Antiretroviral treatment in developing countries: The peril of neglecting private providers
Antiretroviral treatment in developing countries: The peril of neglecting private providers

Ruairí Brugha

Increased access to antiretroviral drugs in the developing world is vital. But unless treatment is properly controlled, these drugs could rapidly become useless. Private medical practitioners, pharmacists, and traditional/informal providers who dispense antiretroviral drugs require oversight.

Back to basics...
Making HIV testing routine

Mark D. Wagner
Improving access to HIV treatment is sometimes thought to be synonymous with providing antiretroviral drugs to those who cannot afford them. We know that these medications could prevent millions of premature deaths in the developing world and so we seek, rightly, to break down the economic barriers that impede their distribution.

We must remember, however, that the reality is not this simple. Airdropping antiretroviral drugs into impoverished regions of the world might help some individuals in the short term—but if a steady supply of drugs cannot be guaranteed and patients cannot have regular consultation with trained healthcare professionals employing appropriate technology (eg, CD4 count), we will have failed. At the individual level, patients will see their treatment options disappear and outcomes will be short of expectation; at the level of global and regional public health, drug-resistant forms of HIV will flourish and whole populations of patients will suffer. It is beyond question that access to antiretroviral therapy in resource-limited countries should be expanded; also unassailable, however, is the concept that improvements are critically needed to the medical infrastructure that will support the use of these powerful medications. Such improvements must be undertaken simultaneously and with equal determination.

Ruarí Brugha reviewed data in a recent British Medical Journal opinion piece, reprinted in this issue of the IAPAC Monthly, that underscores the reasons why bringing antiretroviral therapy to the developing world must be done, while as quickly as possible, with great deliberateness and as part of a true revolution in medical care worldwide.

Separate studies in India, Senegal, Uganda, and Zimbabwe describe patients purchasing antiretroviral drugs from the private sector because public sector care was unavailable or associated with stigma. They speak of unprescribed and incorrect dosages on a massive scale. The authors of the Zimbabwe study, published in the Central African Journal of Medicine, write of “treatment anarchy,” with private healthcare workers and pharmacists dispensing “any [antiretroviral] they could get their hands on.”

Suffering people will always find ways to acquire the medications that can alleviate their pain. This cannot be changed, and neither should it be. As such, we face a situation in which we all bear some personal interest in the treatment of HIV-infected patients around the world.

The world community, led by professional men and women who have committed their lives to healthcare, must come together for an unprecedented show of unity. For it is only through a radical improvement in healthcare throughout the economically challenged countries of the world that we can see antiretroviral drugs used to their ultimate potential.

This was the general consensus at last month’s 2nd IAS Conference on HIV Pathogenesis and Treatment, during which clinicians and researchers from around the world were able to present and review new data on the feasibility of using antiretroviral therapy in the developing world. There was agreement that antiretroviral therapy is possible in resource-constrained settings and the potential for drug-resistant HIV should not be an excuse for further delays. They went further to say, however, that the success of treatment programs will be greatly improved by such things as widespread and appropriate training for HIV care providers and improvements to the physical infrastructure of national healthcare systems.

Brazil’s Paolo Teixiera, Senegal’s Papa Salif Sow, and Botswana’s Ernest Darkor—all physicians with tremendous experience in scaling up antiretroviral programs where resources are limited—were among those who made these points. As Darkor put it, “HIV/AIDS must be addressed in the context of total healthcare delivery.”

The International Association of Physicians in AIDS Care (IAPAC) has an important role to play in bringing about this transition. IAPAC is actively engaging with and training private practitioners, pharmacists, and community healthcare workers on the African continent. We hope to extend this multi-profession outreach within Africa and in other resource-limited regions of the world, particularly as we roll out the Global AIDS Learning and Evaluation Network (GALEN). And, the association plays a leadership role within the International Treatment Access Coalition (ITAC), and is in consultation with the World Health Organization (WHO) on ways to help facilitate the UN General Assembly Special Session on AIDS (UNGASS) goal of three million patients on antiretroviral therapy by 2005.

In these and all IAPAC’s roles, we emphasize the need for improving the capacity to care properly for HIV-infected patients, not simply the disbursement of drugs. And, as always, we count on the active involvement of our members. Your commitment to solidarity in this struggle demonstrates recognition of the fact that we are all in this together.

José M. Zuniga is President of the International Association of Physicians in AIDS Care (IAPAC), and Editor-in-Chief of the IAPAC Monthly.
The US Food and Drug Administration (FDA) approved July 2, 2003, the newest addition to the nucleoside reverse transcriptase inhibitor (NRTI) class of antiretroviral agents—Gilead Sciences’ Emtriva (emtricitabine or FTC). FTC’s approval by the European Agency for the Evaluation of Medicinal Products (EMEA) is expected in early 2004.

FTC is indicated for adult patients ages 18 and older. Safety and effectiveness in pediatric patients have not been established. In antiretroviral-treatment-experienced patients, the use of FTC may be considered for adults with HIV strains that are expected to be susceptible to FTC as assessed by genotypic or phenotypic testing. The recommended dose of FTC is one 200 mg capsule daily, with or without food.

The FDA’s approval of FTC was based on data from two 48-week clinical trials—Study 301A and Study 303.

Study 301A was a double-blind, active-controlled multicenter study comparing FTC (200 mg once daily) + didanosine (ddI) + efavirenz (EFV) versus stavudine (d4T) + ddI + EFV in 571 antiretroviral-naive patients. The proportion of patients who achieved and maintained confirmed HIV RNA <400 copies/mL (<50 copies/mL) through week 48 was 81 percent (78 percent) for the FTC + ddI + EFV group versus 61 percent (59 percent) for the d4T + ddI + EFV group, respectively. The mean increase from baseline in CD4 cell count was 29 cells/mm³ for the FTC arm compared to 61 cells/mm³ for the 3TC arm.

