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INTRODUCTION

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The HIV/AIDS epidemic has already devastated Nigeria, with nearly a million people dead and more than two million children orphaned. By 2003, the virus had infected approximately 5.0% of the adult population (1); within two years, an estimated four to six million Nigerians were carrying the virus.

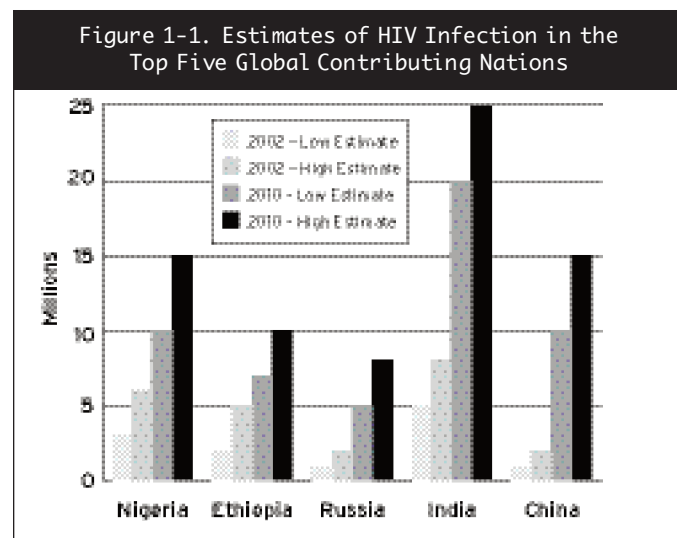
In 2002, the National Intelligence Council identified the five countries expected to bear the heaviest burden of HIV infection in the expanding worldwide epidemic: India, China, Nigeria, Ethiopia, and Russia (2) (Figure 1-1). The council predicted that Nigeria and Ethiopia would be especially hard hit, with the number of people living with HIV/AIDS in Nigeria projected to balloon to ten to fifteen million by 2010, or as much as 26 percent of the adult population. Without effective prevention on a large scale, Nigeria will experience not only the tragedy of countless lives forever altered by the virus, but also untold adverse social and economic effects.

THE NATIONAL RESPONSE

Nigeria, like many countries around the world, initially responded to the epidemic with denial and little action (3,4). In 1987, the Nigerian government formed the National Expert Advisory

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Source: Eberstadt N. The future of AIDS. *Foreign Aff.* 2002;81(6).

established a Presidential Committee on AIDS and a National Action Committee on AIDS (NACA). The government established the three-year HIV/AIDS Emergency Action Plan (HEAP) in 2001. That same year President Obasanjo created the Nigerian National ART Program with the purchase of anti-retrovirals (ARVs) for 10,000 adults and 5,000 children. He also hosted African heads of state for the first Organization of African Unity Summit on HIV/AIDS, Tuberculosis and Other Related Infectious Diseases, and he has continued to be a strong advocate and spokesperson for HIV prevention programs throughout Africa.

More recently, the government devised the National HIV/AIDS Strategic Framework, which is intended to guide the nation's response from 2005 to 2009. The partners implementing these plans include governmental institutions, nongovernmental organizations, community-based organizations, faith-based organizations, and people living with or affected by HIV/AIDS. NASCP, in the meantime, continues to take responsibility for the Nigerian health system's response to HIV/AIDS. It develops guidelines on key interventions and supports monitoring and surveillance of the epidemic.

Although data suggest that Nigeria's nationwide prevalence has not dramatically increased since 1999, the sheer magnitude of the population and the high prevalence rate together indicate a generalized epidemic. Since HEAP was written, all sectors—including advocacy, prevention, care, and treatment—have seen activity, yet the need remains great to scale these activities up significantly. For example, more than one million Nigerians would be considered eligible to receive antiretroviral therapy (ART), yet the fewer than 50,000 eligible patients treated by the end of 2005 represent only a fraction of those who need ART.

Committee on AIDS. A year later, the National AIDS and STDs Control Program (NASCP), coordinated by the Federal Ministry of Health, replaced this advisory board. Yet the response remained tepid.

