# global issues

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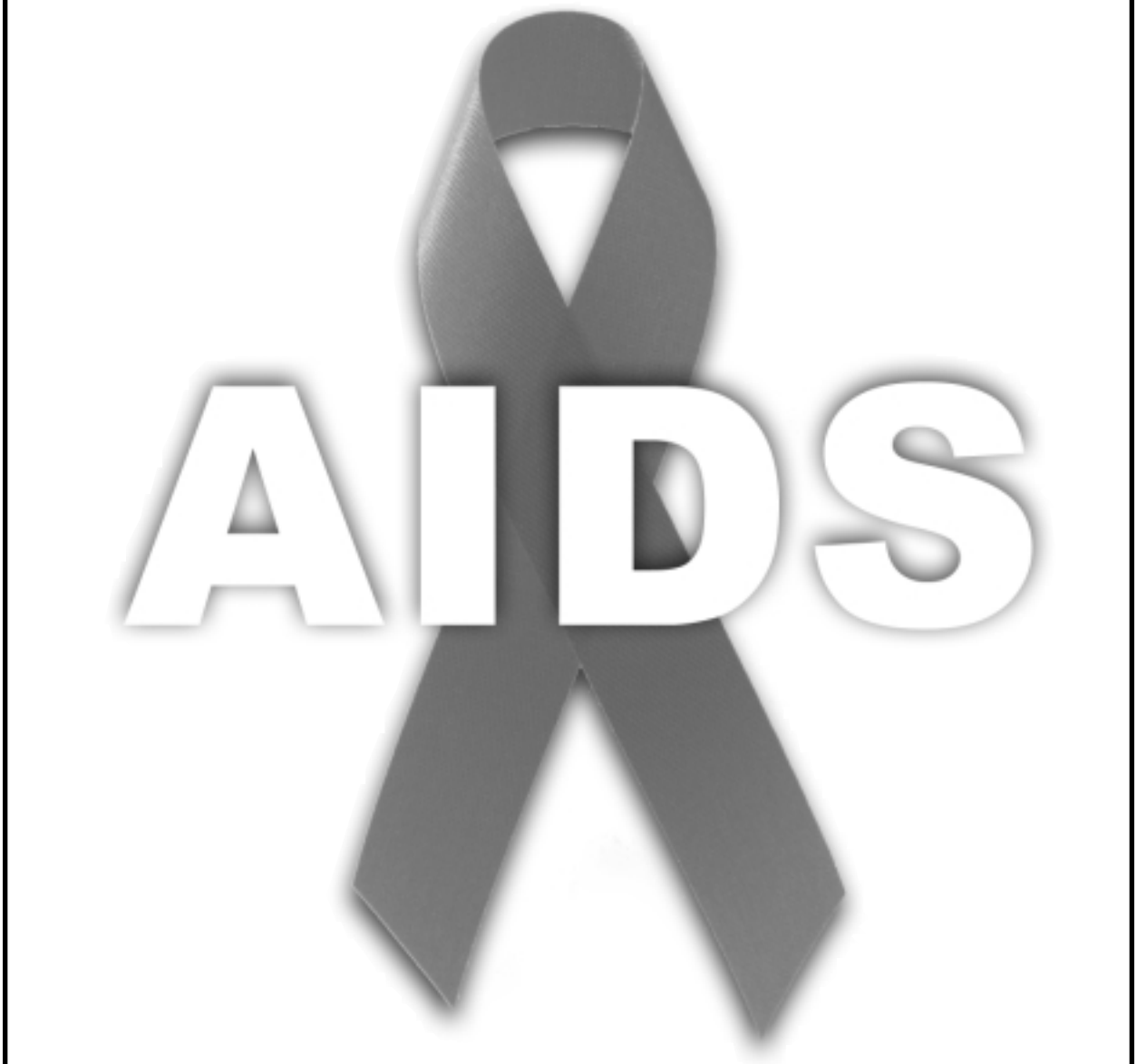


## The Threat to World Security

*We shouldn't pretend that we can give injections and work our way out of this. We have to change behavior, attitudes, and it has to be done in an organized, disciplined, systematic way.*

*President of the United States*

*Keynote Address to the National Summit on Africa*
*February 17, 2000*

# *From the Editors*

*This Electronic Journal goes to press at the time that about 10,000 researchers, physicians, activists, care-givers, and government officials prepare to convene at the XIII International AIDS Conference in Durban, South Africa. The meeting is expected to showcase innovative techniques and strategies for care, treatment, and prevention that could offer new directions for those pursuing this vital work.*

*The weeks before the conference have brought a steady stream of developments in this ongoing story about HIV/AIDS: new statistics on the mounting toll of the disease; initiatives for education and prevention programs; new efforts to encourage the hunt for a vaccine. Perhaps most significant of all, however, is the evolving recognition that a disease, for the first time, presents such an ominous threat to health, prosperity, and development that it deserves the same kind of official attention world leaders have given to more traditional threats to world security. We remain hopeful that this increased attention from around the world will make major contributions as we seek to confront this scourge.*

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The Office of International Information Programs of the U.S. Department of State publishes five electronic journals that examine major issues facing the United States and the international community. The journals—Economic Perspectives, Global Issues, Issues of Democracy, U.S. Foreign Policy Agenda, and U.S. Society and Values—provide analysis, commentary, and background information in their respective thematic areas. All journal editions appear in English, French, and Spanish language versions, and selected issues also appear in Arabic, Russian, and Portuguese. A new English-language issue is published every three to six weeks. Translated versions normally follow the English original by two to four weeks. The order in which the thematic editions appear is irregular, as some editions publish more issues than others.



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# The Shared Struggle Against AIDS

By Sandra Thurman
Director, Office of National AIDS Policy

*The United States, working with other countries, is helping to design model programs based on prevention and community-based care to stem the rising tide of new AIDS infections in Africa and other regions of the world.*

I would like to lay out a vivid picture of the scope of the AIDS pandemic—particularly as it impacts the stability of families, communities, and nations. I would like to share with you some of my experiences with the faces behind these shocking facts. And I would like to outline for you some key components of the Clinton administration's enhanced response to this global pandemic.

By any and every measure—AIDS is a plague of Biblical proportion. And it is claiming more lives in Africa than in all of the wars waging on the continent combined. AIDS is now the leading cause of death among all people of all ages in Africa—and the progression of this pandemic has outpaced all of our projections. In 1991, the World Health Organization predicted that by 1999 there would be 9 million infected and nearly 5 million deaths in Africa due to AIDS. The resulting numbers are two to three times higher with nearly 24 million infected and 14 million deaths.

And yet this war rages on. Each and every day Africa buries 5,500 men, women, and children as a result of AIDS—and that count will more than double in the next few years. It is now projected that by 2005 more than 100 million people worldwide will have become HIV infected. And unlike other wars—it is women and children that are increasingly caught in the crossfire of this relentless pandemic.

In Africa, an entire generation of children is in jeopardy. In several sub-Saharan African countries, between one-fifth and one-third of all children have already been orphaned by AIDS. And the worst is yet to come. Within the next decade, more than 40 million children in Africa will have lost one or both parents to AIDS. Forty million. That is about the same number as all children in the United States living east of the Mississippi River.

