An Unequal Epidemic in an Unequal World

Kevin M. De Cock, MD, FRCP, DTM&H
Robert S. Janssen, MD

In JULY 2002, APPROXIMATELY 15 000 CLINICIANS, RESEARCHers, and other interested persons will gather once again, this time at the XIV International AIDS Conference in Barcelona, to discuss what is arguably the worst plague the world has ever known. These international conferences and their venues are milestones in the history of this tragic epidemic. In 1985, Atlanta hosted the first meeting; in 1996, the Vancouver meeting introduced combination therapy and viral load testing to the world; and in 2000, Durban drew international attention to Africa's plight. Barcelona offers further opportunity for dialogue, reflection on epidemiology and response, and strengthening global resolve.

The United States is the most heavily affected country in the industrialized world with almost 1 million persons living with HIV (human immunodeficiency virus).[1] Important successes have included the prevention of HIV/AIDS (acquired immunodeficiency syndrome) transmitted through blood and blood products; progress toward elimination of pediatric HIV disease as a result of prevention of mother-to-child transmission of HIV; and reductions in AIDS incidence and deaths since 1996 through use of highly active antiretroviral therapy (HAART); however, the trend in incidence and death has now stabilized.[2]

Despite some advances, HIV incidence in the United States has not declined significantly over the past decade, with approximately 40 000 new infections occurring annually.[1] Unfortunately, HIV infection continues to affect disproportionately communities of color, especially African Americans.[1,2] Moreover, with unchanged incidence and longer survival, a slow increase has occurred in the total number of persons living with HIV. Because HAART has delayed the development of AIDS, back calculation, a technique used to model HIV incidence from AIDS case surveillance data,[3] is no longer possible. Of note, in part because of the successes of HAART, there has been a recent resurgence of unsafe behavior among men who have sex with men (MSM), resulting in well-characterized outbreaks of sexually transmitted infections such as syphilis, and, perhaps, increased HIV transmission.[4,5]

Three public health priorities for the United States are: (1) to refashion the national HIV/AIDS surveillance system to focus on HIV[6] and obtain insight into HIV incidence; (2) to reinvigorate prevention efforts nationally; and (3) to promote prevention specifically among HIV-infected persons to prevent onward transmission.[7] Among MSM and other populations with high rates of HIV/AIDS, emphasis must be placed on voluntary counseling and testing, medical evaluation and care, prevention services for HIV-infected individuals, and adoption of the philosophy of personal responsibility not to transmit HIV.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that in late 2001 approximately 40 million persons worldwide were living with HIV/AIDS, that 5 million new HIV infections occurred in that year, and that 3 million HIV-infected persons died.[8] In Central and South America, MSM and injecting drug users account for the majority of infected persons in most countries.[8] In western Europe,[9] HIV/AIDS has become endemic, despite major differences between different countries. In some European countries heterosexual transmission now accounts for the majority of new HIV infections,[9] although a substantial proportion of newly reported infections are imported, especially from Africa.[9]

The most unpredictable epidemiological situations are in eastern Europe and Asia. Extensive HIV testing has been conducted in eastern Europe, but there have been few systematic prevalence studies.[9] The majority of HIV infections are associated with injecting drug use and occur in men; the male to female ratio of reported infections is more than 3 to 1.[9] The number of new infections in the last few years has increased steeply in Ukraine, the Russian Federation, Latvia, and Estonia, but spread is now occurring throughout most of the region.[9] Eastern Europe needs better surveillance data, interventions to reduce drug use and needle and syringe sharing, and prevention of secondary sexual spread of HIV.

