/stavudine (d4T)]. However, Phanuphak urged the symposium attendees to not

only consider the length of time that it has taken Thailand to reach these levels, but to also question the difference between mere access to emergency medicines and actual long-term quality of care.

To begin, Phanuphak listed the armamentarium of ARVs available within Thailand, noting that while generic versions of seven individual ARVs and two coformulations exist, the standard of GPO-Vir as first-line treatment in ARV-naïve patients contradicts what clinical evidence suggests are more appropriate choices [eg, zidovudine (ZDV)/3TC/efavirenz (EFV) or didanosine (ddI)/3TC/EFV]. Further, he noted that despite indication of their high effectiveness, agents such as tenofovir (TDF), lopinavir (LPV), and atazanavir (ATV) are not available to the vast majority of prescribers.

Another area of multiple standards, Phanuphak noted, is in the prevention of mother-to-child transmission of HIV (PMTCT) where single-dose NVP prophylaxis continues to be favored over full-course treatment for HIV-infected mothers—the standard in more affluent countries—with no consideration of ZDV as an alternate prophylactic measure, despite strong evidence of its favorability. The consequence continues to be a high rate of NVP resistance in a context where the recommended first-line treatment regi-

men is an NVP-containing coformulation. Across all treatment concerns, Phanuphak related that while six-month CD4 count follow-up is standard procedure, access to viral load and genotypic resistance testing remains highly limited, rendering patient monitoring and detection of treatment failure complicated.

Phanuphak echoed the concerns Zuniga articulated in his opening presentation in listing the training of healthcare providers, amendment of existing health service practices (eg, allowing select cadres of nurses to prescribe drugs), and the need for more clinical research on strategic treatment options [eg, ritonavir (RTV)-boosted indinavir (IDV) versus the expensive double protease inhibitor (PI) combination of saquinavir (SQV)/LPV] as essential to ART scale-up success and sustainability in Thailand.

Overall, Phanuphak urged his Thai compatriots to continue to earn the country's reputation within the global community by fighting to eliminate HIV-related stigma, to accept the cost-benefit of investing in high-quality HIV care and treatment interventions sooner rather than later, and to act as a global leader in these areas not because of pressure from external sources, but because of a generalized desire for the betterment of Thai society.

Brazil



Of his middle-income nation, Celso Ramos-Filho (Federal University of Rio de Janeiro) delineated a history of successes, followed by an interesting series of current and projected challenges that proved a true education for all. He started by tempering the tendency of some to imply that all is rosy in the world's fifth largest country when it comes to its AIDS epidemic. Although an estimated 600,000⁵ Brazilians are living with HIV/AIDS, and though care and treatment are constitutionally guaranteed and have been largely achieved through political commitment and a flourishing generic drug manufacturing sector, only an estimated 215,000 of those living with HIV are being followed up (of which 142,000 are on ART). And, approximately 385,000 have not entered into the healthcare system for HIV care. Indeed, it is thought that the majority of these 385,000 are not even aware of their serostatus.

To Brazil's credit, a chart presented by Ramos-Filho showed a nearly perfect 45-degree incline, depicting the number of patients who have been placed on ART over the past decade. From 1997 to 2004, these numbers have increased each year, from a base of 20,000 in 1997 to over 140,000 as of early 2004. The result (from 1996 to 2002) has been a decrease of 40 percent in mortality (90,000 prevented deaths) and 70 percent in morbidity; a reduction in hospital admissions of 80 percent (358,000 in total); savings to the economy of US\$1.23 billion in hospital services and treatment of HIV-related opportunistic infections; and a reduction of US\$960 million in drug prices.

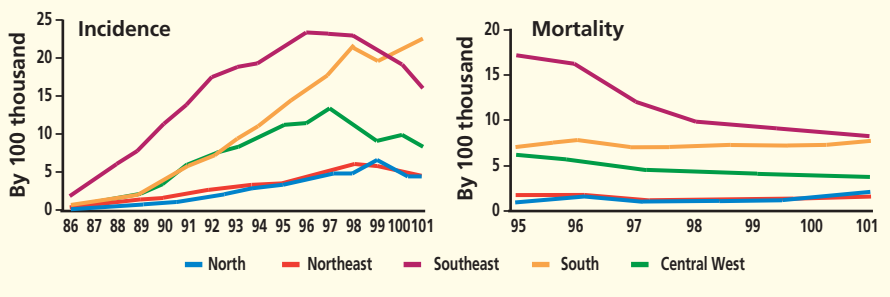
The services responsible for the above

figures are delivered by 950 HIV/AIDS care units across the country, including 388 accredited hospitals, 420 outpatient units, and 63 homecare units. However, these services are disproportionately centered in high-density, urban settings. Though the majority of HIV-positive Brazilians live in these areas, there are alarming gaps between urban and rural care infrastructure, which must lead to differing epidemiological situations in various regions of the country. In other words, while Brazil remains a shining example, if one looks beyond major urban centers such as Rio de Janeiro, Sao Paulo, and Brasilia, discrepancies in incidence and mortality rates across the country's different regions are startling. As Figure 1 shows, there continue to be plateaus or alarming increases in both incidence and mortality in certain regions, such as North and Northeastern Brazil, while in others these rates have declined significantly.

as men. This gender imbalance also has its own regional character. For instance, while the average percentage of HIV-infected pregnant women across Brazil who receive ZDV prophylaxis during labor is 35.5 percent, regionally specific data indicate that this rate varies widely—50 percent receive ZDV in the southeast; 42 percent in the south; 18 percent in the central west; 10 percent in the north; and a mere 8 percent in the northeast. Consequently, these inequities are reflected in vertical transmission rates, with a low of 5.5 percent transmission in the south and a high of 14.86 percent in the north.

Ramos-Filho stated that his country will only retain its global reputation in HIV care and treatment if it is able to grapple with these regional differences and with the feminization of the disease. Finally, he shared various data revealing the relative success of Brazil

Figure 1. Diverse dynamics of the Brazilian epidemic in different regions



This picture of “two Brazils” is compounded by an increasing gender imbalance. In regions where a decline in incidence rates has been experienced, the rate of decline is typically half as slow for women as men, and where incidence rates are growing (again, most notably in the north and northeast of the country), they are increasing twice as rapidly for women

in achieving ARV price reductions through a mixture of generic manufacture and price negotiation for brand name drugs. Of particular note is the fact that the mean price reduction has been nearly twice as great for drugs that are produced locally versus those imported from abroad (83 percent versus 47 percent).