The most common adverse events that occurred in patients receiving FTC with other antiretroviral agents in clinical trials were headache, diarrhea, nausea, and rash, which were generally of mild to moderate severity. Approximately 1 percent of patients discontinued participation in the clinical studies due to these events. With the exception of skin discoloration, which was reported with higher frequency in the FTC-treated group, all other adverse events were reported with similar frequency in FTC and control treatment groups.

Skin discoloration, manifested by hyperpigmentation on the palms and/ or soles, was predominantly observed in non-Caucasian patients. The mechanism and clinical significance are unknown.

FTC is not indicated for the treatment of chronic hepatitis B (HBV) infection, and the safety and efficacy of FTC have not been established in patients coinfected with HBV and HIV. HBV “flare-ups” have been reported in patients after the discontinuation of FTC. Patients coinfected with HIV and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment.

Gilead Sciences plans to co-formulate FTC in one tablet with its nucleotide reverse transcriptase inhibitor (NtRTI) tenofovir (TDF)—a co-formulation that could be marketed by 2005. Already in progress is a Gilead Sciences-sponsored study comparing the FTC/TDF co-formulation to GlaxoSmithKline’s Combivir (ZDV/3TC), using EFV as the third drug. This 48-week study is expected to reveal whether FTC/TDF is superior to ZDV/3TC, or at least whether the Gilead Sciences’ co-formulated drug achieves a lower rate of treatment failure caused by the M184V mutation—the common site of resistance to 3TC and FTC.

**At-a-Glance: Emtriva (FTC)**

- **Generic name:** emtricitabine (FTC)
- **Brand name:** Emtriva
- **Class:** NRTI
- **Manufacturer:** Gilead Sciences
- **Prescribed dose:** 200 mg capsule once a day

**The buzz:** Clinical trials suggest FTC is equally effective as lamivudine (3TC)

**Side effect alert:** Most common side effects include diarrhea, headache, nausea, rash

**Resistance note:** FTC is likely ineffective for patients resistant to 3TC

**Key research:** Study 301A, Study 303, ALIZE-ANRS 99 Study
The US Department of Health and Human Services (HHS) on July 14, 2003, released its updated “Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents” (DHHS Guidelines). The most notable revision to the DHHS Guidelines is the identification of “preferred” and “alternative” antiretroviral regimens for antiretroviral-naive patients.

Previous iterations of the DHHS Guidelines grouped commonly used antiretroviral agents into columns and asked clinicians to construct a combination regimen by adding drugs from one column with those from another. As the number of available antiretroviral medications has increased, constructing an effective regimen based on this “menu” format has become increasingly difficult.

The suggested “preferred” and “alternative” regimens are classified in Table 12a of the revised DHHS Guidelines. According to the Panel on Clinical Practices for Treatment of HIV Infection, which maintains the DHHS Guidelines, “preferred regimens were selected … based on the totality of virologic, immunologic, and toxicity data.” Of note, the DHHS Guidelines stress that “[r]egimens should be individualized based on the advantages and disadvantages of each combination such as pill burden, dosing frequency, toxicities, and drug-drug interactions, and patient variables, such as pregnancy, co-morbid conditions, and level of plasma HIV-RNA.”

In addition to Table 12a, the revised DHHS Guidelines also include two new tables meant to list the advantages and disadvantages of individual components of antiretroviral therapy (Table 12b), and regimens or components that should not be used (Table 13), respectively.

Also new to the DHHS Guidelines are several new sections on special considerations in the initiation of antiretroviral therapy, including once-daily therapy, drug-drug interactions, and initiating therapy in pregnant women or women who may become pregnant. And, reflecting new knowledge and experience on the use of drug-resistance testing in clinical practice, the DHHS Guidelines include a new section and accompanying table entitled, “Drug Resistance Testing,” and “Recommendations for Using Drug-Resistance Assays” (Table 3), respectively.

“We have more clinical trial experience and better strategies for managing so-called ‘treatment failure’ since the last update of the [DHHS Guidelines],” said Mark Dybul, Assistant Director for Medical Affairs at the US National Institute of Allergy and Infectious Diseases (NIAID) and Executive Secretary of the DHHS Guidelines Panel. “Notably, we have gained more experience in using drug-resistance testing to guide the selection of a new treatment regimen once a patient has failed an initial regimen.”

In addition, a revised section on the “Management of the Treatment-Experienced Patient” includes new tables that provide guidelines for patient assessment and management based on specific clinical scenarios; list novel strategies to consider in patients with few available treatment options; and list treatment options following virologic failure on initial therapy (Tables 23-25).

**Editor’s Note:** Members of the International Association of Physicians in AIDS Care (IAPAC) as well as IAPAC Monthly subscribers will receive in September 2003 an abridged version of the DHHS Guidelines as a supplement to the IAPAC Monthly.

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### Table 12a. Antiretroviral regimens recommended for treatment of HIV-1 infection in antiretroviral-naive patients

<table>
<thead>
<tr>
<th>NNRTI-based regimens</th>
<th>Preferred regimens</th>
<th>Alternative regimens</th>
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<tbody>
<tr>
<td>EFV + 3TC + (ZDV or TDF or d4T) — except for pregnant women or women with pregnancy potential</td>
<td>EFV + 3TC + ddI — except for pregnant women or women with pregnancy potential</td>
<td></td>
</tr>
<tr>
<td>NVP + 3TC + (ZDV or d4T or ddI)</td>
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<table>
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<tr>
<th>PI-based regimens</th>
<th>Preferred regimens</th>
<th>Alternative regimens</th>
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<tbody>
<tr>
<td>LPV + RTV + 3TC + (ZDV or d4T)</td>
<td>APV + RTV† + 3TC + (ZDV or d4T)</td>
<td></td>
</tr>
<tr>
<td>IDV + 3TC + (ZDV or d4T)</td>
<td>IDV + RTV† + 3TC + (ZDV or d4T)</td>
<td></td>
</tr>
<tr>
<td>NLF‡ + 3TC + (ZDV or d4T)</td>
<td>SQV (sgc or hgc) + RTV + 3TC + (ZDV or d4T)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Triple NRTI regimen – as an alternative to PI- or NNRTI-based regimens</th>
<th>Alternative regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC + 3TC + ZDV</td>
<td></td>
</tr>
<tr>
<td>ABC + 3TC + d4T</td>
<td></td>
</tr>
</tbody>
</table>

| * Preliminary 96-week data comparing d4T + 3TC versus TDF + 3TC revealed higher incidence of lipodystrophy and lipid abnormalities in the d4T group. |
| † Low-dose (100-400 mg) RTV. |
| ‡ NLF 625 mg tablet – soon to be available. |
Safety and immunogenicity of a heptavalent pneumococcal conjugate vaccine in infants with human immunodeficiency virus type 1 infection

Nachman S et al.