In just a few short years, AIDS has wiped out decades of hard work and steady progress in improving the lives and health of families throughout the developing world—infant mortality is doubling, child mortality is tripling, and life expectancy is plummeting by 20 years or more.

And AIDS is not just a health issue; it is an economic issue, a fundamental development issue, and a security and stability issue.

AIDS is having a dramatic effect on productivity, trade, and investment—striking down workers in their prime, driving up the cost of doing business, and driving down gross national product (GNP). Many companies are already being forced to hire at least two employees for every one job—assuming one employee will die of AIDS.

AIDS is also affecting stability in the region. The U.N. Security Council recently held a daylong meeting on HIV/AIDS. This historic event highlighted the growing awareness that AIDS is a security threat that requires a global mobilization. This reality was also addressed in a report recently released by the National Intelligence Council, which documents that the impact of this pandemic is far more serious a threat than we thought.

Yet my message to you is not one of hopelessness

and desolation. On the contrary, I hope to share with you a sense of optimism. For amidst all of this tragedy, there is hope. Amidst this terrible crisis, there is opportunity: the opportunity for us—working together—to empower women, to protect children, and to support families and communities throughout the world in our shared struggle against AIDS.

It is important to remember that what we are talking about today is not numbers but names, not facts and figures but faces and families. Let me tell you the story of one inspirational grandmother I met in a small village outside of Masaka, Uganda.

Bernadette has lost 10 of her 11 adult children to AIDS. Today, at age 70, she is caring for her 35 grandchildren. With loans from a village banking system, she has begun growing sweet potatoes, beans, and maize, raising goats and pigs, and trading in sugar and cooking oil.

With the money she earns, she is now able to send 15 of her grandchildren to school, provide modest treatment for the five who are HIV positive, and begin construction on a house big enough to sleep them all. In her spare time, she participates in an organization called "United Women's Effort to Save Orphans"—founded by the first lady of Uganda, Mrs. Janet Museveni—linking in solidarity thousands of women allied in the same great struggle.

And these women are not alone. From the young people doing street theater in Lusaka to educate their peers about HIV to the support groups in Soweto providing home and community-based care for people living with AIDS—communities are mobilizing and creating ripples of hope.

These are the faces of children and families living in a world with AIDS. And their spirit, their determination, and their resilience lead us on.

The good news is, we know what works. With our partners in Africa we have developed useful knowledge and effective tools. Together, we have designed model programs and proven that they work. And today, we know how to stem the rising tide of new infections, how to provide basic care to those who are sick, and how to mobilize communities to support the growing number of children orphaned by AIDS. Uganda has demonstrated that with strong political commitment and sustained nationwide programs, HIV prevalence can be cut in half. And Senegal has shown that HIV can be stopped in its tracks and prevalence can be kept low. But there is more, much more that needs to be done if we are to continue these successes.

The United States has been engaged in the fight against AIDS here at home since the early 1980s. But increasingly we have come to realize that when it comes to AIDS—both the crisis and the opportunity have no borders. We have much to learn from the experiences of other countries, and the suffering of citizens in our global village touches us all.

We have done much, but there remains much more that the United States and other developed nations can and must do.

During the past year and a half I have made four trips to eight African countries. Together with members and staff from both parties and chambers of Congress we went to witness firsthand both the tragedies and triumphs of AIDS in Africa. In response to the findings of these trips, the administration requested and Congress appropriated an additional $100 million in fiscal year 2000 to enhance our global AIDS efforts.

This initiative provides for a series of steps to increase U.S. leadership through support for some of the extraordinary community-based programs currently being funded through the U.S. Agency for International Development (USAID) and to provide much needed technical assistance to developing nations struggling to respond to the needs of their people infected and affected by AIDS. This effort more than doubles our funding for programs of prevention and care in Africa, and challenges our G-8 (group of seven major industrialized nations plus Russia) and other partners to increase their efforts as well.

The initiative focuses on four key areas:

- Prevention—Particularly stigma reduction strategies, especially for women and young

people, including HIV education, voluntary counseling and testing, and interventions to reduce mother-to-child transmission.

- Home and community-based care—This will help to create and enhance counseling and support systems, and provide some basic medical care, (including treatment for related illnesses like sexually transmitted diseases (STDs) and tuberculosis (TB).

- Care of children orphaned by AIDS—This will be done through nutritional assistance, education, training, health, and counseling support, in coordination with micro-enterprise programs.

- Infrastructure—These funds will help to increase the capacity for the effective delivery of essential services through governments, NGOs, and the private sector.

Some of the other key components of this initiative include an increase in our efforts to make the AIDS epidemic a part of our foreign policy dialogue, to promote the use of resources freed up by debt relief for HIV prevention, and to engage all sectors including business, labor, foundations, the religious community, and other non-governmental organizations in a broad-based mobilization.

While this new initiative greatly strengthens the foundation of a comprehensive response to the pandemic, UNAIDS has estimated that it will take $1,000 million to establish an effective HIV prevention program in sub-Saharan Africa. Currently, all donors combined are contributing less than $350 million to that end. In addition, UNAIDS estimates that it will take a minimum of $1,000 million to begin to deliver basic care and treatment to people with AIDS in the region. We have not even begun to scratch the surface when it comes to delivering even this most basic treatment.

In the face of such tremendous need, the administration has requested, in the president's 2001 budget submission, an additional $100 million increase to enhance and expand our efforts to combat AIDS in Africa and around the world.

These funds will enable us to bolster our efforts already underway at USAID and the Centers for Disease Control (CDC), and to expand our approach to include the Departments of Labor and Defense for efforts to address HIV/AIDS transmission in the workplace and in the military. Let me repeat, however, that the United States cannot and should not do this alone. This crisis will require the active engagement of all segments of all societies working together. Every bilateral donor, every multilateral lending agency, the corporate community, the foundation community, the religious community, and every African government must do its part to provide the leadership and resources necessary to turn this tide. It can and it must be done.

The bottom line is this: we have no vaccine or cure in sight, and we are at the beginning of a global pandemic, not the end. What we see in Africa today, frankly, is just the tip of the iceberg. As goes Africa, so will go India and the Newly Independent States of the former Soviet Union. There must be a sense of urgency to work together with our partners in Africa and around the world, to learn from both our failures and our successes, and to share this experience with those countries that now stand on the brink of disaster. Millions of lives—perhaps hundreds of millions of lives—hang in the balance. AIDS is a devastating human tragedy that cries out to all of us for help.

We are one world, and in many ways, Africa's destiny is our destiny. There is hope on the horizon, but that hope will only be realized if we take constructive action together. Today, let us commit to seize this opportunity. As South Africa's Archbishop Desmond Tutu said: "If we wage this holy war together—we will win."

# Battling the AIDS Pandemic

By Richard C. Holbrooke
U.S. Ambassador to the United Nations

*The AIDS epidemic, still seen as a taboo and surrounded by cold silence in many cultures, must be talked about publicly at the highest levels.*

I first became aware of the intersection between international security issues and HIV/AIDS in 1992, when as a private citizen I traveled to Phnom Penh and had the opportunity to speak with U.S. and U.N. officials then working on U.N.-sponsored elections in Cambodia. I was so alarmed by what I was hearing about transmission of the virus to and by peacekeeping troops that I wrote a letter to the senior U.N. official in Cambodia, noting that 40 different nations contributed to the U.N. peacekeeping force in Phnom Penh. While the peacekeeping troops were committed to the admirable task of bringing peace to that war-torn country, those troops also had a high potential for contributing to the global spread of AIDS, either bringing it into Cambodia or taking it out.

