Special Contribution

HIV in India

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Although it is estimated that there are fewer than 4 million cases of HIV infection in India, the general consensus is that there are growing localized epidemics. The challenge to the country's infrastructure to respond to this epidemic and the issues of stigma and discrimination faced by HIV-infected persons appear daunting. After initial denial, the government set up the National AIDS Control Organization, which initiated a large-scale surveillance program for prevalence of HIV infection throughout all the states of India. The National AIDS Control Organization also brought significant improvements to blood supply safety in the country. The nongovernmental sector is active in prevention and care; people living with HIV are beginning to organize themselves for advocacy and activism; epidemiologic, interventional, and clinical research have moved forward; yet more could be done. Diagnosis of HIV infection remains a challenge. There are unresolved ethical, technical, and programmatic issues around voluntary counseling and testing. Availability of highly active antiretroviral therapy is not an issue since antiretroviral drugs are manufactured in the country and exported elsewhere, but their affordability and the feasibility of monitoring patients taking the drugs are in question. Almost none of those living with HIV infection receive these medications from the government, except when nevirapine is provided to prevent mother-to-child transmission, or from the nearly nonexistent health insurance sector.

This commentary offers a perspective on the current status of the HIV epidemic in India, focusing on epidemiology, the government response, and diagnosis and treatment.

Introduction

We often hear 2 different descriptions of the HIV epidemic in India. The official version is that the total number of HIV infections in the country is still fewer than 4 million[1] and that the efforts by the government and other public agencies to prevent a rapid escalation of HIV infection are effective. However, a second version asserts that the official account does not present the true picture of the magnitude of the epidemic and the efforts to address it.

No matter which school of thought one believes, those who know India as a country that is populous, large, culturally complex, and economically diverse will agree that HIV adds to its woes. In 1978, India joined other nations in signing the World Health Organization's Alma Alta Declaration, which set the goal of "Health for All by the Year 2000."[2] Although India has not realized this goal, the failure leaves valuable lessons for the health sector to learn about HIV infection.

HIV has yet to cause dramatic, visible turns in the Indian economy or the health sector. Such good fortune may not continue. The first documented HIV infection was among sex workers in Chennai, Tamil Nadu, in 1986,[3] and the 15-odd years since this initial report may have been the best opportunity for response. This first case report and subsequent reports, including those from northeastern India describing HIV infection among injection drug users (IDUs), were received with skepticism and denial by academicians, politicians, and sociologists, thus diluting the promise for an effective response. Some speculate that India is now on the verge of a catastrophe.

Tracking the Spread of HIV Infection: The HIV Sentinel Surveillance System

The National AIDS Control Organization (NACO) is a government institution that was established in 1992 for planning and implementing HIV prevention, control, and management. A NACO brochure titled *India Responds to AIDS* states, "AIDS presents the most serious public health problem in India today."[4] Reports from NACO's sentinel surveillance system present a grim picture. The sentinel surveillance system uses anonymous unlinked sample screening for HIV antibodies to estimate prevalence of HIV in various states and population groups. Surveys are conducted annually, and survey sites include sexually transmitted disease (STD) clinics, antenatal clinics, sites that target IDUs, and those that target men who have sex with men.[1] Table 1 provides surveillance data from 1995 to 1999; in the samples screened, which comprised both individuals at low and high risk for HIV infection, approximately 25.84 per 1000 were infected with HIV as of 1999. A large majority of these infections were attributed to heterosexual transmission, although bisexual and homosexual transmissions were likely underestimated. Possible sources of infection for AIDS cases reported from 1986 to 2001 are listed in Figure 1.

HIV testing is offered by government institutions and by private hospital-based or independent clinical laboratories. There is no national information grid that collects HIV testing information from clinical laboratories in the private sector, so prevalence estimates are based solely on the sentinel surveillance mechanism. Further, all over the country, individuals dying from opportunistic infections associated with HIV are not being test-

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Table **1.** Surveillance for HIV Infection in India

For Period Ending	2/1995	3/1995	3/1996	9/1996	3/1997	9/1997	12/1999
No. Persons Screened	1,273,829	2,679,033	2,798,521	2,787,136	2,941,825	3,170,084	3,572,144
No. Persons HIV-seropositive	6683	19,754	22,389	46,503	52,802	67,067	92,312
Seropositive Persons Per 1000	5.25	7.37	8.00	16.10	17.80	21.15	25.84

Adapted from National AIDS Control Organization, 2000-2001.

ed for HIV infection. Families of those who die from known HIV infection often request that the cause of death be attributed to a cause other than HIV, and physicians oblige. The suboptimal HIV reporting system may thus preclude planners from shaping effective responses.[5]

Based on sentinel surveillance data, HIV prevalence in the adult population can be broadly classified into the 3 following groups of states and union territories in the country (Figure 2). States and union territories not listed below include those for which data are insufficient to estimate prevalence of HIV infection in antenatal women.