OBJECTIVE: Heptavalent pneumococcal conjugate vaccine (PCV) has been shown to be safe and effective in healthy infants and children. However, little is known about its use in children who have human immunodeficiency virus (HIV) infection and are known to be at increased risk of developing pneumococcal infections. This study was conducted to evaluate the safety and immunogenicity of heptavalent PCV in infants with HIV infection.

METHODS: The Pediatric AIDS Clinical Trials Group Study 292 Team randomized infants with HIV infection 2:1 to receive heptavalent PCV or placebo in a double-blinded manner. Infants were vaccinated with three doses at two-month intervals, starting at ages 56 to 180 days. A booster dose was given at 15 months of age. Immunogenicity was evaluated after the third dose of vaccine, before and after the booster dose, and at 24 months of age. RESULTS: Thirty infants with HIV infection received PCV, and 15 received placebo. No differences in baseline characteristics were found across arms. Five severe acute reactions were experienced by four subjects: three in the PCV arm and one in the placebo arm; all occurred among subjects with symptomatic disease at study entry. No differences were found in the two arms with respect to the number or timing of new diagnoses through 24 months of age, including diagnoses of otitis media. However, when symptomatic subjects were examined separately, the first new diagnosis occurred more rapidly among PCV recipients. Three deaths, all judged to be unrelated to study vaccine, occurred during follow-up: two in the PCV arm and one in the placebo arm. The primary immunogenicity measures were based on composites of four-fold changes in serotype-specific immunoglobulin G titers from preimmunization levels. We found a highly significant difference between the vaccine and placebo arms, with the PCV arm showing higher rates of response. Asymptomatic and symptomatic subjects who received PCV had similar immunologic responses for all serotypes.

CONCLUSIONS: This study demonstrates that heptavalent PCV was well tolerated and not associated with vaccine-associated adverse reactions. Most important, this vaccine was immunogenic in the infant with HIV infection. However, additional studies of this vaccine (or others) must pay special attention to patients with symptomatic HIV disease, as they seem to be at higher risk for adverse events to any antigen.

Annals of Internal Medicine

Slower progression of HIV-1 infection in persons with GB virus C co-infection correlates with an intact T-helper 1 cytokine profile

Nunnari G et al.

BACKGROUND: Progression to AIDS is slower in persons infected with both HIV-1 and GB virus C (GBV-C), also known as hepatitis G virus. OBJECTIVE: To compare clinical, virologic, and immunologic variables in HIV-1-seropositive patients with and without GBV-C co-infection. DESIGN: Subanalysis of a prospective cohort study. SETTING: Institute of Infectious Diseases, University of Catania, Catania, Italy. PATIENTS: 80 asymptomatic HIV-1-seropositive patients. MEASUREMENTS: GBV-C RNA level; plasma HIV-1 viral load; CD4+ cell counts; and serum levels of interleukin (IL)-2, IL-4, IL-10, and IL-12. RESULTS: At the start of the study, plasma GBV-C RNA was detected in 17 patients (21 percent). During follow-up, IL-2 and IL-12 levels decreased significantly (P = 0.005 and P = 0.01, respectively) and IL-4 and IL-10 levels increased significantly (P = 0.01 and P = 0.004, respectively) in the GBV-C-negative group but did not change substantially in the GBV-C-positive group. Each measured variable differed significantly between GBV-C-positive and GBV-C-negative groups during follow-up (P < 0.001 for IL-12, IL-4, and IL-10; P = 0.002 for IL-2). CONCLUSION: GB virus C may immunologically interfere with progression of HIV-1 infection to AIDS by maintaining an intact T-helper 1 cytokine profile.

Journal of Adolescent Health

Social and psychological influences on HIV preventive behaviors of youth in Haiti

Holshneider SO and Alexander CS

PURPOSE: To examine HIV/AIDS prevention-related sexual behaviors and identify potential predictors of those behaviors among youth living in Haiti. METHODS: Data were gathered from a cross-sectional survey conducted with 845 youths, aged 15 to 19 years, attending 12 primary and/or secondary schools. A subsample of the 491 students who were sexually active adolescents reported always or sometimes using condoms and 27 percent reported having used a condom the last time they had sex. Over 40 percent (43 percent) had had three or more lifetime sex partners. Findings from the multivariate logistic regression analyses indicate that consistent condom use, condom use at last sexual intercourse, and fewer lifetime sexual partners were significantly associated with high levels of self-efficacy to communicate about HIV/AIDS or use a condom. Significant negative associations were found among consistent condom use, condom use at last sexual intercourse, and high barriers to condom use. Fewer lifetime sexual partners was significantly associated with high peer preventive norms and low traditional gender norms.

CONCLUSION: These findings emphasize the importance of providing HIV prevention programs for young people in the study communities which enhance effective sexual communication and negotiation skills, target prevention-oriented social norms, and address how to overcome barriers to condom use.