Since that time, predictions by epidemiologists on the global spread of HIV-AIDS have come devastatingly true. While education and new drug therapies have offered much hope for stemming the disease in the West, in the developing world infection rates are exploding. Nowhere is the disease's impact more apparent than in sub-Saharan Africa. Although the crescent of states from Kenya to South Africa has only 10 percent of the world's population, it accounts for over two-thirds of the world's HIV positive people and nearly 85 percent of all AIDS deaths. The disease kills 10 times more people in sub-Saharan Africa annually—more than 2.62 million people last year alone—than all of the continent's armed conflicts combined.

Last December, on a 10-nation trip to Africa, I saw firsthand the ravages of AIDS—from thousands of orphans in Lusaka, Zambia, who were forced to live in a bus depot, many already infected with HIV, to six pregnant women in Windhoek, Namibia, all of whom were infected with AIDS and who had to meet with our delegation secretly because of the stigmatization associated with the disease. These women told us that if they even admitted they had contracted the disease they would lose their husbands, families, and jobs, and be completely ostracized from society. HIV/AIDS—untested and untreated—destroys family and kinship relationships, killing breadwinners, teachers, soldiers, and policemen who are the very hope of the next generation.

In January of this year, the U.N. Security Council marked the new millennium by taking an historic step in making HIV/AIDS the subject of its first-ever session devoted to a health issue. This event symbolized something that many of us have believed for a long time —that AIDS is as destabilizing as any war; that in the post-Cold War world, international security is about more than guns and bombs and the balance of power between sovereign states. Vice President Gore, who chaired that Security Council session, put it eloquently when he said AIDS is "a security crisis because it threatens not just individual citizens but the very institutions that define and defend the character of a society."

In the months since that Security Council session, there has been growing media attention to the issue of AIDS in Africa, including a Pulitzer Prize to the Village Voice's Mark Schoofs for his feature series, "AIDS: The Agony of Africa." There have been many new initiatives by the United Nations,

by the U.S. government, by drug companies, and by nongovernmental organizations (NGOs). And, as long as I am ambassador to the United Nations, the U.S. will never again vote for a peacekeeping resolution that does not require specific action by the U.N.'s Department of Peacekeeping Operations to prevent AIDS from spreading by or to peacekeepers.

But we must do more. First and foremost, we urgently need a greater commitment of resources. It's no secret that the level of international resources dedicated to fighting AIDS is far too low by an order of magnitude. According to World Bank President James Wolfensohn, the current level of official international assistance for AIDS prevention in Africa is only $160 million. In last January's Security Council session, Vice President Gore announced that the administration would ask Congress' support for another $100 million to fight the epidemic, bringing the U.S. total this year to $342 million. We will continue to work through diplomatic channels to energize our G-8 colleagues, UNAIDS, the World Health Organization, the World Bank, and other international organizations, the private sector, and the leaders of every country in the world to improve cooperation and bring more financial and political commitment to this global fight.

Secondly, those nations that are in the throes of the AIDS crisis, as well as those that are on the launch pad to a wider outbreak, must accept their own responsibilities. In too many cultures, HIV/AIDS is still seen as a taboo and is surrounded by cold silence. This epidemic and its causes must be talked about publicly at the highest levels. In addition to financial resources, the battle against AIDS requires political capital and will. For this reason, I welcome the 13th Annual International Conference on AIDS, held in Durban, South Africa, this July. This conference provides an excellent opportunity for government and NGO representatives, donor organizations, and medical experts to have open discussions on effective strategies of prevention, on potential treatments, and on international, national, and community mobilization to battle the pandemic that is AIDS.

For it is clear that no government can fight the scourge of AIDS alone. Only through partnership among the community of nations, and among the public and the private sectors can we make progress in preventing a generation of orphans whose futures have been utterly diminished and who have lost all hope. Surely, we owe the world's children nothing less than our best combined efforts to stop the seemingly inevitable spread of this horrific disease.

# Preventing AIDS: An Investment in Global Prosperity

By Lawrence H. Summers
U.S. Secretary of the Treasury

*Today's pace of scientific discovery provides an historic opportunity to make progress against deadly diseases like AIDS that exact such a toll on economic development and threaten the prosperity and stability of the global economy.*

Increasingly, as integration proceeds, the world is confronting a broad class of problems that cross borders and defy easy solution by individual governments and markets. Whether it is money laundering and financial crime, climate change, or reductions in global biodiversity—the solutions to these problems will be global public goods, requiring concerted global cooperation.

The proposals put forward in the President's Millennium Initiative seek to catalyze a global response to one of the most urgent and morally compelling of such problems: the scourge of infectious diseases that hit hardest the countries that are least able to cope.

I would like to address here the three points that form the basis for the president's initiative. First, the development and delivery of vaccines and treatments for infectious diseases is now one of the most effective investments that we can make in successful economic development in the poorest countries. Second, both the lessons of recent development experience and the advance of scientific discovery have put us in a position to have a real impact on the global spread of these diseases. Third, public-private cooperation, both at the national and international level, is needed to achieve this.

**Combating Infectious Diseases as a Moral and an Economic Imperative**

It might seem surprising that the Treasury Secretary is devoting so much attention to the goal of preventing and controlling disease in the developing world. But, as Treasury Secretary, I am constantly aware of the enormous national economic, humanitarian, and security stake that the United States has in the successful development of the poorest countries.

Today, it does not overstate the case to say that the greatest single obstacle to human development in these countries is the specter of disease, such as HIV/AIDS. The spread of HIV/AIDS in recent years has been swift and particularly brutal.

Fifty million people worldwide have been infected with the HIV virus; more than 16 million have died; and annual AIDS-related fatalities hit a record 2.6 million last year. In sub-Saharan Africa, where 85 percent of all AIDS deaths have occurred, life expectancy is now declining sharply in many countries, reversing decades of hard-won gains. In at least five African countries, more than 20 percent of adults are HIV-positive. In southern Africa, life expectancy is expected to drop from a high of 59 in the early 1990s to 45 within the next 5-10 years—a level not seen since the 1950s. And the highest rates of new infection are often among young women who will soon be mothers.

Women are increasingly bearing the brunt of HIV/AIDS, both as the primary care providers and, among the young, as those who are often most vulnerable to the disease. In many places, HIV/AIDS infection among young women is three-to-five times higher than among boys. And in parts

of South Africa, nearly one-third of pregnant women are testing HIV positive, compared to just 1 percent in 1990. On a continent where women perform an inordinate share of the physical labor and contribute in critical ways to the household economy, the debilitation wrought by AIDS is especially cruel.

Most worrisome is the rate at which HIV/AIDS is spreading, and the very real danger that what is happening in Africa is about to happen elsewhere. Infection rates in Asia are climbing rapidly, with several countries on the brink of a large-scale pandemic and needing to take action immediately to forestall the disaster that Africa has suffered. Parts of Latin America and the Caribbean—our own neighbors—also show high and rising rates of infection. And the former Soviet Union countries and Eastern Europe are vulnerable as well, with Russia experiencing the highest increase in infection rates in the world last year.