- High HIV Prevalence States: Includes Maharashtra, Tamil Nadu, Karnataka, Andhra Pradesh, Manipur, and Nagaland, where prevalence of HIV infection is 1% or higher in antenatal women.
- Moderate HIV Prevalence States: Includes Gujarat, Goa, and Pondicherry, where prevalence of HIV infection is 5% or higher among high-risk groups, but lower than 1% in antenatal women.
- Low HIV Prevalence States: Includes remaining states, where prevalence of HIV infection is lower than 5% in any of the high-risk groups and lower than 1% among antenatal women.

The virus is spreading rapidly along India's coasts and inward to all parts of the country, both rural and urban.[6] The epidemic varies widely among regions, a reflection of the country's great diversity. A survey of randomly selected households in Tamil Nadu found that 2.1% of the adult population living in the countryside had HIV infection compared with 0.7% of the urban population.[7] In the northeastern state of Manipur, HIV has already reached epidemic proportions among IDUs.[8]

Early descriptions of HIV epidemiology created a general perception that HIV infection was largely restricted to sex workers, truckers, and IDUs.[6] The rest of the population was, and in many cases, still is, in denial; meanwhile, the infection has spread further into the general population. For example, HIV infection rates are reported to be increasing among monogamous women, through unprotected sex with infected spouses.[9,10]

Poverty creates conditions ripe for HIV transmission. Economic growth has caused rapid urbanization in India, with large urban slum populations composed of migrants, manual laborers, and child laborers.[11] Currently, 260 million persons in India (26% of the population) live below the poverty line.[12] Those with low incomes cannot afford to buy condoms or treatment for STDs. Poor families send their young women into prostitution to make ends meet. Too illiterate to understand prevention messages and with little access to information, the poor succumb to STDs. Untreated STDs increase the risk of HIV transmission, as these infections cause mucosal ulceration with an easy entry for HIV. India has a very high rate of STDs; the current estimates are about 6% to 9% of the population, with more than 40 million new infections per year.[6,13]

Government Responses

The National AIDS Committee, which supervises the work of NACO, was set up under the Union Ministry of Health and Family Welfare in 1986. The committee's objective: ". . . to lead and catalyze an expanded response to the HIV/AIDS epidemic in order to contain the spread of the infection, reduce people's vulnerability to HIV, promote community- and family-based care to people with HIV/AIDS within an enabling environment without any stigmatization and discrimination, and alleviate the epidemic's devastating social and economic impact." NACO is headed by a project director and consists of an additional technical project director, subject specialists, and other technical and administrative staff.

Each state now has a State AIDS Control Society (a body with programmatic and financial autonomy), with a program

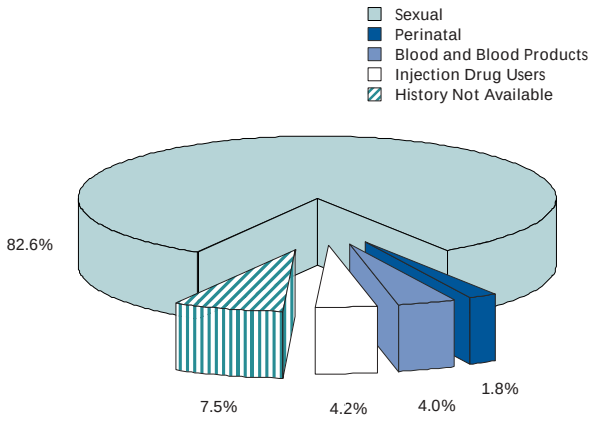

Figure **1.** Probable sources of infection for AIDS cases reported in India from 1986 to 2001. Adapted from National AIDS Control Organization, "Combating HIV/AIDS in India 2000-2001."