AIDS

Survival in an urban HIV-1 clinic in the era of highly active antiretroviral therapy: A 5-year cohort study

Lucas GM, Chaisson RE, and Moore RD

OBJECTIVE: To examine the implications of early virologic response to highly active antiretroviral therapy (HAART) on long-term HAART utilization patterns, development of diabetes or hyperlipidemia, and mortality in an urban HIV-1 clinic. DESIGN: A cohort of 444 patients in an urban HIV-1 clinic, who started HAART prior to January 1, 1999, were categorized by virologic response in the first 18 months of therapy: durable viral suppression, initial suppression followed by rebound, and failure to achieve suppression. Antiretroviral exposure, HIV-1 RNA levels, CD4 cell counts, development of diabetes or hyperlipidemia, and survival were compared in the three groups. RESULTS: Over four years of follow-up, patients in the durable suppression group used HAART 82 percent of the time compared with 60 percent in the rebound group (P < 0.001) and 23 percent in the failure to suppress group (P < 0.001). Through four years of follow-up, patients in the rebound group had a cumulative exposure to a median of seven antiretroviral drugs (interquartile range [IQR]: 6 to 9) compared with five drugs in the durable suppression group (IQR: 4 to 6) and five drugs in the failure to suppress group (IQR: 3 to 7) (P < 0.001 for both comparisons with the rebound group). At five years, the estimated proportions surviving were 89 percent in the durable suppression group, 76 percent in the rebound group (P = 0.04), and 56 percent in the failure to suppress group (P < 0.001). During follow-up, 35 percent in the durable suppression group developed diabetes or hyperlipidemia compared with 24 percent in the rebound group (P = 0.15) and 8 percent in the failure to suppress group (P < 0.001). CONCLUSIONS: This study highlights the long-term implications of early virologic response to HAART for survival, accumulation of triple-class antiretroviral exposure, and development of HAART-associated toxicities.

Antiretroviral treatment in developing countries:
The peril of neglecting private providers
Ruairí Brugha

Increased access to antiretroviral drugs is vital for developing countries with high rates of HIV infection. But unless treatment is properly controlled, these drugs could rapidly become useless.

Only 5 percent of the 5.5 million people in developing countries who need antiretroviral treatment currently receive it. New initiatives and global partnerships are trying to increase access to antiretroviral drugs—for example, the International HIV Treatment Access Coalition, guidelines created by the World Health Organization (WHO) for scaling up antiretroviral treatment, and employee programs under the umbrella of the Global Business Coalition on HIV/AIDS. However, these initiatives largely ignore the fact that most poor people who suspect they have a sexually transmitted infection seek care in the private sector because of the stigma attached. The main care providers for HIV disease in the poorest countries are therefore likely to be private medical practitioners, pharmacists, and traditional and informal providers, such as drug vendors, who are often unregulated and dispense drugs illegally. Improper use of antiretroviral drugs may result in development of resistant HIV, so it is important to take account of private providers and regulate their behavior.

Dangers of unregulated prescribing

Although recent reductions in the price of antiretroviral drugs are welcome, the rapid increase in legal distribution will inevitably increase illegal leakage into the private sector. Evidence of uncontrolled use is already emerging in the formal and, more worryingly, informal private sector. A study from Zimbabwe in 2000 reported that a quarter of 68 private physicians were prescribing antiretroviral drugs and a quarter of 80 pharmacies were dispensing them to patients, although insurance companies did not reimburse for their use. The authors described prescribing practices as “therapeutic anarchy,” with prescribers and dispensers using “any ARV that they could lay their hands on.” Monotherapy, stocked by 82 percent of pharmacies, was prescribed to 17 percent of patients; and most of the 92 patients interviewed believed that antiretroviral drugs cured HIV infection.

A survey of 21 Ugandan private medical facilities reported that only four of 17 facilities prescribing antiretroviral drugs had received CD4 and viral load results in the previous two months for 38 of the 340 patients they were monitoring. Tests cost US$150 to US$165 per sample. Providers had to change patients’ treatments because of differences in drug costs and running out of stock. Alternative sources of antiretroviral drugs were “mainly drug donations from relatives abroad and local pharmacies.” Of 200 HIV-positive patients referred to a specialist center in India because of poor response to antiretroviral treatment, only 10 percent had adhered to treatment; 50 percent had stopped taking the drugs on the advice of traditional healers, and 80 percent had been receiving incorrect doses. In India, 60 to 85 percent of primary care provision occurs in the largely unregulated formal and informal private sector.

In Senegal, nine antiretroviral drugs were available in the informal private sector by 2002, all donations from northern countries that were sold on. The study reported monotherapy, dual therapy, and intermittent treatment, stating that “the patient demand is still very weak, but several sellers in the informal market confirm that they are about to develop marketing strategies to encourage their sale.”

Policymakers cannot afford to wait for conclusive evidence that private providers will soon be at the forefront of providing antiretroviral drugs in developing countries and that their treatment practices will accelerate HIV resistance to these drugs. Private providers are recognized to dominate the market in the treatment of sexually transmitted diseases. However, international and national policymakers have not acted on the available evidence.

Working with the private sector

The public sector needs to learn to compete more effectively in delivering acceptable and high quality services for controlling HIV. Even when users recognize (correctly) that public sector services are technically superior, they choose private providers to minimize stigma. The public sector may therefore be the best channel for delivering...
short course antiretroviral drugs to prevent mother-to-child transmission of HIV. Trusted private providers, like community health workers, may have greater potential for providing continuity of care and supporting treatment, driven partly by the economic incentive to retain client loyalty. They are an untapped potential for ensuring long-term compliance.

Donors need to be more active in helping countries to fulfill their stewardship responsibilities in setting prescribing and dispensing rules (regulation), ensuring compliance (enforcement), and “exercising intelligence and sharing knowledge,” to deal with this private sector. Lack of treatment guidelines, but crucially lack of links between private practitioners and specialists and lack of access to research evidence, were reported in Zimbabwe. If guidelines are to contribute to a public health approach, they need to take into account public health realities in resource-limited settings. Most poor countries lack two proved essentials for working with dominant and uncontrolled private sectors: financial leverage and effective enforcement of regulatory controls. Additional strategies are needed.

Creating policies for treatment

National policies need to take account of the coverage achieved by different types of providers and the profile of people that providers are serving. Quality of care is determined by providers’ knowledge, skills, and access to resources; the influence of user demand (for accessible, acceptable, and short courses of treatment); and policies and practices for drug licensing, importation, and distribution. The problem facing poor countries is that poor people are more likely to use informal providers such as drug shops and vendors as they lack other affordable options.