Transmission of HIV in Asia remains largely restricted to injection drug users and commercial sex workers and their clients, with secondary sexual transmission from these core groups to their steady partners.[8] Generalized heterosexual spread as seen in Africa has not occurred, and vigorous

Author Affiliations: CDC-Kenya, Nairobi, Kenya (Dr De Cock), and Division of HIV/AIDS Prevention—Surveillance and Epidemiology, National Center for HIV, STD, & TB Prevention, Centers for Disease Control and Prevention, Atlanta, Ga (Dr Janssen).
Corresponding Author and Reprints: Kevin M. De Cock, MD, Unit 64112, APO AE 09831-4112 (e-mail: kdecock@nairobi.mimcom.net).

efforts in Thailand to achieve universal condom use in commercial sex settings had rapid impact on decreasing HIV transmission.[10] Although the situation in the 2 most populous countries, India and China, is unclear, the prevalence of HIV infection among pregnant women, still the most useful sentinel population, has remained well below 5% in most of the region.[11] India is estimated to have 4 million HIV-infected persons.[11] China's epidemic is predominantly associated with injection drug use, and HIV prevalence levels of 70% or more have been reported among drug injectors in some areas.[11] Evidence of extensive HIV infection in rural Henan Province in central China has emerged and is related to unsterile practices in the commercial blood trade.[11] Focusing prevention efforts on injection drug use and commercial sex, and ensuring a safe blood transfusion infrastructure, will help prevent the greatest number of new HIV infections in Asia. What happens in this most populous continent, especially in India and China, will profoundly influence the future history of the HIV/AIDS pandemic.

In Africa, where HIV/AIDS is generalized, the epidemic is uniquely severe. Of the world burden of HIV infection, the sub-Saharan Africa region represents 77% of AIDS deaths, 70% of HIV-infected persons, and 68% of new infections.[8] The region has more than 90% of the children with HIV infection and AIDS orphans in the world.[8] Antenatal HIV prevalence is greater than 10% in more than a dozen cities in sub-Saharan Africa, and in some it exceeds 20% and even 30%.[12] In many countries the probability that an adolescent will ultimately die of AIDS is greater than 50%.[13] The impact of HIV/AIDS on all sectors of society is unlike that associated with any other disease. Extreme differences in epidemic severity are seen across the continent, with the east and southern parts most heavily affected.[12,14]

Increased attention is now being paid to the pandemic by international political leaders, evidenced by the creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM).[15] Global health is now seen as an issue with political, economic, and security implications.[16] This increased attention and funding offer the best chance in decades to improve the health of the global poor, but formidable obstacles include the targeting of effort, adequacy of funding, technical limitations, difficulties of implementation, and the limited priority accorded to health in poor countries. Because conditions are most adverse in Africa, which lags behind the rest of the world in virtually all measures of economic and social development, Africa is the absolute test of effectiveness of interventions for HIV/AIDS and other diseases associated with poverty.

Although HIV/AIDS is the most pressing problem, there is under-recognition of the collapse of public health and clinical infrastructure in general in Africa over the past 25 years, independent of, as well as sometimes exacerbated by, HIV/AIDS. For example, chloroquine resistance has resulted in increases in malaria-related mortality in Africa during the 1990s, and resistance to sulfadoxime-pyrimethamine is also increasing.[17] Tuberculosis case rates are increasing by 10% to 15% annually in many countries largely because of HIV/AIDS.[18] Conflict has adversely affected health in numerous settings; an estimated 2.5 million excess deaths occurred in the eastern part of the Democratic Republic of the Congo over a recent 3-year period, largely from infectious diseases and malnutrition.[19] Environmental and social conditions have favored the emergence and reemergence of different infectious diseases, such as sleeping sickness in the Democratic Republic of the Congo.[20] Substantial increases in infant and under-5 mortality have occurred,[21,22] as well as in maternal mortality, a longstanding and neglected problem.[23-25] Thus, there is evidence to suggest that a number of aspects of health status in general show decline both independent of and exacerbated by AIDS.

The Commission on Macroeconomics and Health[26] estimated that to substantially improve global health, donor funding to all low-income countries would have to increase by $27 billion by 2007, from current levels of approximately $6 billion, and by $38 billion by 2015. The call for approximately $8 billion annually for the GFATM is included in these figures. In an analysis of requirements for an expanded response to HIV/AIDS alone, Schwartlander and colleagues[27] estimated that by 2005, $9.2 billion would be needed annually in middle- and low-income countries, with half of the resource needs represented by requirements for sub-Saharan Africa. Currently, less than $2 billion has been pledged to the GFATM.