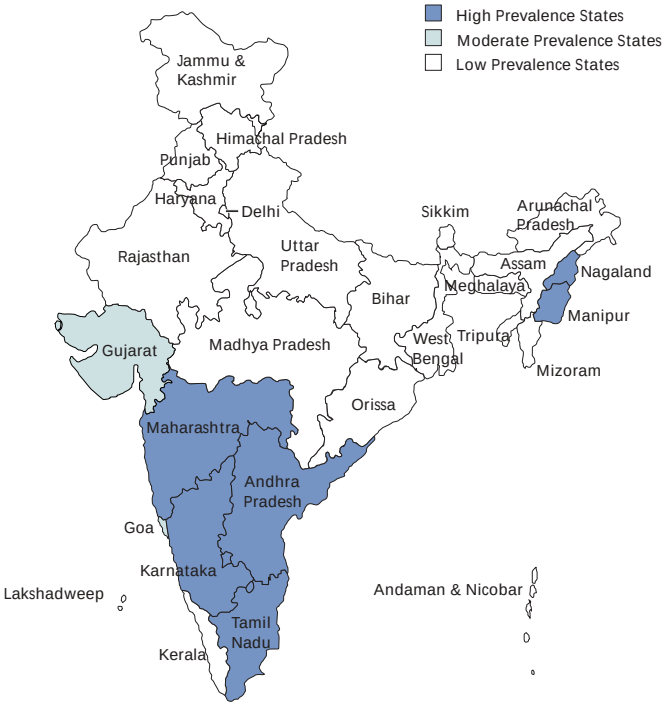

Figure **2.** HIV prevalence in adults in India, 2000. Adapted from National AIDS Control Organization, "Combating HIV/AIDS in India 2000-2001."

officer supported by technical staff. Tamil Nadu was the first state to set up such a cell, the Tamil Nadu State AIDS Control Society (TNSACS), followed by Pondicherry. Their successes led the government of India to ask the other states and union territories to adopt this model.

The strengths of the TNSACS model are program management with flexibility and autonomy; participation of nongovernmental organizations (NGOs) and people living with HIV in the decision-making process; a strategic information, education, and communication campaign; a transparent process of funding NGOs; and the provision of funds for patient-care activities and support groups such as the Indian Network of People Living with HIV (INP Plus).

The efforts of NACO, augmented by the state AIDS societies, include surveillance, information, education, and communication campaigns for HIV prevention, safe blood supply, strengthening STD treatment services, expanding availability of condoms, preventing mother-to-child transmission of HIV, and providing community-based care for those living with HIV. NACO promotes its objectives by working with representatives of people living with HIV and bringing together government, NGOs, and private institutions to tackle HIV infection at various levels.

Of note, in 1989 the government of India declared a ban on the acceptance of blood from professional blood donors—individuals who accept a monetary compensation in return for donating blood. However, this ordinance has not been entirely effective. Although blood banks refuse to transact commercially with these donors, the friends and relatives of those who require blood transfusions regularly bring these donors to blood banks, declaring them voluntary donors or close relatives, and complete the payment to donors elsewhere.

Social Precursors of HIV Infection

In ancient times, Indian culture offered the world the renowned treatise on sexuality *The Kamasutra*. Sexual imagery found a pride of place in temple sculptures. Elaborate rituals covered marriage, nuptial nights, pregnancy, and childbirth, recognizing sex and reproduction as part of the social processes that surrounded them. Such openness about sex and sexuality is now near absent. Talking about sex is taboo, and efforts by policy makers to introduce sex education in schools are half-hearted.[14]

There are many social precursors for the rapid spread of HIV in the country, including inability to talk openly and learn about sex and sexuality, pressures from family to give birth to an heir and an implicit threat to the marriage when a woman is unable to become a mother, the high prevalence and acceptability of domestic violence against women, the moral double standard imposed on men and women, and the lower status of women in general. The pressure to be a mother is so intense that when a woman has to choose between being HIV-seronegative but without children and possible conception with possible HIV infection, she often chooses the latter.[15-17]

Issues in HIV Testing and Diagnosis

Attitudinal Issues

It is important for every nation to have effective, voluntary counseling and testing services for HIV infection. Benefits include early management of HIV infection and thus improvement in quality of life, and the primary and secondary prevention of HIV infection. Only a fraction of persons living with HIV are aware of their infection, and those who do receive clinical testing are usually not provided with counseling.