Policy choices will be difficult. The practices of many private providers are contrary to current policy and hard to monitor. There will be opposition from powerful professional groups to working with informal providers, and projects successful in working with unorganized individual providers are hugely resource intensive. Consequently, working with the more organized formal private sector—doctors, nurses, and trained pharmacists—is the most feasible starting point for governments. No single approach will suffice for all contexts. In settings with low public sector capacity, governments could use nongovernmental organizations to run services to control HIV and manage strategies for working with and monitoring private providers.

The public sector also needs to learn the skills of the corporate private sector in social marketing, franchising, and accreditation of provider networks. Much attention is justifiably given to the potential of companies to provide antiretroviral drugs to employees and their families. A model that combines several elements of good practice is the Direct AIDS Intervention Program, a partnership between a company, a nongovernmental organization, and a health maintenance organization in South Africa. Employees and their families are eligible to receive a free HIV care package including antiretroviral drugs. They can use any of the eligible private practitioners, who are supported by a team of HIV/AIDS medical specialists. However, the poorest people most at risk are not in formal employment.

Cooperation

Drug development, especially for antiretrovirals, is an uncertain and risky venture. It is in the interest of pharmaceutical manufacturers as well as the public sector that prescribing, dispensing, and adherence to treatment are optimal in order to delay the emergence of resistant HIV.

Pharmaceutical distributors have sophisticated strategies for monitoring and influencing prescribing practices, even in resource-poor settings. They could place these at the service of the public sector.

The goal of an AIDS-free world is too important to risk failure through ideological disputes over public or private sector approaches at the local or global level. Each can learn from the other, and the state should be the guarantor of quality, wherever people seek care. A sustained increase in resources to ensure access to antiretroviral drugs through long-term commitments to the Global Fund to Fight AIDS, Tuberculosis, and Malaria; investment in building public sector capacity to manage increasingly complex health systems; and the piloting and evaluation of innovative strategies for delivering antiretroviral drugs are all needed.

At the 14th International Conference on AIDS in 2002, [former South African President] Nelson Mandela talked about the window of hope offered by even a few years of additional life on antiretroviral drugs for people with HIV/AIDS. Accelerated HIV resistance due to widespread uncontrolled use in the private sector will remove that hope and threaten populations in poor and wealthy countries alike.

Ruarai Brugha is a Senior Lecturer in Public Health in the Health Policy Unit of the Department of Public Health and Policy at the London School of Hygiene and Tropical Medicine.

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n June 1987, US Vice President George H.W. Bush was booed during a speech that discussed making HIV testing “routine.” Met with hostility from physicians and AIDS activists alike, the idea was dumped and the event was taken, rightly or wrongly, as evidence of the government’s insensitive response to the disease, one that reflected an urge to limit the civil rights of HIV-infected people and at-risk groups.

In the aftermath, state and local governments passed laws that made HIV testing a special case, requiring that patients sign an extraordinary informed consent document before they could be tested. Though government and private organizations may have encouraged individuals to seek testing, such burdens meant that HIV tests never became a routine part of clinical care in the United States.6

Sixteen years after Bush’s ill-fated speech, the US government has again announced plans to make HIV testing a standard procedure. An HIV prevention initiative announced on April 18, 2003, by the US Centers for Disease Control and Prevention (CDC):

...emphasizes the use of proven public health approaches to reducing the incidence and spread of disease. As with other sexually transmitted diseases (STDs) or any other public health problem, principles commonly applied to prevent disease and its spread will be used, including appropriate routine screening, identification of new cases, partner notification, and increased availability of sustained treatment and prevention services for those infected.3

Given the history of controversy that has surrounded HIV testing, one might suspect that talk of “routine screening” and handling AIDS like “any other public health problem” would have activists marching in the streets. But the CDC’s new strategy has been met with little outright objection. While there have been concerns voiced about particular aspects of the plan, and some fear that focusing more funding and effort on HIV-infected individuals will undercut programs working with seronegative people, most commentators are praising the plan to make HIV testing routine and approach the epidemic with a more traditional public health strategy.4,5,6

What are we to make of this? One interpretation is that science is finally winning out over politics. “AIDS exceptionalism”—through which activists and civil libertarians tie the hands of public health experts and the government by playing up fears of discrimination and invasion of personal privacy—is starting to wane.

Subscribing to this way of thinking, the head of a Texas-based sexual health policy organization wrote in a recent op-ed that the CDC’s new strategy is “a first step toward treating HIV/AIDS like a public health challenge, not a political issue.”7 Other recent accounts of the history of AIDS and the response to it would agree.8,9

This view is correct in the sense that the CDC’s shift represents a closer approximation of science-based disease control and standard public health practice. It is inaccurate, however, to the extent that it
paints the change as a victory over misplaced concerns for rights and freedoms. That it is now possible to approach HIV with a strategy that employs the proven methods of public health management with little fear of resultant discrimination speaks to medical and technical advances—and to victories for the causes of human rights and social equality. It is wrong to see it as the overcoming of obstacles inappropriately raised in the name of these ideals.

A good plan?
But before getting further into a discussion of changes in medical practice, laws, and societal mores that made possible the CDC’s “Advancing HIV Prevention: New Strategies for a Changing Epidemic,” the continuation of a shift begun in 2001, we should ask whether it is indeed a superior model for preventing the spread of HIV in the 21st century.

Though some details remain to be seen, the answer to that question appears to be “yes.” Current strategies are simply not lowering infection rates and reducing unsafe sexual behavior. Additionally, there is a great deal to be gained by employing new technology to make testing more routine and efficient.

After the virtual elimination in the United States of the risk of spreading HIV through blood donations and in clinical settings, and the great reduction of perinatal HIV transmission, the main modes of HIV transmission in the United States became sharing syringes in intravenous drug use and unprotected sex. Partly because testing has been so controversial, and because programs to provide clean syringes to drug users are wrongly banned from receiving federal funding, government HIV prevention at the national, state, and local levels has focused on bringing “safer sex” messages to HIV-negative people—particularly those seen to be “at risk” for infection.