At the same time, it bears emphasis that millions of the world's people still fall prey to diseases that are centuries old. For example, tuberculosis (TB) accounts for more than two million deaths annually, and drug-resistant strains are spreading. Indeed, thousands of people who are HIV-positive actually die of TB; their damaged immune systems allow active TB to develop, which then can spread to people who are not HIV-positive.

All told, infectious diseases are the leading cause of death worldwide, responsible for almost half of all deaths among people under the age of 45. The end result is not merely a humanitarian crisis, but a broader social and economic crisis.

Life expectancy is falling mainly because of rising mortality among prime age adults, and research has shown that economic growth depends importantly on the share of the population that is of working age. A recent World Bank study estimates that AIDS is likely to subtract about 1 percent a year from GDP growth in 30 sub-Saharan African countries. The burden of coping with these diseases further reinforces the poverty that allowed these diseases to take root. Health care budgets and facilities are overwhelmed by the heavy burden of caring for those who are infected. And families that are already impoverished are forced to liquidate assets and defer expenses for essentials such as education in order to pay for costly medical care, thus sending them into a deeper downward economic spiral. AIDS alone has orphaned an alarming number of children—more than 11 million worldwide—with all but one-half million in Africa.

If these countries do not develop, they cannot contribute to the broader global growth in which we have such a stake, at a time when more than 40 percent of our exports already go to developing countries. The national economic distress and political instability that inevitably accompany this scale of human loss can cause greater damage to the global system as a whole.

For all of these reasons, the development and delivery of vaccines and effective treatments for infectious diseases are among the most cost-effective investments we can make, both in successful economic development in these economies, and in the prosperity and stability of the global economy as a whole.

We believe this is fundamentally a humanitarian imperative. It is also a national economic and security imperative. And it is an imperative that global experience and the pace of scientific discovery have now put us in a much stronger position to address.

**The Ability to Make a Real Difference**

We must deal now with the ongoing and immediate impact of infectious and other diseases of poverty. The record of past international efforts to combat infectious disease suggests that there are no easy, simple solutions to this problem. But we are in a much stronger position today than we were even a few years ago to help countries make concrete progress.

First, there has been rapid growth in relevant scientific understanding. Clearly, one reason for the high incidence of infectious diseases is the remaining gaps in our scientific knowledge about those diseases. The development of vaccines and medicines simply cannot exceed the frontiers of available basic science. But, as one pharmaceutical executive said at a recent meeting on this subject

with President Clinton, this is a "golden age" for research and implementation. Important recent advances are being made on malaria, pneumococcus, and AIDS. We believe that public policy can provide a critical boost to private research efforts in this area.

Second, we have new tools for potentially channeling significant internal and external resources toward this effort. A sheer lack of financial resources relative to the cost of even the most basic investments in health is clearly an even greater obstacle to improving health outcomes in these countries.

On average, the poorest nations in the world spend just $15 per person on health care each year—less than it costs to fully vaccinate a child against nine basic diseases including polio, measles, and tetanus. In the United States, we spend thousands of dollars per person on health care each year. In the poorest developing countries, there are only 14 doctors and 26 nurses on average for every 100,000 patients, compared to 245 doctors and 878 nurses in the United States. And 800 million people live on less than $1 a day. The harsh reality is that the cost of caring for patients with AIDS the way we do in the United States far exceeds the per capita income of most developing countries.

We cannot hope to eliminate the relative gap in countries' economic resources. But in the Heavily Indebted Poor Countries (HIPC) initiative we do have a tool for increasing the funds they have available—and ensuring that they are channeled to core human development priorities such as basic health care.

The HIPC initiative, created in 1996 and further enhanced last year, has already helped some of the poorest nations in the world free up precious resources for human development that would otherwise have been spent on servicing debt. Fully funded and implemented, the enhanced HIPC initiative has the potential to be an even more powerful tool for helping countries devote more resources to combating infectious disease.

Last year, the Ugandan government saved $45 million in debt service under the original HIPC program. Its expenditures on health and education increased by $55 million, including a major effort to combat the HIV/AIDS epidemic. Immunization rates for children in Uganda are expected to increase from 55 percent in 1996 to 60 percent in 2002. One of the key priorities for health spending in the future, which would be facilitated by enhanced HIPC debt relief, is to extend HIV/AIDS education outreach, particularly to rural communities.

It bears emphasis that educating girls holds the further benefit of helping to prevent the spread of HIV/AIDS. Studies in Zaire, Zimbabwe, and elsewhere all suggest strongly that higher rates of female secondary school enrollment have been associated with a much slower rate of transmission of HIV. And across the developing world, health care data confirm that levels of education are now highly correlated with the probability that women will practice safe sex. That is why the new approach to official lending that is part of the HIPC initiative puts core investments in female education, along with other core social investments, at center stage.

Finally, we have greater understanding of the importance of—and prerequisites for—the effective delivery of vaccines and treatments. Clearly, it does no good to ship vaccines and medicines to the ports of poor nations if they do not end up in the arms or throats of the people who need them. Just as clearly, it does little good to administer vaccines and medicines to people who do not receive basic tools for maintaining health, such as nutritional interventions like vitamin A and iron, or for preventing disease, such as bed nets for malaria and education to prevent the spread of HIV/AIDS. These problems have often been important obstacles to international efforts to combat heart disease in the past. However, the tight linkages between different aspects of health care are now well understood in the development community and are being successfully put into practice.

This is reflected in both the President's Millennium Initiative and plans now being developed by the World Bank, which focus on shifting significant resources to improving the delivery of basic health services, including vaccines and medicines.

We also understand better that this is not a problem of money alone—but one of competence and enduring commitment. Specifically, developing country governments need to commit themselves to specific targets for improving health care delivery and health outcomes. And donor countries, international organizations, and non-government entities in developing nations need to cooperate to find solutions that will work best for the country in question. And applying these principles is yielding concrete results.

For example, in Uganda and Thailand, recent innovative programs supported by the international community have begun to reverse HIV infection rates of high-risk groups. And in Senegal, an early investment in prevention programs has helped to keep HIV infection rates low. In Bangladesh, which spends only $4 per person per year on health, the World Bank, USAID, and other donors have supported the development of networks of non-physician personnel fanning out to thousands of villages and urban slums, helping to reduce the infant mortality rate from 132 to 75 between 1980 and 1997.

**The President's Millennium Vaccine Initiative**

The President's Millennium Vaccine Initiative, outlined in his State of the Union address, draws on both of these realities: the scale and urgency of the problem, and the greater scope that we have today for launching an effective global response.

In these efforts, we are building on the support of the private sector, including pharmaceutical companies that can provide the research and development that is so necessary to developing the right vaccines. We are also drawing on the commitment of the non-profit sector, including organizations like the foundation created by Microsoft Chairman Bill Gates, which has contributed so generously to the fight against disease; and we are utilizing the expertise of government so that it can act as a catalyst to ensure that these efforts are expanded on an international scale.