Nigeria's political leadership has since taken a more proactive approach to HIV/AIDS control (5), with an increase in local activities and external donor support. President Olusegun Obasanjo, elected in 1999, has been actively involved in HIV/AIDS prevention and control. In January 2000, the federal government, recognizing the need for a multisectoral approach,

SPECIAL CHALLENGES FOR NIGERIA IN TACKLING THE EPIDEMIC

Nigeria faces a number of important challenges in its efforts to control the HIV/AIDS epidemic, including widespread poverty, a large and youthful population, extensive variation in epidemic trends, and viral heterogeneity.

An Impoverished Population

With its annual income per capita below the average for other low-income countries, Nigeria is considered a "poor" nation (Table 1-1). The country's health status indicators also are worse than average; Nigeria spends less than average on health and has received less external aid than other low-income countries. The United Nations Development Programme has ranked Nigeria 152 out of 175 on the Human Development Index, a composite measure of income coupled with access to education and health services (6). By some estimates, two-thirds of Nigerians live on less than US\$1 per day. Youth unemployment is a major problem, with estimates ranging between 40% and 60% (7).

Poverty—combined with economic vulnerability, institutional weaknesses, and sociocultural complexity—exacerbates the difficulties inherent in tackling the Nigerian epidemic. At the same time, an increased commitment by the government, local professionals, and civil society organizations and a growing international attention provide a basis for cautious optimism that the epidemic can be contained. The deciding factor may be the extent to which the country deploys local and international expertise to meet the challenge within the local context. The fact that the national HIV prevalence rate has been hovering in the 5% range suggests that such cautious optimism may be warranted. Increased efforts to demonstrate the efficacy of current programs will further support the view that the HIV prevalence has reached a plateau as a result of the national response.

A Youthful and Populous Nation

Nigeria's population has grown rapidly in recent decades. In 1991 the total population was 88.9 million, and projections by the National Population Commission of Nigeria estimated that by 2003 the population would rise to 133 million (8). The annual rate of growth of the Nigerian population is estimated at 2.8%. Nigeria has been undergoing a demographic transition from a high-fertility and high-mortality population to a low-fertility and declining-mortality population. The effect of this transition has brought about a population structure with a wide base of people younger than 15 years. While the median age of the population is 17 years, the 15-to-24-year age group constitutes about 20% of the population. Life expectancy rose from 45 years in 1963 to 51 years in 1991. More recently, however, the life expectancy has been falling, at least in part because of the HIV/AIDS epidemic. In 2002, life expectancy in Nigeria was estimated at 45 years. The infant mortality rate is 88.4 per thousand and the under-five mortality rate is 201 per 1,000.

Table 1-1. Selected Indicators of Development, Health Expenditures, and Outcomes		
Indicators	Nigeria	Low-Income Countries (average)
Population (millions, in 2002)	133	
Gross national income per capita in 2002 (US\$)	300	430
Under-five mortality rate per 1,000 live births in 2002	201	121
Incidence of tuberculosis per 100,000 people in 2002	304	226
Average life expectancy at birth (years, in 2002)		
• Male	45	58
• Female	46	60
Dependency ratio (young dependents as percent of working age population) in 2002	80	60
Health expenditure (in 2001, US\$)		
• Total as % of gross domestic product	3.4	4.4
• Public as % of gross domestic product	0.8	1.1
• Health expenditure per capita	15	23
Aid dependency (as of 2002)		
• Aid as % of gross national income	0.8	2.7
• Per capita (US\$)	2	12

Source: World Development Indicators. Washington, DC: World Bank, 2004.
 Note: Low-income countries are those with a gross national income per capita of \$735 or less in 2002.

Wide Variations in Epidemic Trends

In just a few decades the HIV epidemic has reached global proportions, with approximately 40 million people infected worldwide. Since Nigeria’s first AIDS case was reported in 1986, as many as six million Nigerians may have become infected with HIV. To estimate HIV prevalence rates in the country, beginning in 1991, the Federal Ministry of Health began conducting a countrywide survey of HIV infection in pregnant women, a representative population. These surveys show that the adult HIV prevalence increased from 1.8% in 1991 to 4.5% in 1996 and to 5.8% in 2001.