Health counseling is a new concept in India. Patients here are much less proactive in seeking health care than in developed countries. In the context of HIV-test counseling, the process of building a risk inventory involves discussing the sexual lifestyle of the client. This falls into the realm of taboo. Worse, high-risk behavior is viewed as morally wrong; hence, few visit the voluntary counseling and testing (VCT) centers.

At the other end of the spectrum are health care facilities that test without consent. HIV testing is performed either as part of a differential diagnosis or, in the case of surgical candidates, to provide reassurance for surgeons. Hospitals are widely known to refuse to perform any invasive procedures on persons with HIV infection. Anecdotal evidence indicates that hospital staff commonly tell HIV-seropositive patients, "You have a problem in your blood. Come back once it is treated."

Hence the majority of HIV testing in India is not accompanied by pretest or posttest counseling.[18] Individuals who receive an HIV-seropositive result are handed a virtual death sentence when they are told, "You have AIDS."

Another issue for any person undergoing an HIV test is realizing that his or her test is neither anonymous nor confidential.

With scant regard for the privacy that such clients are entitled to, laboratories readily provide test results over the telephone or share them with families and workplace supervisors.

The story of Mr V, who worked for a very large government-run company, is heartrending. Following frequent illness and a prolonged hospital admission, an HIV test performed on him without his consent was seropositive. The test result was shared with the company physician, who was excited by his "first" HIV case. Sadly, when Mr V returned to his workplace, he came to know of his HIV serostatus from a doorman who refused entry to him. Mr V attempted suicide but did not succeed.

By yielding a seropositive result or just by its very use, an HIV test can be stigmatizing. Appropriate skills and attitudes could reduce this stigma. At the Y R Gaitonde Centre for AIDS Research and Education (YRG CARE), an AIDS service organization in Chennai City, several thousand people have received HIV counseling and testing, and follow-up services if seropositive. The organization preserves its clients' anonymity by assigning each client a unique serial number on entry. The steady increase in the numbers of persons who have sought counseling and testing over the years reflects the positive reception of this program in the community.

Cost Issues

When laboratory resources are limited, consideration should be given to using total lymphocyte count (TLC) levels in lieu of CD4+ levels, at least for decisions on treatment initiation. In a study at YRG CARE, researchers found a high degree of correlation between 650 paired CD4+ and TLC counts (r=0.744).[19] The cost of a single CD4 test is US $30 versus US $0.80 for a single TLC count, which translates into a substantial annual cost saving.

Many clinicians use plasma HIV RNA testing to monitor HIV infection; however, inexpensive assays with faster turnaround time are needed in resource-limited settings. The p24 antigen level is of potential, but has not been validated as a prognostic tool.[20-24]

Quality Issues

The majority of the laboratories in India do not take part in quality-assurance and quality-control exercises for HIV testing, and poor techniques are commonplace.[18] HIV test results are often inaccurate for several reasons: test kits are used after the expiration dates; kits are not stored at the correct temperature; electricity is shut down at night; air-conditioning for the testing equipment is erratic; poor-quality water is used; and tubes, tips, and other equipment are often recycled. With makeshift laboratories that have scant respect for quality control or assurance, patients cannot necessarily be sure of their test results, especially when these laboratories do not provide patients with an opportunity to discuss their lifestyles and risk histories with a counselor who could then help them place the result within that context.[18]

In a 2001 survey (unpublished and under further compilation) in Chennai City, conducted in association with the Brown-Tufts Fogarty Program, 972 laboratories were studied, of which 64% (n=619) offered HIV testing. More than 50% (n=510) offered HIV test results on the basis of a single rapid test. A fourth (n=249) performed the enzyme-linked immunosorbent assay (ELISA), a tenth (n=24) of which offered, on request, confirmation by Western blot. There was a small percentage of laboratories (n=15) that either performed HIV RNA polymerase chain reaction assays or branched DNA assays, or acted as collection centers for others that did these tests. About 1% of the laboratories offered p24 antigen tests.

In a previous study that described the first 5 years of YRG CARE,[18] 9% of clients (n=156) accessed services for reconfirming a prior HIV-seropositive test result. Of this group, only 78% (n=122) tested seropositive under the clinic's conditions for quality assurance and quality control.

Issues in HIV Treatment and Care

A wide spectrum of opportunistic infections has been documented in those living with HIV in India (Figure 3). Emerging opportunistic infections include *Pneumocystis carinii* pneumonia, toxoplasmosis, and cryptococcal meningitis. HIV infection has made tuberculosis, syphilis, and herpes more aggressive.