It has been pointed out that measuring the efficacy of such programs is very difficult. The safer sex message reaches millions and one cannot be sure, it is argued, how many of these people might have become infected were it not for learning how to protect themselves. There may be some truth to these assertions, but the numbers that we do have point quite clearly to an overall strategy of AIDS prevention that is simply not working.

While the total estimated number of new infections appears to have stagnated in the early 1990s at around 40,000 per year, reliable evidence shows an increase in the last several years. From 1999 through 2001, in the 25 states where laws have allowed hospitals and clinics to report newly diagnosed cases of HIV infection since 1994, the number of infections increased by 14 percent among men who have sex with men and 10 percent among heterosexuals. More recent data from individual states and urban centers point to a distinct rise in other sexually transmitted infections—a trend that bespeaks more people having unsafe sex and putting themselves at risk for HIV infection. (It is particularly disturbing that a higher percentage increase would be seen among gay males because they are precisely the group that has been most targeted for safer sex programming.)

At the same time that existing programs do not appear to be inspiring behavior change and adequately preventing HIV infection, there is an unmet need among at-risk populations for greater knowledge of personal infection status. A recent report, which confirmed the findings of previous studies, presented data showing that a majority of urban HIV-infected males who are young, gay, and sexually active did not know they were infected. Fully 91 percent of African Americans in this group were unaware of their seropositivity status and 60 percent of white males were unaware of it. These data, drawn from studies in urban areas, are particularly disturbing. But the total estimate of Americans who do not know they are living with HIV is also shocking: as many as 280,000 of the nearly 1 million Americans who are HIV-infected are unaware of it—approximately 25 percent of the total.

There is good reason to believe that many new infections could be prevented if more HIV-infected people were made aware of their status and targeted with safe sex messages. Several studies have shown, for example, that the majority of people surveyed adopt safer sexual behavior after learning of their infection and beginning treatment. If the approximately 25 percent of infected Americans who do not know their status could be tested and brought into treatment, we could greatly reduce the number of potentially HIV-transmitting sex acts.

There will be further benefit in making HIV testing a more routine part of care in all clinical settings because data show that the many sexually active gay men who do not disclose their sexual orientation avoid testing locations that are associated with the homosexual community. This is especially true of minority men who have sex with men and it is doubly significant in light of the fact that minorities are over-represented among new HIV diagnoses.

Another major hurdle preventing HIV-infected people from being made aware of their status is overcome by the CDC’s adopting the new OraQuick testing technology that can determine within 20 minutes the presence of antibodies that indicate HIV infection. Older HIV tests required one to two weeks for processing, and a significant percentage of people who were tested would simply not return to retrieve the results. Unpublished CDC data show that 31 percent of people who tested positive for HIV in 2000 did not return to the testing site to learn of their infection. Experienced HIV test providers estimate that number is actually as high as 50 percent in some regions of the country. With results prepared while the individual waits, there is no danger of his or her not returning to learn them.

Again, such new methods as more portable tests may be better able to reach minority populations and other groups that do not have a community association with existing prevention centers.

Not perfect
Though it takes many steps in the right direction, the CDC’s “New Strategies” plan could nonetheless be improved upon. First, despite its general emphasis on proven initiatives, it continues a long and unfortunate US government practice of not funding risk reduction initiatives for individuals who practice illegal activities that put them at high risk for HIV infection.

There are copious data showing that programs providing intravenous drug users with clean syringes reduce the spread of HIV and do not increase the use of illicit drugs. In other areas of the world, and in some US urban areas, there has been some success with helping commercial sex workers to reduce their risk by using condoms. The CDC would do well to fund these strategies. (Though, in fairness, doing so would require a political wind change at federal, state, and local levels that might be far beyond anything that one CDC administration could bring about.)
and informed them of the shift in priorities of the new CDC strategy, he held a conference call with prevention advocates and informed them of the shift in priorities away from safer sex programming for people uninfected with HIV. At this writing, the new plan is only now taking effect, with rollout beginning June 27, 2003, for co-sponsored promotion of increased testing among the population as a whole. How exactly prevention money will be spent, then, remains to be seen. It would be inadvisable to change course entirely and leave out all other forms of HIV prevention.

Third, it is unfortunate that the plan is not being implemented as part of a general increase in federal support for HIV prevention, care, and treatment efforts. If thousands more individuals are to be made aware of their HIV infection and brought into treatment, there should be more money available to pay for that treatment. But the federal budget includes only a minimal increase, one that will not cover the increased need, for state AIDS Drug Assistance Programs.

How did we get here?

On balance, however, focusing prevention strategies on HIV-infected individuals and implementing routine HIV testing, partner notification, and other traditional public health approaches should have a good effect in lowering incidence rates. It is fair to ask, then, why it was not implemented in 1985, as soon as the antibody test was developed. What was behind the fear and disapproval of routine testing made evident in Vice President Bush being booted for suggesting it? What has changed since then?

It must be made clear that this is not simply a long delayed public health victory, a matter of sound policy finally trumping political quibbling. Rather, this policy shift was made possible by a series of medical advances, legal developments, and changes to society’s attitudes. Understanding this confluence of forces can help us to build on them in the United States and should be applicable in other contexts as well.

The medical advancements that have taken place to engender the routinization of HIV testing are the most obvious. Nine years after the development of HAART, we must not lose sight of the fact that an HIV diagnosis once meant nothing to the diagnosed but a painful death (as it still does in much of the developing world). When there is no effective treatment, and there are, as we shall see, significant psychosocial drawbacks to a positive diagnosis, routine testing or screening is far more an imposition on the individual, regardless of any gains to the community at large. It is a step that should be taken more carefully and one that will be made less effective through resistance from individuals and affected groups.