In 2001, the survey was expanded nationwide and readily demonstrated the incredible capacity of the country in its implementation. Conducted over a three-month period, the survey included approximately 300 pregnant women from each of 85 sites, which represented all 36 states and the Federal Capital Territory (FCT). More than 24,200 samples were collected and tested for HIV. A nationwide median prevalence rate of 5.8% was reported, ranging from 0.8% to 16.4% by state (9). In 2003, the nationwide survey was repeated, with a countrywide prevalence of 5.0% (10). All states and the FCT reported HIV infection, which in all cases exceeded 1%. Thus, Nigeria is experiencing a “generalized” epidemic, in which transmission within low-risk populations not only is occurring, but also is independently fueled by transmission from higher risk and “bridge” groups. In a country with such a sizable population, this represents a significant fraction of the worldwide pandemic.

A review of the prevalence figures from each of the states and the FCT demonstrates tremendous diversity in the rates of HIV infection, ranging from 1% to 16.4%. Although subject to continued discussion and speculation, it seems clear that multiple determinants must be considered to explain this tremendous heterogeneity in infection rates. HIV is thought to have entered the Nigerian population in the mid-1980s, just as it did with Nigeria’s West African neighbors; however, the origin of the infection and the factors responsible for its early spread in the country remain unknown. Geopolitical zones and differences in ethnic, religious, and sexual networking are but a few of the many possible factors that contributed to the differences in HIV infection that we now appreciate decades later. As HIV continues to spread, it has become increasingly apparent that the epidemic does not follow the same course in different locales or among various subpopulation groups. This variation has complicated the task of monitoring the epidemic’s course, planning intervention measures, and projecting needs for the care and support of infected people. Therefore, a thorough understanding of the nature of the epidemic, especially the factors enhancing the spread of the virus among different subpopulations, is still needed.

Until 2002, the federal government had monitored the epidemic primarily using cross-sectional serosurveys of HIV infection. While this method has its merits, its inability to provide specific behavioral information on at-risk subpopulations or to explain changes in levels of infection in mature epidemics creates serious limitations. According to UNAIDS, such an understanding can only be achieved with more information on the most-at-risk subpopulations and on the behaviors that place them at risk (1). The second generation of HIV surveillance provides warning signals for the spread of HIV along with some important biological markers of spread. It also allows the identification of relevant high-risk and bridge populations. These data then provide the basis for development of targeted interventions. Because Nigeria demonstrates such cultural and ethnic diversity, obtaining up-to-date surveillance data with the best available methods is a critical first step in developing targeted interventions. To accomplish this step, it is crucial to have continued high-quality surveillance and monitoring systems as well as expanded scientific research.

Viral Heterogeneity

HIV, the first human lentivirus from the retrovirus family, was first described in the early 1980s coincident with the description of AIDS in the developed world. HIV integrates its genetic material into the infected host’s DNA; therefore, infection is lifelong, even with currently available treatment. Although mortality is high without treatment, the incubation time from infection to AIDS can range from eight to ten years in the developed world.

Perhaps the most striking feature of HIV is its tremendous genetic diversity. Viral dynamics studies have indicated that 10^{12} virus particles are generated each day, with mutation occurring at every round of replication, suggesting that the high replication rate also contributes to viral genetic diversity (11).

This high degree of diversity has a number of important implications. First, there are two HIV types—HIV-1 and HIV-2—with a number of related viruses in non-human primates. Both HIV-1 and HIV-2 have been described in Nigeria and other parts of West Africa. Second, HIV-1 has multiple subtypes

(A–D, F–H, J, and K) and a number of circulating recombinant forms (CRFs), which are associated with significant transmission and disease in various populations worldwide (12). Molecular surveillance studies have made use of polymerase chain reaction (PCR) and molecular sequencing techniques to characterize the viral subtypes and describe their prevalence and geographic distribution worldwide. Subtype B, for example, accounts for an estimated 12.3% of cases worldwide, but infections with this subtype are primarily seen in the Americas, Western Europe, and Australia. Conversely, subtype C is estimated to have caused more than 47% of the worldwide infections, with highest incidence in southern African countries, Ethiopia, and India.

Areas of the world with a significant circulation of multiple viral subtypes also appear to have a unique and heterogeneous distribution of CRFs. CRF_02 A/G, originally described by David Olaleye from the University of Ibadan, has been considered the prototype West African HIV-1 subtype; the “IbNG” strain name designates Ibadan, Nigeria, as the source. CRF_02 A/G is responsible for a significant proportion of the new infections in Nigeria, as it is in other West African countries (12).