Botswana

Botswana is the first African nation to embrace the challenge of ART delivery on a national scale, in the face of the second highest HIV prevalence rate in the world (37.3 percent).⁶ Ernest Darkoh (Botswana National ARV Program, Gaborone) endeavored to describe how HIV care and treatment efforts in the diamond-rich country are unfolding.

Nestled in the current epicenter of the AIDS pandemic, Botswana benefits from a longstanding civil peace and from a commitment at the highest political levels to combat the nation's AIDS epidemic. In 2001, the government of Botswana made the commitment to provide ART to all those in need. This promise has been coming to fruition gradually through "Masa," the national ART program (named after a Setswana word meaning "new dawn") and its various governmental and private sector components, including a collaboration between Botswana's government, the Bill & Melinda Gates Foundation, and the Merck Company Foundation, known as the African Comprehensive HIV/AIDS Partnerships (ACHAP).

Describing the difficulties of poverty and logistics in developing countries attempting to treat with ARVs, Darkoh argued that even if treatment for HIV/AIDS consisted of nothing more than a glass of clean water every day, it would be an enormous task to deliver it to all the people in need. Darkoh stressed that the greatest obstacles to effective HIV treatment in the country are the severe shortage of trained healthcare personnel, the challenge of reducing numbers of patients presenting at late stages of disease, and the

logistical complications of reaching disparate populations with a steady supply of drugs and regular follow-up.

Despite great odds, Botswana has achieved notable success in mounting care and treatment programs in recent years. As of June 2004, Darkoh said of the estimated 260,000 Botswana living with HIV/AIDS, 27,699 persons have been diagnosed with CD4 counts of <200 cells/mm³ or an AIDS-defining illness (the criteria for ART initiation), of which 24,087 have been placed on ART. This number, however, still falls short of the 110,000 that are estimated to be in immediate need of treatment. Nonetheless, it demonstrates a broad reach across the country's 16 public treatment sites and additional private sector centers. In addition, across all public treatment sites (accounting for 17,387 out of about 24,000 persons on ART) the average mortality rate for those receiving ARVs has been 7 percent.

Darkoh related that ZDV/3TC/EFV is prescribed as the first-line regimen, substituting NVP for EFV in the case of children and pre-menopausal women of child-bearing potential. Although no information was shared regarding the frequency of regimen failure, he made clear that second- and third-line regimens are available through the national program (ddI/d4T/nelfinavir (NFV) and RTV/SQV, respectively). Unlike most other resource-poor countries, however, a high level of diagnostic testing and monitoring is provided in Botswana. Although resistance testing continues to be unavailable publicly, the standard work-up for patients on ART through the national program includes a CD4 count, viral load, chemistry, and hematology tests five times a year, and hepatitis and syphilis tests annually.

Darkoh listed several very practical recommendations as lessons learned from Botswana's experience. Foremost, he reiterated that HIV testing through voluntary counseling and testing (VCT) centers has proven the key entry point for all interventions—treatment, support, and prevention—and that the quality of these services has a marked impact upon the success of any national effort. In scaling up from no or few ART sites to many, Darkoh stated that the best approach appears to be establishment of small pilot programs, followed by rapid roll-out, as opposed to a phased roll-out scheme.

To these recommendations, however, he added several important caveats. Most notable among them were, first, to appreciate that typically, the sickest patients will present first, and so there is a need to ensure a balance between equitable access and emergency care; second, to appreciate that the greatest burden of service delivery relating to ART is in monitoring and evaluation, and to therefore establish these systems early on in the scale-up plan; and, third, to ensure coordination and alignment of all stakeholders from the outset of the process in order to foster project ownership and avoid redundancies and operational inefficiencies.

Darkoh reminded the audience that the single greatest obstacle to effective and appropriate ART delivery, namely the lack of health service capacity, predated the AIDS pandemic. As such, he urged countries not yet faced with the devastating prevalence rates experienced in countries such as Botswana (and especially those now touted as "next wave" countries) to seize the opportunity to invest in this capacity in advance of escalating HIV incidence rates.



Haiti

B

ouncing back across the Atlantic, attendees were next presented with the case of the small Caribbean island of Haiti.

Haiti holds two unfortunate titles. It is both the Western Hemisphere's poorest nation and the country outside of Africa with the highest HIV prevalence rate (5.6 percent).⁷ Having returned to his native country in 1980 from the United States, Jean William Pape (Centres GHESKIO, Port-au-Prince) has dealt with Haiti's epidemic from its outset, and he drew from this formidable experience in relating the challenges and opportunities for HIV care at this crossroads in the global movement.

Despite its poverty and the tremendous political turmoil that has gripped the nation over the past half-century (13 different governments over the past 18 years alone), Haiti has mounted successful programs in prevention of and care for HIV over the past two decades, stemming the tides of a potentially much more devastating epidemic. With commitments of funding and reductions in the price of ARVs over the past few years, the country has shifted into high gear to add the outstanding component of a truly comprehensive national program, namely ART.

Pape noted that 2002 national guidelines dictating first-line ARV regimens (ZDV/3TC and either NVP or EFV), and recommendations for treatment of HIV-related opportunistic infections, have been implemented using modified urban and rural testing entry point models, the former designed by Centres

GHESKIO and the latter by Harvard University's Partners in Health program. These services are being provided in 27 VCT centers nationwide, with several being developed to act as centers of excellence. The rapid scale-up of ART and high-quality patient care in Haiti, he noted, is shaped by several concurrent activities currently underway. The focus on VCT services as the key entry point to care, support, and prevention interventions is being paralleled by a program to rapidly train scores of new physicians, nurses, and allied healthcare providers at those centers and elsewhere, through dedicated on-site and mobile training teams. Additionally, a system of data management is being implemented across that network of testing and treatment centers to monitor patient clinical and laboratory indicators, drug inventories, and site-specific epidemiological indicators.