State of the art HIV treatment is still far from perfect, but it has advanced a great deal in the last two decades, and its effect is increased when it is implemented before a patient is symptomatic for AIDS. These facts, considered alongside the development of extremely accurate HIV tests that can be performed by a physician, allied healthcare professional, or trained volunteer, without lab work, have altered the scales. The potential benefit to any individual of learning his or her serostatus has increased relative to the potential harm.

Other changes to the balance of benefits and harms are to be seen in the area of legal and policy changes. In 1987, a representative for National Gay Rights Advocates explained the gay community’s fears to a Los Angeles Times reporter: “All those who test positive are going to get their insurance canceled and go on Medicaid, possibly lose their jobs, their apartment.”

These were not irrational concerns at the time, and they contributed to an understanding of HIV as an extraordinary disease, not to be treated with the same disease control approaches as would be employed to fight other infections.

This from a 1989 article in the American Journal of Public Health:

HIV infection is not like any other clinical conditions, even those that are potentially lethal. It carries not only great psychological burdens but the possibility of severe stigma and discrimination, including rejection or avoidance by healthcare workers and poor-quality treatment.

This is the era, it should be remembered, when hemophiliic children in the United States who tested positive for HIV were being banned from attending public schools. Internationally, countries were officially outlawing people with HIV or those who belonged to potential risk groups, such as homosexuals and commercial sex workers.

Since then, many states have written methods to prevent such discrimination into their laws, eliminating a major impetus for the public—particularly the already marginalized groups who were most at risk for AIDS—to resist routine testing. By creating government programs that pay for treatment of HIV-infected patients while they remain in the asymptomatic stage of disease progression, the government also added a benefit to early detection of HIV-positive status.

Outside of the United States, Jonathan Mann deserved a good deal of credit for preventing the legal discrimination of patients with HIV/AIDS. He organized the agreement of 150 nations to swear off such practices and convinced the World Health Organization to prioritize human rights within its response to the pandemic.

As US Supreme Court Justice Sandra Day O’Connor remarked in a recent collection of essays, “rare indeed is the legal victory—in court or legislature—that is not a careful byproduct of an emerging social consensus.” The outlawing of discrimination against HIV-infected individuals in US law and government policy indicates a general shift in attitudes toward those who test positive and the groups seen to be at high risk for testing positive.

Such cultural changes are nebulous. It is more difficult than is the case with medical and legal advancements to point to them, establish a record of how they came about, and elucidate their effects. But they are nonetheless real, and they have had an impact on what approaches to HIV public health are acceptable.

Continuing on a trajectory that began in the late 1960s, gays and lesbians in the United States have become more accepted within society as a whole. This can be seen in everything from pop culture (where they are characters on hit television shows—inconceivable a decade ago) to national jurisprudence and the US Supreme Court decision to disallow laws banning gay sex—a ban the court upheld in 1986.
harm associated with an HIV diagnosis and increasing the individual’s potential benefit to getting tested.

Having reached this point, US HIV/AIDS advocates should recognize the current possibilities for employing proven public health strategies more broadly in the fight against HIV. While remaining wary of sliding back into discrimination, and advocating for increased funding for treatment and prevention, they would also do well to encourage local and state authorities to reduce barriers to practices such as routine testing, confidential partner notification, and national reporting of incidence and prevalence rates.

The US experience also shines light on steps for improving prevention efforts that could be applicable elsewhere, particularly in the developing world. If we are to routinize testing in these settings, access to effective treatment and accurate testing should be improved; laws and public policy should be altered to reflect anti-discrimination positions; and efforts should be made to de-marginalize HIV-infected people and those seen to be at high risk for infection.

Most clearly, we need to move beyond the notion of a dichotomy that separates public health from human rights. When individuals and groups have reason to fear the effects of disease control measures, they will resist them—and forcing such measures on the populace is both morally questionable and impractical. In light of this, society’s interest in fighting infectious diseases should be seen as cause to protect the rights of infected individuals and implement strategies that encourage their cooperation in public health interventions.

Mark D. Wagner is Director of Communications of the International Association of Physicians in AIDS Care (IAPAC).

References

Ibrahim M. Shoaib

Vanity Fair readers have every month since 1993 enjoyed The Proust Questionnaire, a series of questions posed to celebrities and other famous subjects. In June 2002, IAPAC Monthly introduced “In the Life,” through which IAPAC members are asked to bare their souls.

This month, IAPAC Monthly is proud to feature Ibrahim M. Shoaib, who is Professor of Public Health at Tanta University, Tanta, Egypt.

If you could live anywhere, where would it be?
Vancouver, Canada, is the place [where] I [would] adore to live. An extremely beautiful city, which I visited in July-August 1996 while attending the XI International AIDS Conference. I simply fell in love with her streets, hills, buildings, suburbs, people, waterfronts, and the Pacific Ocean.

Who are your mentors or real life heroes?
Both my mother and my wife; because their unconditional love and [because their] heartfelt sacrifices have made possible the person who I am today.

With what historical figure do you most identify?
Abraham, the nobody, who became the father of all heavenly prophets, who in turn brought God’s word and wisdom to the whole [of] mankind.

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

If you could have chosen to live during any time period in human history, which would it be?
Ancient Egypt during the era of the Great Pyramid builders, the birthplace of not only the dawn of civilization but also the dawn of consciousness.

If you did not have the option of becoming a physician, what would you have likely become given the opportunity?
I would have loved to become a diplomat.

In your opinion, what are the greatest achievements and failures of humanity?
The Internet and eradication of smallpox are the greatest achievements of humanity, whereas the greatest failures are the persistence of poverty, inequity, and injustice.

What is your prediction as to the future of our planet one full decade from present day?
Within one decade I am hopeful to see vaccines being used against malaria and HIV; within 20 years from now I predict [we will] see the first human clone.

What proverb, colloquial expression, or quote best describes how you view the world and yourself in it?
“Be strong, be good, be pure! The Right only shall endure.”

What activities, avocations, or hobbies interest you?
I love travel and reading. Presently I am reading W. Durant’s “History of Civilization.” I also like swimming, fishing, and jogging.
In July 2003, the International Association of Physicians in AIDS Care (IAPAC) welcomed 38 new and renewing dues-paying members from five countries. IAPAC thanks the following physicians and allied health workers for their support of the association’s mission to improve the quality of care provided to men, women, and children who are living with HIV/AIDS.