The status of HIV genetic diversity appears to be ever changing, with the possibility of additional new recombinant forms ever present. The potential for this event is highest in Africa, where multiple subtypes are actively circulating. The underlying causes of the varied geographic distributions are unknown and could conceivably represent founder effects, whereby viruses present in a given locale would predominate over time. This heterogeneity may also represent a complex interaction between viral parameters, however, such as infectivity, transmissibility, and immunogenicity, as well as host characteristics, such as genetic background and immune system competence.

Research continues into the mechanisms and impact of viral diversity, which represents a major obstacle to vaccine development. Current vaccine development approaches are often subtype specific, with most developed for the prototype subtype B, which is found predominantly in the United States and Europe. In recent years, some vaccine candidates have been developed for trials with non-B subtypes. A vaccine candidate for West African CRF_02 A/G has yet to reach human trials.

Triple-drug regimens have been shown to significantly prolong life in the developed world, yet HIV/AIDS treatment is complex and expensive. When Nigeria embarked on its national ART program in 2001, initial data indicated early efficacy in the first 50 patients treated with generic ARVs (13). It is well recognized, however, that the ultimate success and longevity of ART depend heavily on patient adherence. In addition, toxicity to different drugs in the multiple-drug regimens will be responsible for a significant proportion of patients who fail to benefit from ART over time. The Nigerian experience with these drugs is limited and based on clinical trials data conducted in the United States and Europe. The circulating HIV subtypes in Nigeria are distinct from subtype B; thus, it remains to be seen whether this distinction will alter the efficacy of these drugs or the rate at which drug resistance develops. Early data suggest a 10% to 17% baseline resistance to major classes of ARVs in viruses from Nigerians not undergoing ART (14,15). Therefore, the genetic diversity of Nigerian HIV-1 subtypes would seem to suggest that drug-resistance mutations might lower the overall efficacy of ART in Nigeria.

HIV/AIDS has created new challenges for physicians, other health care providers, and laboratory investigators. New methods to detect antibodies to HIV were needed for diagnosis, and although the simple rapid test and the enzyme-linked immunosorbent assay formats have been improved, they remain expensive for Nigerian patients. Furthermore, voluntary counseling and testing (VCT) programs are still based in urban centers, where they remain inaccessible to many Nigerians. Clinical management of HIV infection requires the regular measurement of CD4+ lymphocytes in the blood; these laser-based flow techniques are expensive and require a significant infrastructure to perform. In addition, the measurement of quantities of virus in the blood—known as viral load—is an important clinical parameter to evaluate the severity of disease and to monitor the efficacy of therapy. These expensive laboratory tests require complex technologies not previously used in much of the developing world. Scientists are devising new methodologies that they hope will be as sensitive as existing methodologies yet more cost effective. To accommodate these new and critical diagnostic clinical tools, Nigerian institutions will need ongoing training, capacity building, and infrastructure development. These requisites will grow even more acute as the country scales up its ART program.

THE POWER OF TARGETED INTERVENTIONS

Despite the rising toll of the global HIV/AIDS epidemic, compelling evidence—based on work in Senegal, Uganda, and Thailand—has emerged that early interventions can make a significant difference in reducing HIV infection rates and preventing explosive increases in AIDS (1). The most effective interventions have been multisectoral, with a high-level government commitment to tackle the problem, policy changes resulting from an awareness of the impact of HIV/AIDS on society, and the development of communications and media efforts, health interventions targeting high-risk populations, laboratory and field research, and scientific training.

HIV prevention initiatives include an array of education, behavioral change, and condom promotion programs. Through second-generation surveillance, the epidemiologic and behavioral characterization of high-risk and bridge populations provides the necessary data to design such interventions for maximum efficacy. The promotion of VCT centers provides a venue for community education and risk reduction messages, as well as the identification of HIV-infected individuals for intervention and treatment.