Pape noted that 2,400 patients in Haiti had been placed on ART as of July 2004. While this figure remains low when contrasted against the estimated 240,000 Haitians living with HIV/AIDS, he noted that the comprehensive approach being undertaken throughout the country to integrate services at VCT centers, coupled with the new promise of access to treatment, will surely cause this number to grow exponentially in the short term. He shared figures from Centres GHESKIO, for example, demonstrating that the number of people tested for HIV had more than doubled from 2000 (10,310) to 2003 (21,328). To accommodate these new numbers of patients entering into formal care services, Pape's centers commenced aggressive healthcare profes-

sional training programs in 2000 in cooperation with Cornell University, and have also ensured that patients placed on ART receive extensive adherence counseling and peer support, nutritional support, telephone calling cards, and free transportation to and from treatment sites.

Speaking of Centres GHESKIO's experiences as an example of the national picture, Pape expressed an optimistic outlook on next stages of ART scale-up, based upon results thus far. Of the past year's scale-up efforts he noted that only 4 percent of patients (out of a total of 1,091) placed on treatment have been lost to follow-up, with a 6 percent mortality rate, largely due to very advanced stage disease complications. A greater concern, and one shared by most presenters, was the event of toxicities requiring regimen change in 10 percent of those patients (most commonly due to anemia and rash). In addition to this concern, both for clinical and financial reasons, Pape cited several other issues that must be addressed in Haiti. Among them are the scarcity of diagnostic technologies, including very limited CD4 count availability; the administration and coordination of differing drug supplies, for example generic drugs procured through funds from the Global Fund to Fight AIDS, Tuberculosis, and Malaria versus brand-name versions purchased through the US President's Emergency Plan for AIDS Relief (PEPFAR) funds; and the continuing medical education and mentoring required by trained healthcare personnel.



Russia



From a mood of optimism to one of greater doubt and frustration, symposium attendees were next asked to shift their imagination across another vast expanse of geography and experience, as Julie Stachowiak (AIDS Infoshare Russia, Moscow) presented snapshots from one of the potential “next wave” countries that has captured global attention over the past year—Russia.

As Stachowiak unraveled her presentation about the status quo of care and treatment in the former Soviet stronghold, it became ever clearer that there was as little in common between the spirit of busy antiviral progress in Haiti and the state of affairs in Russia as there is commonality between the humid languor of Port-au-Prince and the steely nerve of Moscow.

What most distinguishes the AIDS epidemic in Russia—and those of much of Eastern Europe for that matter—from its existence elsewhere, is its overwhelmingly predominant mode of transmission. Unlike most other affected regions, where sexual contact or tainted blood supplies account for the bulk of transmissions, Russia suffers from an HIV epidemic spurred forward by a co-epidemic of intravenous drug use (IDU). Stachowiak explained that of the official number of 274,808 reported HIV cases (as of early 2004), anywhere from 80 to 93 percent of those are IDU-related. High-risk sexual behavior, she noted further, is a growing concern, as is the likeliness of vertical transmission of the virus from mother to child, absent effective PMTCT programs. Although the actual rate of transmission of HIV from mother to child seems unclear,

8,458 babies have been born to mothers with reported seropositive status.

In a slide aimed at describing what Stachowiak called, “the horror behind the official numbers,” she noted morbidity and mortality figures that bespeak utter neglect of the disease. Most notably, Stachowiak related that of the officially reported number of HIV cases—itsself felt by most experts in the region to grossly misrepresent the actual number of people living with HIV—4,403 had died thus far. Of those, only 1,009 individuals had been diagnosed with AIDS-defining symptoms; 700 of them ultimately dying. This means that of those who have died in Russia, with known HIV seropositive status, 84 percent die before being diagnosed with AIDS, with a staggering 70 percent mortality rate in those individuals who are diagnosed with AIDS.

Reasons for this horror run the full gamut of the possible. At its core, a lack of political (and in turn financial) commitment to fighting HIV/AIDS, and discrimination against and a punitive approach toward injection drug use has resulted in widespread stigma, covert high-risk behavior, and a stagnant healthcare system response. In an overall context where a highly limited number of healthcare professionals are trained to diagnose and care for HIV, where state policy remains to deny treatment of injection drug users (including use of opioids), and where ARVs are prohibitively expensive (average cost of ART is US\$5,000 to US\$15,000 per year compared to US\$300 to US\$700 in the Ukraine), the virus continues to run rampant.

Currently, Stachowiak stated, while the WHO estimates that 50,000 people need immediate ART, only 2,800 are provided for by national and local budgets; 700 of whom are currently receiving ART; the remainder are left to the dubious benefit

of monotherapy. Little patient counseling is afforded, clinical follow-up and monitoring is inconsistent, and in combination with widespread stigma and the behavior patterns that often accompany IDU, adherence in those who are able to access treatment of some sort remains a tremendous problem.

Stachowiak noted the limited signs of hope seem to be appearing either from external sources or from courageous civil society groups fighting against stigma and for healthcare rights, under great strain. Recently, for instance, the Global Fund approved a fourth round proposal for Russia that will infuse a desperately needed US\$120 million into the country, largely for treatment efforts. Astride this ray of hope, the World Bank and others continue to support ARV price reduction efforts. And, in the trenches, a new social movement called “Shagi” aims to reduce HIV-related stigma, to expand acceptance of ART for people living with HIV/AIDS, and to harness the energies of groups such as AIDS Infoshare.

In ending her remarks, Stachowiak appealed for greater attention to the potentially disastrous situation that is unfolding in Russia. As for the general state of care and treatment in 2004, her final slide described a chaotic state of affairs that begs no elucidation: “What we have in Russia is not [highly active antiretroviral therapy]. It is pills, and the supply of those is not even consistent. There is discrimination in determining who has access to these medications. There is very little laboratory monitoring, no emphasis on adherence, little communication between patient and doctor.”