Technical limitations concerning interventions for Africa's major health challenges also are overlooked in the enthusiasm of advocacy and fund-raising. There is no uniform HIV/AIDS prevention program to roll out internationally, the efficacy of sexually transmitted disease control as an HIV prevention strategy is not entirely clear,[18] mother-to-child transmission prevention is proving more difficult programmatically than in clinical trials (Anja van't Hoog et al, unpublished data, 2002), and there is no consensus about the appropriate balance between prevention and care, or how to expand access to HAART in Africa.[28] HIV/AIDS prevention initiatives may have underemphasized the importance of HIV testing and partner notification in Africa's high prevalence, generalized epidemic.[29] As an example of limitations in successfully tackling major diseases in Africa, DOTS (directly observed therapy—short course), the tuberculosis control strategy of the World Health Organization, is failing in areas of high HIV prevalence.[30] In addition, drug resistance challenges effective antimalarial treatment, a component of the World Health Organization Roll Back Malaria program.[31] Science-based solutions to these and myriad other problems are required for the high aspirations of the GFATM to be met.

A particular challenge in Africa is to convert increased funding into better services at the local level, through what the Commission on Macroeconomics and Health referred to as "close-to-client" systems.[26] The GFATM will be judged

on the degree to which enhanced prevention and clinical services affect the health of the poor. This will require linkages between industrialized and developing country governmental and other institutions and groups, and investment in rebuilding health infrastructure. In addition to enhanced preventive services, there is a need for simple, quality health care services for infectious diseases in children and adults, pregnancy and its complications, and surgical conditions, especially trauma.[32]

In conclusion, the XIV International AIDS Conference in Barcelona will be a contrast of extremes. Although the impact of AIDS is now less obvious in the industrialized world, HIV transmission continues in specific groups such as MSM, and a disproportionate burden of disease exists in underprivileged communities. The situation in the former Soviet Union epitomizes epidemic spread of HIV through injection drug use, a problem for which global control is elusive. Injection drug use and commercial sex fuel HIV transmission in Asia. Focused interventions for these focal epidemics can have great effect. The situation in Africa is different in scale and scope, with a devastating, generalized HIV/AIDS epidemic superimposed on an eroding health infrastructure burdened by other health threats. A fundamental question is to what extent public health strategies can reverse Africa's current adverse health trends without long-term economic development or an HIV vaccine. Despite the obstacles, the increased attention to and resources for global health, the moral challenge of this era, offer hope and opportunities not seen before in the history of the HIV/AIDS pandemic.