The standard of care that NACO supports is limited to the provision of drugs for treatment of opportunistic infections.[1] Resource constraints limit the distribution of drugs to those institutions that qualify through a NACO state-level selection process. Unfortunately, since there are additional people living with HIV who only have access to the centers not selected to receive drugs, the provision of drugs for opportunistic infections is limited.

A spate of antiretroviral drugs, evolving incrementally but rapidly and being approved at a brisk pace, has changed the treatment horizon. However, these drugs were not within reach of even middle-class Indians until recently, and they are still inaccessible to most. For example, only about 15% of YRG CARE's patients can afford antiretrovirals. Although antiretrovirals do not offer a definitive cure, the appropriate use of these

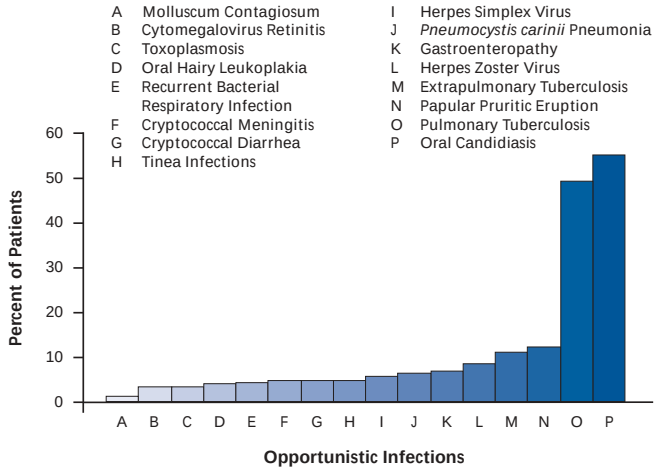

Figure **3.** Spectrum of opportunistic infections at Y R Gaitonde Centre for AIDS Research and Education, Chennai, Tamil Nadu, India. Adapted with permission from: Kumarasamy N. *Studies on Human Immunodeficiency Virus Disease Progression in South India* (PhD thesis). Chennai, India: University of Madras; 2001.

drugs in combination has demonstrated a significant decrease in mortality and substantial clinical improvements and has helped individuals lead healthier, longer lives and enjoy a better quality of life.

These new drugs can also prevent mother-to-child transmission of HIV infection and prevent development of the infection in health care workers following occupational exposures to the virus or in cases of other exposures such as rape. To this extent, these drugs are definitely recommended. With regard to use of antiretroviral drugs in the setting of occupational exposure, NACO recently ordered hospitals to stock postexposure prophylaxis kits. Detailed guidelines on postexposure prophylaxis have been distributed to all the hospitals.[1] With regard to prevention of mother-to-child transmission, there are 27 million pregnancies a year in India and an overall estimated 0.3% prevalence rate of HIV infection among pregnant women; it is estimated that about 100,000 HIV-infected women deliver each year. In January 2000, a pilot study was initiated in 11 antenatal clinics to assess the feasibility of administering zidovudine for the prevention of mother-to-child transmission; a subsequent study of nevirapine was initiated in October 2001 in the same 11 clinics. The option of breast feeding was left to the mothers.[25]

The major Indian pharmaceutical companies have changed the landscape of drug availability and affordability by taking advantage of Indian laws that protect process patents but not product patents. In a rare show of boldness and business wisdom, drugs that cost no less than $8000 to $12,000 a year in the United States are now being offered in the Indian and international markets for only a few hundred dollars a year. Whether the recent dramatic reductions in the pricing of AIDS drugs will make a difference to the very few who already know their HIV serostatus, and whether they foretell a standard of care in India on par with that in the developed world, remain contentious issues.

Treatment with antiretroviral therapy of 1 or perhaps more than 1 person in a family presupposes large savings, disposable incomes, or a benevolent government. Contrast these assumptions with the real current situation: a US $400 per capita income and a government program allocating $0.06 per capita per year on HIV/AIDS until 2004.[1]

In a country where only a small portion of physicians have willingly learned about HIV infection and its management, finding a competent opinion on HIV treatment options may not be easy. Further, in India, where prescription drugs are available over the counter, some wonder how much longer it will be before HIV treatments are available for self-medication.