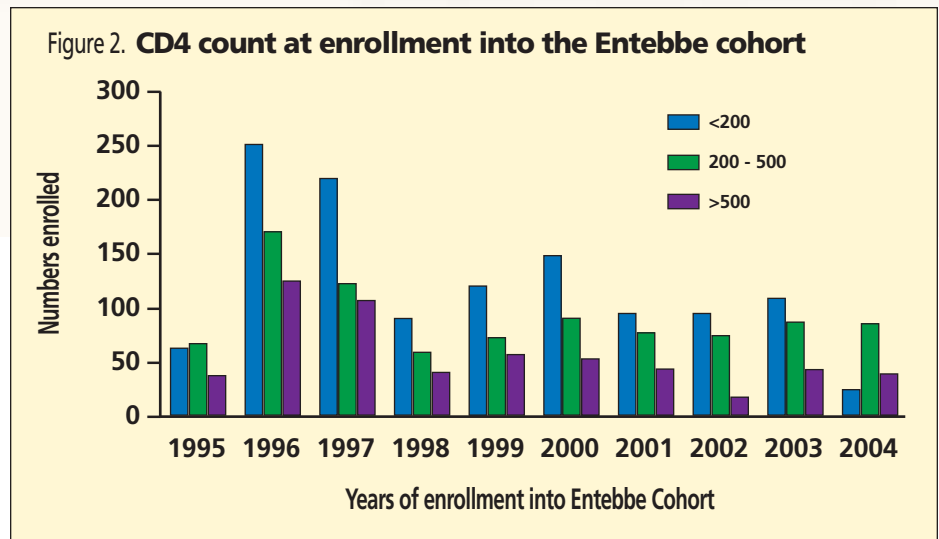
Uganda



The final country-specific presentation of the evening focused on the African nation of Uganda.

The east African country, widely acknowledged as the crown jewel of the African fight to prevent the spread of HIV/AIDS due to the host of measures that it effected to reverse its high prevalence rates relatively early on in the days of the burgeoning global pandemic, has seen a decrease of 4.1 percent, according to the Joint United Nations' Programme on HIV/AIDS (UNAIDS). Controversy continues to surround the Ugandan case with respect to just what in fact was responsible for this marked success. The discussion is focused largely on the oft-cited "ABC approach" (Abstain, Be faithful, use Condoms), with actors from all scientific, social, and religious walks of life—and from all corners of the earth—measuring in on the debate. Amid this tumult, however, discussed far less often is where the country stands with respect to actual HIV/AIDS care and treatment.

Paula Munderi (DART Trial, Entebbe) delved into the matter from the highly informed perspective of a site investigator at one of the African continent's largest multi-site, multi-country treatment projects. Munderi told the symposium attendees that, in advance of the UNAIDS 2003 figures released at the XV International AIDS Conference, Uganda's National AIDS Control Programme reported that prevalence rates stood at 5 percent for the general adult population (15 to 49 years) and an average of 6.2 percent across the country's antenatal care sentinel sites. Ministry of Health figures for 2002 also included 70,170 new infections for the year; 73,830 new



AIDS cases; and 75,290 AIDS deaths. Given a total estimate of 530,000 people living with HIV/AIDS at the end of 2003,⁸ these figures, depicting the continued progression to advanced disease in large numbers of patients, and a high AIDS mortality rate, bespeak far less success in Uganda with regard to caring for and treating HIV than in preventing its spread.

As with many African nations, the reasons for limited achievement in HIV/AIDS care and treatment do not include a lack of political will or clinical and scientific leadership, nor an inactive advocacy community. Rather, they are rooted in conditions of poverty, lack of healthcare infrastructure, and until fairly recently, the almost complete absence of ARVs.

For its part, the Ugandan Ministry of Health has developed a very robust National AIDS Control Programme that includes a five-year strategy to scale up comprehensive care and support, with attention to implementation of national HIV care and treatment guidelines, broad capacity-building measures, and firm government policy support. This has been supported at the highest political levels.

Given the existence of all of the above, more recent commitments of donor assistance, reductions in the price of many antiretroviral agents, and the initiation of larger ART programs is cause for great hope. As of May 2004, Munderi noted, a total of 23,152 patients had been placed on ART, although the vast majority (16,300) were seen at a few "specialized" and centralized HIV care and research centers such as the Joint Clinical Research Centre (JCRC) in the capital city, and DART Trial sites, rather than geographically diverse public health centers and hospitals. This total of 23,152 patients—were one taking count so as to measure future success—may be compared against the 120,000 Ugandans who are estimated to be in need of immediate treatment. Another target that observers may wish to keep in sight is the WHO "3 x 5" initiative target for Uganda of placing 60,000 on ART by 2005, and a full 120,000 by 2007.

These ambitious, but reachable, goals may be frustrated by numerous care delivery challenges. Citing one of the perennial challenges across Africa, Munderi noted



that with 18,600 Ugandans for every physician; 133,514 Ugandans for every pharmacist; and 3,065 Ugandans for every nurse/midwife, the challenge of managing drug supplies and providing effective and appropriate care and treatment for this complex disease is immense. To this challenge is added the fact that most patients placed on treatment continue to present at later stages of disease progression, where the relative burden of care and monitoring is greatly increased. A slide depicting experience with patient cohorts in Entebbe exemplified this phenomenon, which is common to many resource-constrained settings (Table 2).⁹

Viewing these figures, one might suppose that the increased proportion of patients presenting at clinic with earlier-stage disease in 2004 than in previous years suggests greater uptake of care services due to the actual promise of treatment, and societal acceptance of its benefits. One hopes data from years to come will substantiate this interpretation. And there are many signs at this point to suggest that hope, rather than pessimism, is in order.

Regarding other challenges to effective care provision, Munderi noted the enhancement of laboratory capacity and greater accessibility of these services as paramount. Currently, vital microbiology, histology, and special imaging tests, for instance, are available only at select centers of excellence in the capital city. These will become ever more critical with the advent of large-scale ART in order to ensure earlier diagnosis of disease and subsequent monitoring for ARV toxicities. To compliment this clinical component, she added, are required greater patient adherence support interventions, measures to ensure equity in access to care and treatment, and a forward-looking, multi-sector approach to the pandemic that will ensure the sustainability of treatment services.