The president's initiative has four basic components. First, mobilizing additional international resources to help the poorest countries purchase existing vaccines for their children. Many poor countries often cannot afford to buy vaccines. To help address this problem, the president's fiscal year 2001 budget proposes a $50 million contribution to the Global Alliance for Vaccines and Immunization (GAVI) to purchase existing vaccines for children. This contribution should help catalyze significant contributions from other countries and foundations. It will also add critical credibility to the international community's commitment to provide a market for new vaccines, including vaccines for AIDS, when they are developed. Further, the president has helped stimulate commitments from the pharmaceutical industry to donate hundreds of millions of dollars worth of existing vaccines.

Second, shifting existing international resources toward building infrastructure in poor countries that can deliver vaccines and medicines and provide essential basic health services.

President Clinton has called on the multilateral development banks to shift an additional $400 million to $900 million annually of concessional resources into basic health care. Of course, an essential element of such care is prevention and treatment of infectious diseases, including AIDS.

Third, intensifying the search for more effective ways of treating and preventing diseases that widely afflict developing countries, especially HIV/AIDS, malaria, and tuberculosis.

The president's fiscal year 2001 budget for the National Institutes of Health includes a significant increase in research critical to creating vaccines for deadly diseases that afflict primarily developing countries. Funding for AIDS vaccine research will increase substantially in fiscal year 2001 and will have more than doubled since fiscal year 1997.

The president has also proposed an additional $100 million for HIV prevention and AIDS treatment in Africa, Asia, and other developing countries. We can make crucial headway against HIV and AIDS by providing clear information on prevention strategies and treating sexually transmitted diseases. We are calling on other countries to join us in committing money for these purposes.

Fourth, harnessing the scientific and technological skills of the private sector in the development of new vaccines for infectious diseases.

While important progress is being made, it is widely recognized that the market does not provide sufficient incentive for pharmaceutical companies to develop vaccines and medicines for diseases that disproportionately affect developing nations. Indeed, the World Health Organization estimates that only perhaps 10 percent of the $50,000-$60,000 million spent worldwide each year on health research is directed towards diseases that afflict 90 percent of the world's population.

To start to address this problem, the president is proposing a new tax credit for sales of vaccines against malaria, tuberculosis, HIV/AIDS, or any infectious disease that causes over one million deaths annually worldwide. Under the proposal, the seller of a qualified vaccine could claim a credit equal to 100 percent of the amount paid by a qualifying nonprofit organization (such as UNICEF) that received a credit allocation from the U.S. Agency for International Development (AID). The tax credit would match the purchaser's expenditures dollar-for-dollar, thereby doubling its purchasing power.

For 2002 through 2020, AID could designate up to $1,000 million of vaccine sales as eligible for the credit. This credit would provide a specific and credible commitment to purchase vaccines for the targeted diseases once they become available. The president is calling on other governments to make similar purchase commitments so that we can ensure a future market for these critically needed vaccines.

In addition, the Clinton administration has expressed its willingness to support a tax credit for qualified clinical testing expenses for certain vaccines, similar to the existing orphan drug tax credit. The credit would be for 30 percent of the expenses for human clinical testing of vaccines for the diseases targeted by the president's initiative. This credit will provide an additional incentive for drug manufacturers to undertake research on new vaccines and accelerate their development.

**Conclusion**

The sheer magnitude and complexity of the challenge of combating infectious diseases, and their resistance to the efforts of the past, have a tendency to overwhelm hope with a sense of futility. Around the world, infectious diseases—including AIDS—are killing millions of children and weakening and killing tens of millions of prime-age adults. The devastating human and economic consequences are clear.

However, in Uganda, Thailand, Senegal, and elsewhere we have now seen compelling examples of concrete progress. And we have seen in the past that well-coordinated global efforts can have an enormous impact. One need only consider the eradication of smallpox; the nearly complete campaign against polio; and the remarkable global effort to combat river blindness (onchocerciasis), which has halted the transmission of that disease in 11 African countries and prevented 185,000 who were already infected from going blind.

As I have said, we believe that we now have a historic opportunity to make headway against the other killer diseases that today exact such a toll on the developing economies. What is crucial is that we act now to catalyze a broad international effort to address the problem at its root.

# The AIDS Epidemic: Considerations for the 21st Century

By Dr. Anthony S. Fauci
Director of the National Institute of Allergy
and Infectious Diseases

*The HIV pandemic, ranking as one of the most destructive microbial scourges in history, can be controlled in both developed and developing countries through such things as education, behavior modification, and the use of antiretroviral drugs.*

Humankind has been besieged throughout its evolution by microorganisms that pose a continual challenge to the survival of the species.[1] Although such ancient killers as tuberculosis and malaria persistently take a toll of millions of lives per year, occasionally the emergence or reemergence of a microbe results in an unexpected, catastrophic pandemic with global public health consequences. As we enter a new century, it is worth reflecting on the fact that within the framework of an enormous but constant burden of a variety of infectious diseases, as well as a number of mini-epidemics, the 20th century witnessed two such unexpected cataclysmic events.

One, the influenza A pandemic of 1918 was due to an old, but reemerging microbe. Influenza had been a problem for centuries, but in that one winter of 1918-1919 it was responsible for the deaths of approximately 25 million people worldwide and 550,000 people in the United States.[2]

The other pandemic, the acquired immunodeficiency syndrome (AIDS), is due to a newly recognized microbe, the human immunodeficiency virus (HIV).[3] The world first became aware of this new disease in the summer of 1981, and it has exploded in successive waves in various regions of the world. The catastrophic potential of the pandemic may still not have been fully realized. As this new millennium begins, it is appropriate to reflect on the origins of this epidemic, what has occurred over the past 18 years, what has been accomplished from a scientific and public health perspective, and what the prospects are for the future.

**The Origins of HIV**

Recent molecular epidemiologic data have clearly indicated that HIV type 1 (HIV-1) evolved with the *Pan troglodytes troglodytes* subspecies of chimpanzee and was present in that subspecies for centuries.[4] The virus apparently does not readily cause disease in the chimpanzee. As is the case with many viruses, HIV at a particular point (or points) in time "jumped" species to infect human beings; hence, it almost certainly originated as a zoonotic infection. HIV type 2, the less prevalent and less virulent species of HIV, is remarkably similar genetically to the simian immunodeficiency virus that is endemic among sooty mangabeys.[5]

The most likely mechanism of transmission of HIV-1 from chimpanzees to humans was by contamination of a person's open wound with the infected blood of a chimpanzee, probably when the chimpanzee was being butchered for the purposes of consumption.[6] Chimpanzees have traditionally served as a source of nutrition for humans in certain parts of sub-Saharan Africa. Any of a number of mutations in the viral genome that would have allowed successful transmission of the virus from chimpanzees to humans probably took place intermittently over the centuries.[4] Indeed, it is likely that sporadic cases of transmission to humans were continually occurring unnoticed over the course of decades, and perhaps centuries.

Only when demographic and social conditions allowed rapid spread of the virus among people did an epidemic actually begin to emerge. These conditions included massive migration from rural areas to urban areas; the breakup of family units due to the migratory nature of employment opportunities, with its attendant sexual promiscuity and extensive frequenting of commercial sex workers; and contamination of the blood supply.[7]

The introduction of the epidemic to developed countries, such as the United States, followed relatively soon after the "gay revolution" that had its origins in the riot at the Stonewall Inn, a bar frequented by homosexual men, in New York City in 1969.[8] The demographic setting of the high-risk homosexual practices that were concentrated in cities such as New York, San Francisco, and Los Angeles in the 1970s and early 1980s unfortunately made this population of predominantly young adults a perfect target for an epidemic of sexually transmitted disease. Similar patterns soon followed in other developed countries, such as Canada, Australia, and those of western Europe.