Ekema Anjorin, Cameroon
Joan Atkinson, USA
Susan Ball, USA
Happy Benson, USA
Norman Bernstein, USA
Bruce Blacker, USA
Jack Boghossian, USA
Kurt Brotherson, USA
Margarita Cancio, USA
Lysette Cardona, USA
A.J. Cennerazzo, USA
Charles Craig, USA
Kathryn Crooks, USA
Sven Danner, The Netherlands
Elizabeth Elbert, USA
Donna Futterman, USA
P. Greiger-Zanlungo, USA
Catherine Hankins, Switzerland
Bruce Hirsch, USA
John Hostetler, USA
Elizabeth Huttlinger, USA
Vincent Jarvis, USA
Jeffrey Klausner, USA
Mark Krueger, USA
Rhoda Manu, Ghana
Lawrence McGlynn, USA
Amar Munsiff, USA
Jeff Palmer, USA
Robert Salata, USA
William Sanchez, USA
Leonia Tacs, USA
Dixon Valdruten, USA
Karen Van Der Veer, USA
Jonathan Weiss, USA
Olga Wildfeuer, USA
James Zachary, USA

Also, the following are new and renewing institutional members: Canadian AIDS Treatment Information Exchange (CATIE) and Greater Community AIDS Project.

To learn more about professional and institutional memberships, call (312) 795-4935 or send an e-mail to member@iapac.org. For more information regarding Corporate Partner opportunities, call (312) 795-4941 or send an e-mail to partner@iapac.org.

Health professionals who join the International Association of Physicians in AIDS Care (IAPAC) benefit from the research and expertise disseminated through the association’s journals, Web site, care tools, and annual symposia. Greater membership in IAPAC also means more support for the association’s training programs. These programs are making great strides in helping professionals learn best practice care techniques in the developing world, where the pandemic is taking its heaviest toll. Finally, as IAPAC continues to find strength in numbers, and represent more and more of the world’s health professionals, expanded membership means a more powerful voice in discussions that can lead to increased funding for medications, more effective inter-organizational cooperation, and simply better quality of life for those living with HIV disease.

These reasons should be more than enough to encourage you to recruit colleagues to join IAPAC. Nonetheless, we want to provide you with personal rewards for your recruitment efforts.

Through the end of 2003, every new recruit who lists you as the member who referred him/her to IAPAC brings you closer to winning free travel and/or a complimentary membership extension. For each member you recruit, your name will be entered in a drawing for one roundtrip airline ticket within your continent or region of the world. If you recruit five new members before the end of the year, you will receive 12 months of dues-free membership.

Battling complacency and advancing commitment in the international struggle against HIV/AIDS requires a strong, coordinated effort. Encourage your colleagues to join that effort as members of IAPAC.
Editor’s Note: The following quotes were compiled during the 2nd IAS Conference on HIV Pathogenesis and Treatment, held July 13-16, 2003, in Paris. Look to the September 2003 issue of the IAPAC Monthly for full clinical coverage.

**We have systematically underestimated the impact of AIDS on the economy. It doesn’t just kill workers; it kills young adults, and young adults make children and raise children—human capital. When you take that into the equation, you find a very different impact on the economy.**

French economist Jean-Paul Moatti in a July 13, 2003, opening ceremony speech during which he argued that economic considerations, taken together with the potential to further lower the price of antiretroviral drugs, mean that, from a purely economic standpoint, antiretroviral therapy should be implemented as quickly as possible throughout the developing world.

Prime Minister Tony Blair had urged other EU leaders to promise up to US$1 billion, but diplomatic sources said Germany, Denmark, and The Netherlands blocked increased EU funding. Last month, France committed to tripling its contribution to the Global Fund to 150 million Euros (US$167.7 million). The Global Fund faces an estimated shortfall of around US$400 million this year.

It may mean the [major] companies bringing their price low enough to be part of the program. It does not exclude generic drugs.

Anthony Fauci, Director of the US National Institute of Allergy and Infectious Diseases, quoted in a July 16, 2003, The Guardian article entitled, “US AIDS Fund Opens Door to ‘Pirated’ Drugs.” In what some labeled a departure from the close relationship the Bush Administration has enjoyed with brand-name pharmaceutical manufacturers, Fauci and US Secretary of Health and Human Services Tommy Thompson (on the eve of a July 16, 2003, meeting of the Global Fund to Fight AIDS, Tuberculosis, and Malaria’s leadership) articulated their boss’s position on generic drug purchases through the US Emergency Plan for AIDS Relief.

If the infrastructure is not there, we are going to create multi-drug-resistant mutants.

Robert Gallo, Head of the Institute of Human Virology, speaking during a July 14, 2003, special plenary session in which he called for strengthening medical infrastructure to accompany the scale up of access to antiretroviral therapy in the developing world. Gallo shared the stage with Luc Montagnier, Director of the World Foundation for AIDS Research and Prevention. The two researchers are credited with the discovery of the human immunodeficiency virus.

[Resistance] is a fact of life. It happens with antibiotics, it happens with TB. If you use drugs, you’ll eventually see resistant strains.

Joep MA Lange, Professor of Internal Medicine at the University of Amsterdam, quoted in a July 16, 2003, New York Times article featuring researchers’ reactions to an HIV drug resistance study, the results of which were presented at the 2nd IAS Conference on HIV Pathogenesis and Treatment. The CATCH study found that about 10 percent of all newly infected patients in Europe have drug-resistant HIV strains.

This is completely unacceptable. It, too, is a travesty of human rights. Yes, these countries are poor but we know they have the capacity to do more, much more.

Nelson Mandela, former South African President, in a July 14, 2003, plenary speech stating that while there is a moral imperative for wealthy nations to vastly increase funding for global treatment of HIV, many African nations must do more themselves to address their domestic AIDS epidemics within the context of broader human development agendas.