Vukile: South Africa's new day

A global darling and story of inspiration in many respects, South Africa has, over the past decade, managed to shake off many of the shackles of a repressive political system, trudging forward progressively through a period of political and social transition. Not resting contented, the state has set its sights on rising to even greater global stature by welcoming myriad international congresses and conferences and even declaring its readiness to act as host to prestigious global events such as the 2010 FIFA World Cup of football (soccer, to some). Why then, ask many South Africans and foreigners alike, has the country not become the shining example of compassion and African pride in the realm of HIV/AIDS, as would be expected? This, undoubtedly, is the underlying question—opinions aside—when South Africa and HIV are mentioned in the same breath.

With a blemished track record in its past, and a new generation of infections and preventable deaths staring it in the face, the government of President Thabo Mbeki finally took the long-awaited step in 2003 to announce measures to provide for the care and treatment of those out of the estimated 5.3 million South Africans living with the virus that are in immediate need. A strategic plan to do just that, released in November 2003, was a sign that this was more than mere rhetoric. Months later, South African Minister of Health Mantombazana (Manto) Tshabalala-Msimang was poised to present the case of South Africa's future outlook at the IAPAC July 2004 symposium when emergency budget meetings forced her to return prematurely from Bangkok to cabinet in Pretoria. In her stead, Minister of Health for Gauteng province—home to Johannesburg, Pretoria, and many of the country's most severe HIV problems—Gwendoline Malegwale Ramokgopa, addressed the conference audience to describe the state of affairs in the continent's southern-most country.

Minister Ramokgopa described South Africa's strategic plan to fight HIV/AIDS, and implementation in Gauteng province according to four fundamental pillars: prevention; treatment, care and support; research, monitoring and surveillance; and legal and human rights. In the absence of curative measures for the disease, she stressed that prevention of new infection continues to serve as the core of all national programs, while care and treatment interventions are being gradually strengthened. Among the key components of this central prevention objective are a broad campaign aimed to encourage sexual abstinence or fidelity to a single relationship among youth, massive distribution of condoms (distribution has increased by 80 percent over the past six years, she noted), widespread programs focused on prevention of vertical transmission of virus from mother to child (now undertaken in over 1500 public health facilities nationwide), and aggressive training of healthcare workers in preventative measures and post-exposure prophylaxis (PEP).

Of course, while these measures were of interest, and are critical to any comprehensive national strategy, audience members waited in greater anticipation of word from the Minister on recent care and treatment activities. Of these, Ramokgopa related that the government is quickly scaling up efforts to meet goals set in President Thabo Mbeki's State of the Nation Address, which announced the target of establishing 113 service points and getting 53,000 people on treatment by March 2005. This includes achieving access in all the 53 districts of South Africa within the current financial year and at least one service point in every local municipality within the next five years. Currently, she noted, there are about 6,000 people who are receiving antiretroviral drugs free of charge through a temporary supply measure, and more than a third of them are in Gauteng province.

Of challenges, the Minister described financial and human resource constraints as the greatest obstacles to universal access in South Africa, as well as the difficulty of expanding necessary services to rural areas. Importantly, Ramokgopa described the serious attention being paid within the national strategy to nutritional support for those receiving treatment. Surely, in the face of scarcity of income and food for many South Africans, the relative success of these nutritional interventions will be eagerly observed by other nations embarking upon the journey of ART scale-up that are faced with similar or greater food and water crises.

With a hint of regret at the slow pace of progress in South Africa over the past decade, the Minister nonetheless declared her pride in the success of South Africa's public health sector response to the pandemic. Though some would disagree, the Minister described the slow and methodical approach of tending to HIV/AIDS within the scope of comprehensive, multi-faceted healthcare services, as the unfortunate lot of an African nation faced with multiple public health crises and continuing financial shortfalls. Certainly, challenges and disagreement on past decisions can be discussed, but the determination to provide ART within South Africa for all in need will soon yield data and anecdotes that will permit true judgment on the relative prudence of past action and inaction.

A country most resplendent in beauty, natural and man-made, and endowed with tremendous potential, South Africa nonetheless now labors under the watchful eye of spirits that have fallen over the course of its long journey to freedom. The latest episode of this ongoing saga, borne out in the realm of infectious disease—the new apartheid, one might say—will hopefully soon pass the way of its political antecedent. More than the fate of South Africans, but rather hope itself, lies in the balance.

3 x 5: A global challenge

Focus on Uganda provided a perfect segue to a presentation dedicated to the WHO's initiative to place 3 million people living with HIV/AIDS in the developing world on ART by 2005—a presentation which in turn reinforced the host of factors raised by country presenters. Gottfried Hirschall (WHO, Geneva) unveiled the institution's strategic plan to reach the targets contained within the "3 x 5" initiative. He highlighted the initiative's chronology, and outlined its five pillars: global leadership, strong partnership and advocacy; urgent, sustained country support; simplified, standardized tools for delivering ART; effective, reliable supply of medicines and diagnostics; and rapid identification and application of new knowledge.

This foundation in place, Hirschall noted, the WHO looks forward to an aggressive capacity-development program geared not only toward addressing HIV, but also to revitalizing health service systems in broad terms. The components of this comprehensive approach include drug procurement systems, robust financing, training of the healthcare workforce in sufficient numbers, establishment of health information systems

and logistics management systems, development of public-private partnerships and community participation, and overall quality improvement. These components, already being implemented in a total of 56 countries that have requested assistance from the WHO, are based on careful needs assessment revealing generally agreed-upon priorities.

Of successes to date, Hirschall reported that 192 WHO member states have endorsed "3 x 5" and the institution has raised US\$218 million to support of the initiative. Additionally, he stated, 12 countries have established national ART targets in support of the "3 x 5" goals; 15,000 care providers have been trained; core medical education curricula have been developed; and a host of key 2004 milestones have been reached or surpassed. Concerns include the fact that only three countries thus far have published national ART scale-up plans to cover 50 percent of the estimated national need, that average ARV drug prices remain higher than projected for this point in time, and the fact that the projected overall resource gap for WHO activities in 2005 is still at US\$62 million. ■

Editor's note: Scott A. Wolfe was formerly Director of Global Health Policy with the International Association of Physicians in AIDS Care (IAPAC), and currently acts as Policy and Research Associate with the University of Toronto Faculty of Medicine's Centre for International Health.