**Scope of the Epidemic**

AIDS continues to exact an enormous toll throughout the world, in both human and economic terms. In the United States, an estimated 650,000 to 900,000 people are infected with HIV,[9] of whom more than 200,000 are unaware of their infection.[10] Through 1998 (the latest figures available), 688,200 cumulative cases of AIDS and 410,800 AIDS-related deaths had been reported to the Centers for Disease Control and Prevention (CDC).[11]

The demographic characteristics of those affected by the epidemic have changed dramatically since the first cases were reported in 1981. Unlike the early days of the HIV and AIDS epidemic in the United States, when the affected population consisted overwhelmingly of homosexual men, leading some to assume incorrectly that the epidemic would remain contained within the gay population, today new cases of HIV infection result predominantly from injection-drug use and heterosexual contact, with a disproportionate representation among minority populations.[11] The numbers of cases of AIDS (per 100,000 population) reported in 1998 in the United States were 66.4 for non-Hispanic blacks, 28.1 for Hispanics, 8.2 for non-Hispanic whites, 7.4 for American Indians and Alaska Natives, and 3.8 for Asians and Pacific Islanders. Women are increasingly affected; the proportion of U.S. cases reported among women and adolescent girls more than tripled between 1985 and 1998, from 7 percent to 23 percent.[11]

It is often said that the HIV and AIDS epidemic in the United States and other developed countries has reached a plateau, since the number of new infections per year is no longer on an accelerating trajectory but has leveled off. However, in the United States it is estimated that this plateau has reached an unacceptable level of 40,000 new infections per year, a rate that is believed to have remained relatively constant throughout the 1990s.[12] Of these newly infected people, the CDC estimates that half are younger than 25 years of age and were infected sexually.[13] As the number of new cases per year among homosexual men has decreased dramatically, the number of new infections among heterosexuals, particularly among women, has accelerated greatly, producing a deceptive plateau. In the United States we are in fact seeing new waves of the epidemic among different demographic groups.

The same phenomenon of successive waves is reflected dramatically in the global pattern of the epidemic, with sub-Saharan Africa currently bearing the greatest burden of the epidemic worldwide.[14] In addition, the number of HIV infections in the countries of the former Soviet Union has escalated sharply over the past few years.[14] However, the trajectory of the infection rate in the Indian subcontinent and Southeast Asia indicates that without dramatically successful preventive measures, these regions will bear the greatest burden of the epidemic as we enter the 21st century.[14] The estimated number of infections in China is still relatively low; however, there is potential for an explosive spread of HIV in that nation of more than 1 billion people.

The magnitude of the epidemic is huge. As of the end of 1998, there were more than 33 million people worldwide with HIV infection or AIDS, 43 percent of them female, according to estimates by

the Joint United Nations Program on HIV/AIDS (UNAIDS).[14] An estimated 5.8 million new HIV infections occurred worldwide during 1998—approximately 16,000 each day. More than 95 percent of these new infections occurred in developing countries. In 1998, HIV infection or AIDS was the fourth leading cause of death worldwide, resulting in an estimated 2.3 million deaths.[15] If the current trend in the incidence of HIV infection continues, more than 40 million people will be infected with HIV as we enter the new millennium.

**The Successes and Limitations of Antiretroviral Therapy**

In the United States and other developed countries, the numbers of new AIDS diagnoses and deaths have fallen substantially during the past three years. The age-adjusted death rate from AIDS declined 48 percent from 1996 to 1997; [16] similar decreases have been noted in western Europe and Australia.[17,18] These trends are due to several factors, including improved prophylaxis against opportunistic infections and improved treatment, the growing experience among health professionals in caring for HIV-infected patients, improved access to health care, and the decrease in the number of new HIV infections due to prevention efforts and to the fact that a substantial proportion of persons with high-risk behavior are already infected.

However, the most influential factor has clearly been the increased use of potent anti-HIV drugs, generally administered in combinations of three or more agents and usually including a protease inhibitor.[17,19-21] Such combinations are known as highly active antiretroviral therapy. The development of therapies for HIV infection has been remarkably successful, reflecting an effective synergy among government, industry, and academia. Sixteen anti-HIV drugs are now licensed by the U.S. Food and Drug Administration. These drugs have had dramatic effects in reversing the extent of illness in many patients with advanced disease, as well as in preventing the progression of disease in those who are relatively healthy.

Consensus guidelines have been developed for the use of highly active antiretroviral therapy in adults and adolescents, as well as in children and in HIV-infected pregnant women. [22-24] These guidelines, when appropriately applied, have greatly improved the prognosis for HIV-infected people and have markedly reduced the risk of HIV transmission from mother to baby.

Despite the enormous beneficial effects of highly active antiretroviral therapy, many HIV-infected people have unfortunately not had adequate responses to the regimens, cannot tolerate the toxic effects, or have difficulty complying with treatment that involves large numbers of pills, myriad interactions with other drugs, and complicated dosing schedules in which intake of food and liquids must be taken into account.[22] Even in patients who are successfully treated with highly active antiretroviral therapy and have extremely low levels of HIV-1 ribonucleic acid (RNA) in plasma, the virus persists in sanctuaries where the drugs cannot reach it or in a latent form on which drugs haveno effect.[25-28] In addition, the emergence of strains of HIV that are resistant to currently available drugs is a widespread and growing problem.[29]

Although there is evidence of improvement in immune-system function in most patients who receive combination antiretroviral therapy, complete normalization of the immune system and complete eradication of the virus from the body appear unlikely with currently available therapies. The persistence of latent HIV despite therapy that successfully suppresses detectable levels of HIV-1 RNA in plasma is particularly problematic and suggests that lifelong treatment may be necessary with drugs that are currently expensive and difficult to tolerate for prolonged periods.[30-34] In patients in whom plasma HIV-1 RNA had been suppressed by highly active antiretroviral therapy to below detectable levels for a median of 390 days, levels invariably rebounded within three weeks after the cessation of therapy.[35]

Therefore, the development of a new generation of therapies remains a major priority. Currently, all licensed antiretroviral medications are directed at one of two viral enzymes, reverse transcriptase or protease. Many new treatment strategies are being developed and tested, including the use of drugs that prevent the virus from entering a cell and those that prevent the integration of the provirus into nuclear DNA. In addition, approaches to

purging the virus from its latent reservoirs in certain cells and tissues are being vigorously pursued, as are methods to boost HIV-specific immune responses.[36]

**Prevention of HIV Infection**

In developing countries in which the per capita allocation for health care spending may be only a few dollars a year, anti-HIV therapies are invariably beyond the reach of all but the privileged few. This situation underscores the need for effective, low-cost tools for HIV prevention that can be used in these settings as well as in the United States and other developed countries. Even if such therapies were feasible on a global scale, it is clear that treatment is not the solution to the global HIV problem. Unlike microbial scourges, such as malaria and tuberculosis (among many others), for which there is very little that people can do to prevent infection, HIV infection in adults is entirely preventable by behavior modification. Researchers have shown that several approaches to prevention, when properly executed, can be effective. These approaches include education and behavior modification, the promotion and provision of condoms, the treatment of other sexually transmitted diseases, drug-abuse treatment (for example, methadone maintenance for injection-drug users), access to clean needles and syringes for injection-drug users, and the use of antiretroviral drugs to interrupt the transmission of the virus from mother to infant.[37]