Programs that prevent sexually transmitted infections (STIs) through education, early diagnosis, and treatment are considered critical components to HIV prevention and intervention, as STIs are significant cofactors for HIV transmission. Population groups at high risk for HIV are similarly at high risk for STIs; therefore, HIV and STI prevention are often integrated. The monitoring of the efficacy of HIV prevention programs may include lowering of HIV incidence rates, while STI rates may serve as important proxy indicators of the success of HIV prevention programs.

In much of the developing world, HIV infection in pregnant women contributes to the spread of the epidemic through mother-to-child transmission. In 2004, more than 640,000 children under the age of 15 were infected with HIV, the vast majority in Africa. In that year alone, more than 75,000 infants were born with

HIV in Nigeria (16). Prevention-of-mother-to-child-transmission (PMTCT) programs that provide ARVs such as zidovudine and nevirapine to infected pregnant women and their exposed babies can significantly reduce HIV transmission rates. The use of triple-drug regimens to HIV-infected pregnant women can further reduce transmission to negligible rates; however, this has yet to be implemented in most of Africa.

PMTCT trials have demonstrated disturbing levels of nevirapine resistance (12% to 40%) in the HIV virus sequences from mothers receiving a single dose of nevirapine as part of typical developing country PMTCT programs (17). The nevirapine resistance in these mothers may diminish the efficacy of ARV regimens that include nevirapine, which becomes problematic because nevirapine is often used in the first-line drug regimens in most developing country ART programs.

Sentinel surveillance in Nigeria conducted on pregnant women throughout the country can help predict the magnitude of the impact of mother-to-child transmission on the epidemic. Nigeria has one of the world's highest numbers of children orphaned by AIDS, and already an estimated 290,000 Nigerian children are infected with HIV (1). PMTCT programs have been an important part of the Nigerian national response to the epidemic since 2001. Federal PMTCT centers were first established in seven target states providing HIV testing to pregnant women and single-dose nevirapine to thousands of HIV-infected women and their babies. Expansion and refinement of the Nigerian PMTCT program is under way, with different and more effective ARV combinations administered to both mothers and infants. Nonetheless, there is a critical need to provide broader coverage of these programs across the country. This will no doubt constitute a major challenge to the Nigerian PMTCT program in the short term. The infrastructure and capacity building needed for such a scale-up is substantial, as the PMTCT program is both expensive and medically complex.

Effective treatment is available to HIV-infected populations in most of the developed world. However, the costs and complexities of these treatment programs have prevented these lifesaving therapies from reaching the developing world. In recent years, international donor organizations have committed tremendous funds to provide treatment and care programs to African nations. In addition, many African governments, including that of Nigeria, have committed substantial resources to initiate and scale up national treatment and care programs. ART programs require enormous resources, training, capacity building, and infrastructure development. Training of physicians in HIV care and treatment is required, accompanied by significant bolstering of health care systems that are already constrained in most African nations. Thus, ensuring the sustainability of such programs needs to be considered in their design.

In 2004, more than 16,000 people living with HIV/AIDS were treated under the national ART program. The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) program has since augmented the national program, providing treatment to 25,000 people and care to tens of thousands more by the end of 2005. Yet these treated individuals still represent only a fraction of the millions of Nigerians living with HIV/AIDS who will eventually require treatment. It is hoped that the increased access to treatment and care will augment prevention efforts, by decreasing societal stigma and lowering the transmission potential of treated patients.

CONCLUSION

Nigeria faces many challenges in dealing with its HIV/AIDS epidemic. Public education must play a key role in the success of prevention programs and increase the uptake of HIV testing. Behavioral change programs must encourage individuals to reduce their risk of HIV acquisition. The stigmatization and discrimination that have typified societal responses must be dealt with promptly, as they compromise the effectiveness of prevention programs. The early involvement and support of the government in the HIV/AIDS campaign set the necessary groundwork for a continuing strong leadership that will be critical for initiating and sustaining an effective nationwide prevention program. As Nigeria and much of Africa await more effective and affordable ARV interventions, additional scientific research will be necessary to monitor the epidemic, to consider unique aspects of the viruses required for therapeutic intervention, and to develop an appropriate HIV vaccine. Nigeria's remarkable progress in the past several years demonstrates the country's capacity and resolve to combat the epidemic. We remain optimistic that the country will rise to the occasion and meet its many challenges.

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