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6. UNAIDS. 2004 Report on the Global AIDS Epidemic. Botswana's prevalence rate (adults 15-49) is second only to Swaziland's (38.8 percent).
7. Ibid
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9. P Munderi, et al. The introduction of ART in an active community based cohort in Uganda and its impact on HIV related mortality. XV International AIDS Conference. July 13-16, 2004. Bangkok. [abstract TU0RC1158]





A B S T R A C T S

HIV Medicine

A significant proportion of HIV-infected patients admitted to hospital have immunosuppression as a result of failure of highly active antiretroviral therapy

Manavi K, McMillan A.

OBJECTIVES: To investigate the immunological and virological features of patients on highly active antiretroviral therapy (HAART) admitted to a tertiary care center. **METHODS:** A retrospective study was carried out on HIV-infected patients on HAART admitted to the Regional Infectious Disease Unit in Edinburgh between June 2002 and July 2003. **RESULTS:** A total of 125 patients who had been on HAART for at least six months were admitted during the study period. The frequencies of hepatitis C virus (HCV) and hepatitis B virus (HBV) coinfection were 52 percent (78 of 150 patients) and 48 percent (72 of 150 patients), respectively ($P > 0.05$ for comparison of frequencies of hepatitis B and C). Of patients who had been on HAART for at least six months, 50 percent (63 of 125 patients) were immunosuppressed and had significantly higher bed-days (3-12) compared with those with CD4 counts >200 cells/mL ($P < 0.002$). Among immunosuppressed patients, 38 percent (24 of 63) had undetectable viral load after at least six months of therapy. Those patients were mostly (67 percent) intravenous drug users and had a significantly higher median age (43 years; range 38 to 47 years) than other patients ($P < 0.001$). **CONCLUSIONS:** Earlier start of HAART and addition of interleukin (IL)-2 to the treatment regimens of patients at risk of slow CD4 T-cell count recovery may reduce the duration of their subsequent hospital admissions.

HIV Med 2004;5(5):360-363.

Journal of Acquired Immune Deficiency Syndromes

Impact of highly active antiretroviral therapy on anemia and relationship between anemia and survival in a large cohort of HIV-infected women: Women's Interagency HIV Study

Berhane K, Karim R, Cohen MH, et al.

BACKGROUND: Anemia is common in HIV-infected individuals and may be associated with decreased survival. **OBJECTIVE:** To ascertain the impact of highly active antiretroviral therapy (HAART) on anemia and the relationship between anemia and overall survival in HIV-infected women. **METHODS:**

A prospective multicenter study of HIV-1 infection in women. Visits occurred every six months, including a standardized history, physical examination, and comprehensive laboratory evaluation. The setting was a university-affiliated clinic at six sites in the United States. Participants were 2,056 HIV-infected women from the Women's Interagency HIV Study (WIHS). The outcome measure was anemia, defined as hemoglobin (Hb) <12 g/dL. Survival analysis was based on overall mortality during the follow-up period. **RESULTS:** Among HIV-infected women who were not anemic at baseline, 47 percent became anemic by 3.5 years of follow-up. On multivariate analysis, the use of HAART was associated with resolution of anemia even when used for only six months (odds ratio [OR] = 1.45; $P < 0.05$). In the multivariate model, a CD4 count <200 cells/mL (OR = 0.56; $P < 0.001$); HIV-1 RNA level $\geq 50,000$ copies/mL (OR = 0.65; $P < 0.001$), and mean corpuscular volume (MCV) value <80 fL (OR = 0.40; $P < 0.001$) were also associated with an inability to correct anemia. Similarly, use of HAART for 12 months or more was associated with a protective effect against development of anemia (OR = 0.71; $P < 0.001$). Among HIV-infected women, anemia was independently associated with decreased survival (hazard ratio [HR] = 2.58; $P < 0.001$). Other factors associated with decreased survival included a CD4 cell count <200 cells/mL (HR = 5.83; $P < 0.001$), HIV-1 RNA level $\geq 50,000$ copies/mL (HR = 2.12; $P < 0.001$), and clinical diagnosis of AIDS (HR = 2.83; $P < 0.001$). **CONCLUSIONS:** Anemia is an independent risk factor for decreased survival among HIV-infected women. HAART for as little as six months is associated with resolution of anemia.

J Acquir Immune Defic Syndr 2004;37(2):1245-1252.

Sexually Transmitted Diseases

A case-control study of syphilis among men who have sex with men in New York City: Association with HIV infection

Paz-Bailey G, Meyers A, Blank S, et al.

OBJECTIVE: The objective of this study was to determine factors associated with syphilis among men who report sex with other men in New York City. **DESIGN:** We conducted a case-control study among 88 men who reported sex with men in the previous year, 18 to 55 years old and diagnosed with primary or secondary syphilis during 2001; and 176 control subjects frequently matched by age and type of health provider. **RESULTS:** HIV prevalence among syphilis cases was 48 percent compared with 15 percent among control subjects ($P < 0.001$). Variables associated with syphilis in a multivariate

model were HIV infection (odds ratio [OR], 7.3; 95 percent confidence interval [CI], 3.5-15.4), income greater than US\$30,000 per year (OR, 2.7; CI, 1.4-5.2), and barebacking (OR, 2.6; CI, 1.4-4.8). The median time since HIV diagnosis for HIV-positive was six years for cases and seven years for control subjects ($P = 0.70$). Among HIV-infected participants, syphilis cases were more likely than control subjects to report being on antiretroviral therapy (69 percent versus 44 percent, $P = 0.05$) and to report having undetectable viral load (58 percent versus 24 percent, $P = 0.02$). **CONCLUSION:** HIV infection was strongly associated with syphilis in this study. High-risk behavior reported by both cases and control subjects indicates the potential for increased HIV transmission.

Sex Transm Dis 2004;31(10):581-587.

Journal of Public Health

Antenatal screening for HIV: Are those who refuse testing at higher risk than those who accept testing?

Boxall EH, Smith N.