The use of antiretroviral drugs in pregnant women with HIV infection and their infants is an extraordinarily successful prevention strategy.[38] The rate of mother-to-child transmission of HIV in the United States has been cut to negligible levels among women and infants treated with an extended regimen of zidovudine therapy. Recent studies by the CDC, the National Institutes of Health (NIH), and others have shown that substantially shorter regimens of antiretroviral drugs, which would be more feasible in poorer countries, can also reduce perinatal HIV transmission dramatically.[39-40] A brief and affordable regimen of therapy administered to the mother around the time of delivery could potentially prevent HIV infection in hundreds of thousands of babies per year. An interim analysis of a study in Uganda indicates that two doses of nevirapine—one given to the mother at the onset of labor and one given to the infant within 72 hours after birth—can markedly reduce the incidence of perinatal transmission of HIV.[41]

Other methods of preventing HIV transmission may also help slow the epidemic of HIV and AIDS. For example, researchers are developing and testing topical microbicides, substances that a woman could use in her vagina before sexual intercourse to prevent the transmission of HIV and other sexually transmitted diseases.[42] UNAIDS and other organizations have also facilitated the widespread use of the female condom in Africa. These interventions may help empower women to protect themselves in situations in which they are unable to avoid sexual relations with HIV-infected partners or cannot persuade their partners to use a condom.

**Development of an HIV Vaccine**

Historically, vaccines have provided a safe, cost-effective, and efficient means of preventing illness, disability, and death from infectious diseases.[43] The solution to the HIV pandemic is the development and availability of a safe and effective vaccine against the infection. Indeed, such a goal remains the highest priority of AIDS research. A major scientific obstacle to the accomplishment of this goal has been the difficulty in establishing the precise correlates of protective immunity against HIV infection. To speed the pace of discovery, many public and private agencies have dramatically increased the resources devoted to research on HIV vaccines. For example, at the NIH, funding for HIV-vaccine research rose from $100.5 million in fiscal year 1995 to an estimated $194.1 million in fiscal year 1999. To date, more than 3,000 uninfected volunteers have enrolled in more than 50 HIV-vaccine studies sponsored by the NIH (including two phase 2 intermediate-sized trials), involving 27 vaccines.

As part of a broad portfolio of research, recent NIH-supported studies have assessed so-called vectored vaccines: harmless viruses (e.g., canarypox) that are genetically altered to make HIV proteins. These vaccines have been administered to volunteers in combination with a

separate vaccine made of a purified HIV envelope protein. Results have been encouraging. In phase 1 and phase 2 studies, the combination approach has appeared safe and has evoked both cellular and humoral immune responses that may have a role in providing protection from HIV infection.[44] Three vectors, as well as other HIV proteins, are currently being compared to determine which combination produces the most vigorous immune response.

Meanwhile, a large-scale study of a vaccine based on the surface proteins of two strains of HIV was recently undertaken in the United States by a private company, with an additional phase 3 study to be conducted in Thailand.[45] Finally, a phase 1 trial of canarypox-vectored vaccine for HIV infection has been initiated in Uganda in a growing effort to involve scientists from developing countries in the research effort.

### Conclusions

The HIV pandemic has posed a formidable challenge to the biomedical-research and public health communities of the world. What began as a handful of recognized cases among homosexual men in the United States has become a global pandemic of such proportions that it clearly ranks as one of the most destructive microbial scourges in history. We are at a pivotal point in the evolution of this historic event. Biomedical research has provided the tools for the development of treatments as well as a still elusive vaccine. It has become apparent over the past few years that minimizing the destructive impact of this epidemic will require partnerships between the public and private sectors as well as a stronger political will among the nations of the world. Unless methods of prevention, with or without a vaccine, are successful, the worst of the global pandemic will occur in the 21st century.

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# Reaching a Turning Point

By Peter Piot
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*While AIDS in Africa has become a full-blown development catastrophe, an historic line has been crossed in the battle against the deadly disease as political leaders speak out and new international resources are mobilized.*

AIDS has become the number one killer in Africa, taking more lives—10 times more—than the wars on that continent in 1998. Since the pandemic began, more than 16 million people have died worldwide and 13.7 million of them have been Africans, according to a global survey on the disease conducted by UNAIDS and the World Health Organization (WHO) at the end of 1999.

These staggering statistics mean that AIDS stands to reverse the developmental progress Africans have made over the last two decades in health care, education, life expectancy, economic growth, and human security. AIDS in Africa has become a full-blown development catastrophe.

The facts emerged starkly from a survey conducted by the United Nations Development Program (UNDP) in late 1999. African nations suffered downward changes this year in the Human Development Index, a ranking based on levels of health, wealth, and education. Almost all of the major changes in rank could be attributed to declining life expectancy as a result of AIDS:

- Average life expectancy at birth in southern Africa, which climbed from 44 in the early 1950s to 59 in the early 1990s, is expected to drop back to 45 sometime between 2005 and 2010.
- The United Nations Development Program estimates that fewer than 50 percent of South Africans currently alive can expect to reach the age of 60, compared with an average of 70 percent for all developing countries and 90 percent for industrialized countries.

Yet even amidst these grim figures I am optimistic. I believe we are now at a turning point in the 20-year history of the AIDS epidemic in Africa. Everywhere I go, I hear top African leaders speaking out about AIDS as the major threat to the continent's development.

In Ghana two months ago, for example, First Lady Nana Konadu Agyeman Rawlings participated in the launch of a new female condom program, calling the introduction of these prophylactics a "long-awaited global dream come true for Ghanaians."

I believe an historic line has been crossed in our battle against this disease as political leaders speak out and new domestic resources are directed to prevention and care programs and new international resources are being mobilized. When governments begin to focus on AIDS as a national priority, tough decisions can be made to create more favorable conditions for those affected by the epidemic, and establish better protections for the poorest and the most vulnerable.

The International Partnership Against AIDS (IPAA) in Africa is working toward those goals in a cooperative effort involving national governments, international organizations, and private sector

groups. African governments are leading broad-based national responses. United Nations organizations are coordinating the global response and providing program and financial support to country-level efforts. Donor governments are also supporting action at all levels, providing input into substantive development of the partnership in addition to financial assistance. The private sector is providing expertise and resources to help turn the epidemic around in the workplace, among organized labor, and in the business community. And, finally, nongovernmental organizations, including groups of people living with HIV, are working to ensure ownership of the partnership within local civil society and to strengthen regional and country networks.