REFERENCES

1. Karon JM, Fleming PL, Steketee RW, De Cock KM. HIV in the United States at the turn of the century: an epidemic in transition. *Am J Public Health.* 2001;91:1060-1068.
2. *HIV/AIDS Surveillance Report.* Atlanta, Ga: Centers for Disease Control and Prevention; 2001;13(No. 1):1-41.
3. Rosenberg PS, Biggar RJ. Trends in HIV incidence among young adults in the United States. *JAMA.* 1998;279:1894-1899.
4. Stall RD, Hays RB, Waldo CR, et al. The Gay '90s: a review of research in the 1990s on sexual behavior and HIV risk among men who have sex with men. *AIDS.* 2000;14(suppl 3):S101-S114.
5. Katz MH, Schwarcz SK, Kellogg TA, et al. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health.* 2002;92:388-394.
6. Centers for Disease Control and Prevention. Guidelines for human immunodeficiency virus case surveillance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep.* 1999;48(No. RR-13)1-27.
7. Janssen RS, Holtgrave Dr, Valdiserri RO, et al. The serostatus approach to fighting the HIV epidemic: prevention strategies for HIV-infected individuals. *Am J Public Health.* 2001;91:1019-1024.
8. UNAIDS/WHO. *AIDS Epidemic Update, December 2001.* Geneva, Switzerland: UNAIDS/WHO; 2001.
9. EuroHIV. *HIV/AIDS Surveillance in Europe.* Saint-Maurice, France: European Centre for the Epidemiological Monitoring of AIDS; 2001;65:1-61.
10. Kilmarx PH, Supawitkul S, Wankrairoj M, et al. Explosive spread and effective control of human immunodeficiency virus in northernmost Thailand: the epidemic in Chiang Rai province, 1988-1999. *AIDS.* 2000;14:2731-2740.
11. UNAIDS. Epidemiological Fact Sheets by Country. Available at: http://www.UNAIDS.org. Accessibility verified June 12, 2002.
12. *Recent HIV Seroprevalence Levels by Country: June 2001.* Washington, DC: US Bureau of The Census; 2001.
13. Zaba B. Lifetime risk of AIDS death for 15-year old boys, assuming unchanged or halved risk of becoming infected with HIV, selected countries. In: UNAIDS. *Report on the Global HIV/AIDS Epidemic, June 2000.* Geneva, Switzerland; UNAIDS/WHO; 2000:26.
14. Buve A, Carael M, Hayes RJ, et al. The multicentre study on factors determining the differential spread of HIV in four African cities: summary and conclusions. *AIDS.* 2001;15(suppl 4):S127-S131.
15. The Global Fund to Fight AIDS, Tuberculosis and Malaria. Available at: http://www.globalfundatm.org. Accessibility verified June 12, 2002.
16. Central Intelligence Agency. The Global Infectious Disease Threat and Its Implications for the United States. Available at: http://www.cia.gov. Accessibility verified June 12, 2002.
17. Ronn A, Msangeni HA, Mhina J, et al. High level of resistance of *Plasmodium falciparum* to sulfadoxine-pyrimethamine in children in Tanzania. *Trans R Soc Trop Med Hyg.* 1996;90:179-181.
18. Corbett EL, Steketee RW, ter Kuile F, et al. HIV/AIDS and the control of other infectious diseases in Africa. *Lancet.* 2002;359:2177-2187.
19. *Mortality in Eastern Democratic Republic of Congo: Results From Eleven Mortality Surveys.* New York, NY: International Rescue Committee; 2001.
20. Van Nieuwenhove S, Betu-Ku-Mesu VK, Diabakana PM, et al. Sleeping sickness resurgence in the DRC: the past decade. *Trop Med Int Health.* 2001;6:335-341.
21. *Kenya Demographic and Health Survey 1998.* Calverton, Md: National Council for Population and Development, Central Bureau of Statistics (Office of the Vice President and Ministry of Planning and National Development) [Kenya], and Macro International Inc; 1999.
22. McElroy PD, ter Kuile FO, Hightower AW, et al. All-cause mortality among young children in western Kenya, VI: the Asembo Bay Cohort Project. *Am J Trop Med Hyg.* 2001;64(1-2 suppl)S18-S27.
23. Hill K, AbouZhar C, Wardlaw T. Estimates for maternal mortality for 1995. *Bull WHO.* 2001;79:182-193.
24. Bicego G, Boerma JT, Ronsmans C. The effect of AIDS on maternal mortality in Malawi and Zimbabwe. *AIDS.* 2002;16:1078-1081.
25. Ahmed Y, Mwaba P, Chintu C, et al. A study of maternal mortality at the University Teaching Hospital, Lusaka, Zambia: the emergence of tuberculosis as a major non-obstetric cause of maternal death. *Int J Tuberc Lung Dis.* 1999;3:675-680.
26. Commission on Macroeconomics and Health. *Macroeconomics and Health: Investing in Health for Economic Development.* Geneva, Switzerland: World Health Organization; 2001.
27. Schwartlander B, Stover J, Walker N, et al. Resource needs for HIV/AIDS. *Science.* 2001;292:2434-2436.
28. Weidle PJ, Mastro TD, Grant AD, et al. HIV/AIDS treatments and HIV vaccines for Africa. *Lancet.* 2002;359:2261-2267.
29. De Cock KM, Mbori-Ngacha D, Marum E. Shadow on the continent: public health and HIV/AIDS in Africa in the 21st century. *Lancet.* 2002;360:67-72.
30. DeCock KM. Chaisson RE. Will DOTS do it? a reappraisal of tuberculosis control in countries with high rates of HIV infection. *Int J Tuberc Lung Dis.* 1999;3:457-465.
31. White NJ, Nosten F, Looareesuwan S, et al. Averting a malaria disaster. *Lancet.* 1999;353:1965-1967.
32. World Bank. *World Development Report 1993: Investing in Health.* Oxford, England: Oxford University Press; 1993.