BACKGROUND: The UK Department of Health recommends that all pregnant women are offered screening for infection with human immunodeficiency virus (HIV) and had encouraged maternity units to achieve uptake targets of 90 percent by the end of 2002. Many maternity units fail to meet this target and there is concern that those women who are still refusing testing may include a higher proportion of women at high risk of infection. In consequence, those infected with HIV are not being identified and are not receiving the antiviral treatment, which would be of benefit to them and reduce the risk of transmission of HIV to their babies. **METHODS:** A retrospective audit of HIV screening uptake in women who were found to be infected with hepatitis B virus (HBV) and in those who were not infected with HBV was carried out in order to explore further the characteristics of "acceptors" and "refusers" of HIV screening. **RESULTS:** The overall uptake rate of HIV screening in the West Midlands population served by the National Blood Service was 60 percent in 2001 and 74 percent in 2002. The prevalence of HBV infection was found to be twice as high (0.39 percent) in those who had refused an HIV test compared with those who had accepted a test (0.21 percent) ($p = 0.022$). **CONCLUSION:** There is good evidence that women refusing HIV antenatal screening have a higher prevalence of another blood-borne virus, indicating clearly that further effort must be made to increase the screening uptake and fully integrate HIV screening with other antenatal tests.

J Public Health 2004;26(3):285-7.

Hepatitis coinfection and LPV/RTV

Michael Carter

HIV-positive patients who are coinfecting with hepatitis B virus (HBV) or hepatitis C virus (HCV) have a significantly increased risk of developing elevated liver enzyme levels when taking an antiretroviral regimen including lopinavir/ritonavir (LPV/RTV), according to a study published in the September 2004 *HIV Medicine*. The study's Italian investigators believe that the results emphasize the importance of testing patients for hepatitis coinfection at baseline and the importance of monitoring liver function before and during antiretroviral therapy.

A retrospective Canadian study, presented at the XV International AIDS Conference in Bangkok, found that the use of LPV/RTV by patients coinfecting with HBV or HCV was significantly associated with the development of grade 3/4 elevations in alanine aminotransferase (ALT) levels.

It is well known that protease inhibitor (PI)-containing antiretroviral therapy regimens can cause liver toxicities. Two reasons for this side effect have been suggested: the intrinsic toxic effects of this class of drugs, and the recovery of cell-mediated immunity brought about by antiretroviral therapy leading to the damage of HBV- or HCV-specific liver cells.

Investigators in northern Italy wished to determine the incidence of, and risk factors for, elevations in liver enzymes in PI-experienced patients taking LPV/RTV as part of their antiretroviral therapy.

In a prospective study, a total of 782 patients were followed for 12 months, or until the appearance of elevated liver

enzymes. Patients were taking the standard dose of LPV/RTV (400 mg LPV boosted by 100 mg RTV), unless they were also taking a nonnucleoside reverse transcriptase inhibitor (NNRTI), in which case the dose of LPV/RTV was increased (533 mg LPV with 133 mg RTV).

Alanine aminotransferase, aspartate aminotransferase (AST), lipid levels, CD4 count, and viral load were evaluated at baseline, one month after starting LPV/RTV, and then at three-month intervals. Tests were also performed for the presence of HBV and HCV.

Elevated liver enzymes were graded according to severity. Alanine aminotransferase levels 2.6 to five times the upper limit of normal were described as grade 2 toxicity, ALT levels five to 10 times the upper range of normal as grade 3 toxicity, and ALT levels over 10 times the upper limit of normal were described as grade 4 toxicity.

Of the 782 patients recruited to the study, a total of 269 (34 percent) had elevated liver enzymes at baseline, and elevated ALT and AST levels on entry to the study were significantly related to infection with hepatitis B or C ($p < 0.001$).

The most common nucleoside reverse transcriptase inhibitor (NRTI) backbones taken with LPV/RTV were didanosine (ddI) and stavudine (d4T) (18 percent) and lamivudine (3TC) and d4T (13 percent). A total of 18 percent of patients were taking an NNRTI, and just under 10 percent were taking a second PI.

Median duration of follow-up was 349 days. A total of 185 patients (24 percent) discontinued LPV/RTV a median of 198 days after starting antiretroviral therapy. Of these patients, 88 stopped because of side effects, including 13 who experienced hepatic toxicities.

Across the study population, a total of 9 percent experienced elevations in liver enzymes during LPV/RTV therapy. Alanine aminotransferase levels increased significantly at months 3 ($p = 0.006$), 6 ($p = 0.005$) and 9 ($p = 0.04$). However, these increases were principally confined to coinfecting patients, with a total of 16 percent of HBV- or HCV-infected patients developing elevated liver enzymes compared to only 3 percent of patients without these infections.

In the patients who did develop elevated liver enzymes, almost 75 percent had grade 2 toxicity, 20 percent grade 3 toxicity, and 5 percent grade 4 toxicity.

Thirteen patients stopped LPV/RTV, but continued with their other antiretroviral drugs, because of elevations in liver enzymes, and this led to a normalization of liver function in 11 patients. There were four hospitalizations and one death.

In multivariate analysis, the investigators found that coinfection with HBV or HCV ($p < 0.001$), younger age ($p = 0.005$), elevated ALTs at baseline ($p = 0.005$), and concomitant use of efavirenz (EFV) ($p = 0.008$) were predictive for the development of increased liver enzymes during LPV/RTV-containing antiretroviral therapy.

The investigators conclude that hepatitis coinfection should be tested for prior to the initiation of antiretroviral therapy, and that liver function should be carefully and closely monitored during antiretroviral therapy. They also suggest that therapeutic drug level monitoring could prove a useful tool to enable physicians to adjust doses of drugs to prevent drug-related liver damage. ■

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International Association of
Physicians in AIDS Care





IN THE LIFE



Ronald Hirsch

For more than two years the *IAPAC Monthly* has featured members of the International Association of Physicians in AIDS Care (IAPAC) who are asked to bare their souls by answering a series of questions similar in nature to those asked in the famous *Proust Questionnaire*.

This month, *IAPAC Monthly* is proud to feature Ronald Hirsch, who practices Internal Medicine at the Chicago-based Signature Medical Associates.

What proverb, colloquial expression, or quote best describes how you view the world and yourself in it?

"No. Try not; do or do not. There is no try."—Yoda to Luke Skywalker when Luke said he would try to levitate his sunken fighter.