The viability of implementing wide-scale antiretroviral therapy in the country cannot be generalized. Although in urban centers there is remarkable excitement over the new combination antiretroviral therapies, this should not obscure the other elements of quality medical care for patients infected with HIV for whom antiretroviral therapy is out of reach. Affordability of antiretroviral drugs aside, logistical and financial challenges hinder access to CD4+ cell count and HIV RNA measurements. Drug supply logistics are convoluted; for example, only a small percentage of Indian households own or have access to refrigerators to store those drugs that require refrigeration. Drugs tend to be available only in urban centers, as those centers have more purchasing power than rural towns, where the demand for the drugs is lower and the cost of stocking them, which may involve use of refrigerators, is high.

Low levels of literacy require additional effort from an overburdened, and more importantly, reluctant medical system to make the complex drug regimens more easily understood. In the absence of quality adherence counseling, both the rich and the poor are not adherent. When HIV-infected patients attain a good quality of life, usually after about 6 months of initiating therapy, the rich take a break and the poor run out of money.

We have important lessons to learn from the indiscriminate use of antibiotics, which has led to many a microbe winning the war. The global concern that suboptimal use of antiretroviral drugs may result in resistant strains of the virus is valid; however, there are as yet no facilities in India that perform resistance-testing assays.

The viability of implementing wide-scale antiretroviral therapy is not determined solely by the cost of the medications. It is affected by the public health infrastructure, site-specific natural history, costs of monitoring, and adherence levels. Data on these cofactors are incomplete and merit independent studies.

Pervasive Magic Cures

Although India predominantly follows the medical system practiced in the West, there are many conditions, such as viral hepatitis, that are treated with Indian traditional medicine.[26-28] Although the Western medical system is often relied upon, if the condition does not respond to treatment, faith in that system becomes fatigued. Families turn to traditional systems as the last hope, and this moment has been seized by a number of self-proclaimed "experts" offering magic cures for HIV. India is in the grip of such a mania. These drugs often masquerade as natural and herbal, though anecdotal reports suggest that they contain steroid-like additives as well as minute quantities of heavy metals. After an initial sense of well-being, the health of persons who take such drugs deteriorates and they end up with life-threatening conditions. While the government is battling vagrant "healers" through legislation, demand from the general public fuels their greed. This is an ongoing and contentious issue, as drugs that are based on traditional systems do not have an approval process and often have never been investigated, even when compelling evidence of harm is presented.

What Is Relevant?

Pilot study data suggest that when antiretroviral therapy becomes universally available in India, there will be less morbidity and mortality from opportunistic infections.[29] However, even in the absence of antiretroviral therapy, opportunistic infections could be managed and prevented through improved health-seeking behaviors as well as shifts in the attitudes of medical establishments, in terms of friendliness to clients and adherence education. Simple chemoprophylaxis protocols effectively prevent the occurrence of opportunistic infections.[30]

HIV Presents a New Opportunity

The time has come for India to change the way it treats its sick. Perhaps HIV will be able to jolt the health system awake and

pave the way to holistic treatment. Experiences from around the world clearly show that patients and their families require extensive education on nutrition, stress reduction, and exercise, as well as counseling and emotional support, to improve their quality of life.

India should begin to invest in promoting good practices in HIV/AIDS VCT, use of related drugs, routine clinical approaches, and relevant treatment guidelines. India also should promote a change in attitudes toward HIV/AIDS. It is a shame that HIV-infected persons continue to live in a secret world, hoping to shield themselves from the stigma, scorn, and discrimination of the members of their community by not talking about their infection. To them, even government support of antiretroviral drugs would be of little relevance.

Conclusion

The exploding epidemic in India calls for radical and courageous steps, and a departure from previous public health planning. We need to remind ourselves of the enormous task at hand: the establishment of quality-assured HIV testing centers, expansion of clinical facilities that provide HIV care, increased access to drugs with attendant laboratory facilities, and enhanced psychosocial support for those living with or affected by HIV. Additional resources are urgently required to tackle the raging twin epidemics of HIV and tuberculosis.

Investment in areas of research such as in the prevention of mother-to-child transmission of HIV infection and primary prevention of HIV transmission among women, perhaps using women-friendly and women-controlled methods (such as the female condoms or microbicides), and development of low-cost alternatives to laboratory markers such as the CD4+ cell count[31,32] and plasma HIV-1 RNA level must be encouraged and accelerated.

The HIV situation in India may not have been alarming at first glance; however, a small percentage-point rise in HIV incidence must be viewed in absolute numbers as a multiple of a billion inhabitants.

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