What activities, avocations, or hobbies interest you?

I enjoy road cycling. Nothing is more serene than the sounds on a country road on an early weekend morning.

If you could live anywhere in the world, where would it be?

I would live in Southern California by the beach. What could be better than a sunset over the Pacific?

Who are your mentors or real life heroes?

My real life hero is my wife. Not only has she raised three amazing children in this hectic world, but she also keeps my priorities in order.

With what historical figure do you most identify?

The historical figure with which I identify was a man who was a good father and husband, a loyal friend; a man who enjoyed his work and worked with local civic organizations and was active in sports: Fred Flintstone.

Who are your favorite authors, painters, and/or composers?

David Foster Wallace, whose "Infinite Jest" is a 1,079-page masterpiece that is nearly incomprehensible.

If you could have chosen to live during any time period in human history, which would it be?

I would live in the Middle Ages and help with the quest for the Holy Grail. Specifically 932 AD.

If you did not have the option of becoming a physician, what would you have likely become, given the opportunity?

In high school my vocation testing said that I should become a criminologist. I didn't know what that was so I became a doctor.

In your opinion, what are the greatest achievements and failures of humanity?

Achievements: Technology and computers creating a global community. Failures: Inability of people in our society to accept responsibility for one's own actions.

What is your prediction as to the future of our planet one full decade from present day?

In 10 years the potential of alternate fuel sources will be realized and there will finally be respect for our environment. In 10 more years, the problems of overpopulation will finally affect the entire world and starvation will no longer be a Third World problem. ■



SAY ANYTHING

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I don't think there's any way to defend the fact that we have not been sensitive [to gays]... and there's still a lot of homophobia out there. We've made some progress, but we still have a long way to go [and] there's no excuse for what happened in the past.

Former US Surgeon General David Satcher during an October 15, 2004, town hall meeting held at the Morehouse School of Medicine in Atlanta, responding to questions from two gay activists who were calling attention to what they defined as the "invisible deaths" of African-American gay men lost to the AIDS epidemic in the United States.

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Why, why give me this shell? [The government] must keep him, because I cannot do what they have failed to do. I cannot afford [antiretroviral drugs]. It is traumatic for the children to see their father in this way.

The wife of an HIV-positive Zambian ex-prisoner as quoted in an October 21, 2004, Inter Press Service report entitled, "HIV-Positive Prisoners Find Freedom a Mixed Blessing." More than 300 HIV-positive inmates have been freed since late 2001 on compassionate grounds by Zambian President Levy Mwanawasa. Commissioner of Prisons Jethro Mumbuwa says Zambia's jails simply lack the resources to look after convicts who are seriously ill. Surprisingly, some of the strongest opposition to the releases has come from the prisoners' families.

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[The region has] made good progress in the last couple of years but like most of Asia, it is moving too late and too slow. The time is now for regional institutions to step up and accelerate their action at a regional level and with individual countries.

Kathleen Cravero, Deputy Executive Director of the Joint United Nations Programme on HIV/AIDS (UNAIDS), speaking October 20, 2004, at a forum hosted by the Association of Southeast Asian Nations (ASEAN) and the Asia-Pacific Economic Cooperation forum (APEC) in Manila. She warned that if governments across the Asia-Pacific region do not step up efforts to combat HIV/AIDS they risk a crisis similar in scale to Africa's AIDS pandemic.

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[South African President Thabo] Mbeki scared a lot of patients. They are just terrified of the side effects.

Francois Venter, a South African HIV/AIDS-treating physician who coordinated an antiretroviral therapy program at Johannesburg General Hospital, as quoted in an October 21, 2004, Washington Post article entitled, "South Africans Shun a Remedy for AIDS." Venter estimated that one of three patients who need antiretroviral therapy refuses it in large measure because Mbeki has repeatedly questioned the use of antiretroviral drugs on the grounds that they may have serious side effects. According to other experts cited in the article, widespread skepticism of Western medicine and reverence for traditional healers also lead many patients to shun the drugs.

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In 10 or 15 years, if there isn't important prevention work, we are going to have a frightening epidemic, starting on the coast and spreading to the entire country.

Paul Martin, a United Nations Children's Fund (UNICEF) representative, from an October 19, 2004, Associated Press report about an explosion of new HIV/AIDS cases in Ecuador's most populous coastal

province. Martin predicted that in certain zones on the coast in Guayas the levels of new infections are approaching those reached 10 years ago by Africa and the Caribbean. Ecuador's Health Ministry said there are more than 5,000 reported AIDS cases in the country of 12 million, but that unreported cases could be as high as 50,000.


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The population in this densely populated slum is extremely socially and economically vulnerable... disease is rife, with the biggest killer in the slum being HIV/AIDS-related illnesses.

From an October 21, 2004, Médecins Sans Frontières (MSF) press release announcing the launch of a new health center in Nairobi. The Kibera South Health Center will provide residents of Kibera, a slum in Kenya's capital, benefits of comprehensive HIV/AIDS care, including antiretroviral therapy. In the statement, MSF said it aimed to demonstrate through this project that a full package of quality healthcare, integrating HIV and AIDS treatment, could successfully be provided in an urban slum setting.

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[A]lthough both candidates look good on paper, neither has made the prospects for poor countries a central part of his campaign. The fact that 3 billion people, half of all humanity, live on US\$2 a day has not been featured in the candidates' speeches or in the debates. Nor was the fact that some 5 million people are newly infected with HIV each year (though the global AIDS pandemic was discussed briefly in the vice presidential debate, thanks to the candidates' inability to respond directly to a question about domestic infection rates among black women).

Excerpt from an October 21, 2004, Washington Post editorial entitled, "Silent Commitments."

WHY DOES DESTINY'S CHILD WEAR THE BRACELET?

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Destiny's Child appears courtesy of Columbia Records
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Purchasing a UTAC bracelet contributes directly to the International Association of Physicians in AIDS Care (IAPAC) and its mission to improve access to quality treatment for all people living with HIV/AIDS. A full 25 percent of the price of each bracelet goes directly to IAPAC programming. Please be sure to mention IAPAC when shopping at www.until.org.