The partnership's mission is as ambitious as it is simple. Over the next decade, it will help reduce the number of new HIV infections in Africa, promote care for those who suffer from the virus, and mobilize society to halt the advance of AIDS. Specific goals promoted by the partnership include:

- giving young people aged 15-24 the information and skills they need to prevent infection;
- providing HIV-positive pregnant women with access to HIV testing and counseling and to drugs that can increase their chances of having healthy babies;
- including people living with HIV/AIDS actively in all aspects of social, economic, and political life;
- furnishing AIDS orphans with the means to grow up and lead meaningful lives;
- providing HIV-positive people with access to care in accordance with locally established standards;
- ensuring that national and international firms operating in Africa are fully involved in the fight against the epidemic;
- encouraging decentralization of HIV/AIDS programs and participation of communities;
- promoting an end to stigma and discrimination by social and legal means.

Governments in a dozen African nations have already accelerated their own actions in order to contain the disease. Burkina Faso and Cote d'Ivoire have established a national solidarity fund, for example.

The African partnership will also better enable these nations to exchange ideas on the "best practices" already emerging in the sub-Saharan region. In Uganda, sex and health education information and in-school HIV prevention programs for teenagers and youth have contributed to a demonstrated reduction in the rate of infection—a decline as high as 40 percent in urban areas.

In Senegal, a rapid, broad-based response to the epidemic, supported by both Islamic and Christian leaders, has kept the rate of HIV infection below 2 percent. Recent behavioral surveys indicate that more than 60 percent of men and 40 percent of women aged 15-24 are now using condoms in casual sexual encounters.

The IPAA and partnerships like it will be the foundation on which to build more effective resistance to this epidemic. Individual sectors can not be successful alone; government, business, educators, and all society's players must be engaged to achieve success. We see it happening not only in these African programs, but elsewhere too—the cooperation between government, nongovernmental organizations, and others is working.

Thailand's government demonstrated the importance of partnership when it launched an impressive program after a 1989 study showed that 44 percent of the sex workers in Chiang Mai were HIV positive. Despite the illegal status of prostitution in Thailand, the government worked with brothel owners to urge 100 percent condom use in brothels. They launched mass media campaigns to encourage respect for women and discourage men from visiting sex workers, and improved access to care for people living with AIDS. As a result, HIV prevalence has declined significantly—especially among young people.

Success stories like these can help other nations

and communities shape future programs. We need to work harder to ensure that "best practices" in the fight against this disease are shared.

We have learned that success in reducing transmission is not random; the most effective HIV prevention programs have key features. They benefit from political commitment and work on many levels at the same time, promoting safe behavior and providing care and support for people affected by HIV. They offer a broad range of prevention measures, including access to cheap and good quality condoms, confidential counseling and testing, prevention of mother-to-child transmission, and early treatment for other sexually transmitted diseases, which multiply the risk of infection with HIV. Other critical elements are long-term education and mass media campaigns to ensure broad public awareness about HIV. Finally, the communities affected and people living with HIV are actively involved in the planning and execution of AIDS programs.

Attention to youth, during their most sexually active and experimental years, is critical. About half of all the new cases of HIV infection involve young people between 15 and 24 years of age. While the young may be the most vulnerable population, we also find that they are the most receptive to prevention messages and will adopt more responsible behaviors.

Besides explanations of what the disease is and how it's transmitted, it is also important to challenge harmful concepts of masculinity, including the way adult men look on risk and sexuality and how boys are socialized to become men. At the same time, young women must be educated to recognize their vulnerability to infection, their responsibility to protect themselves, and their right to insist upon protection in sexual relationships.

Prevention programs will help us contain future HIV infections, but we must not forget the needs of more than 33 million infected people who need our care today. The UNAIDS Secretariat and WHO. are trying to provide well-founded guidance and support to countries to assist in building health systems that can respond to the epidemic.

To that end, together with WHO., UNICEF, the World Bank, and UNFPA, we have opened a new dialogue with five international pharmaceutical companies to explore ways to accelerate and improve the provision of HIV/AIDS-related care and treatment in developing countries. The pharmaceutical companies involved—Boehringer Ingelheim, Bristol-Myers Squibb, Glaxo Wellcome, Merck & Co., and F. Hoffmann-La Roche—have indicated their willingness to work with other stakeholders to find ways to broaden access to care and treatment, while ensuring rational, affordable, safe, and effective use of drugs for HIV/AIDS related illnesses. The companies are offering, individually, to improve access to, and availability of, a range of medicines. Other pharmaceutical companies have also expressed interest in cooperating in this endeavor.

But that's but one step in improving the lives of HIV infected persons. We need to ensure that the lowering of the price of some medicines stimulates the development of more comprehensive care strategies. We recognize that even at heavily discounted prices, the cost of antiretroviral therapies will continue to be beyond the reach of public sector subsidies and therefore unavailable to the majority.

This is a time of great opportunity when it comes to AIDS in the developing world—a time of political opportunity, as exemplified by the strong commitment to respond to AIDS by numerous heads of state, and by the debates on AIDS in Africa at the U.N. Security Council in January 2000, initiated by Ambassador Richard Holbrooke, and at the World Bank/IMF Development Committee last April. It is also a time of opportunity in terms of resources, with the U.S. government, as well as other donors, greatly increasing funding for AIDS programs in the developing world. Africa alone will need $1,600 to $2,600 million per year to ensure effective prevention programs and basic care.

But amidst all this analysis of costs, programs, strategies, and multi-sectoral cooperation, there is one commodity that does not emerge, perhaps the most precious one. That is hope, which is certainly critical to reversing this appalling epidemic. It is my role, and that of all those engaged in this struggle, to keep that hope alive.

# reports & documents

## A Primer: HIV Infection and AIDS

*The following fact sheet, prepared by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health, provides basic information about AIDS, including how it is transmitted, diagnosed, treated, and prevented.*

**Overview**

AIDS was first reported in the United States in 1981 and has since become a major worldwide epidemic. AIDS is caused by the human immunodeficiency virus (HIV). By killing or damaging cells of the body's immune system, HIV progressively destroys the body's ability to fight infections and certain cancers. People diagnosed with AIDS may get life-threatening diseases called opportunistic infections, which are caused by microbes such as viruses or bacteria that usually do not make healthy people sick.

More than 700,000 cases of AIDS have been reported in the United States since 1981, and as many as 900,000 Americans may be infected with HIV. The epidemic is growing most rapidly among minority populations and is a leading killer of African American males. According to the U.S. Centers for Disease Control and Prevention (CDC), AIDS affects six times more African Americans than whites and three times more Hispanics than whites.

**Transmission**

HIV is spread most commonly by having sex with an infected partner. The virus can enter the body through the lining of the vagina, vulva, penis, rectum, or mouth during sex.

HIV also is spread through contact with infected blood. Before blood was screened for evidence of HIV infection and before heat-treating techniques to destroy HIV in blood products were introduced, HIV was transmitted through transfusions of contaminated blood or blood components. Today, because of blood screening and heat treatment, the risk of getting HIV from such transfusions is extremely small.

HIV frequently is spread among injection drug users by the sharing of needles or syringes contaminated with very small quantities of blood from someone infected with the virus. It is rare, however, for a patient to give HIV to a health care worker or vice-versa by accidental sticks with contaminated needles or other medical instruments.

Women can transmit HIV to their babies during pregnancy or birth. Approximately one-quarter to one-third of all untreated pregnant women infected with HIV will pass the infection to their babies. HIV also can be spread to babies through the breast milk of mothers infected with the virus. If the mother takes the drug AZT during pregnancy, she can reduce significantly the chances that her baby will be infected with HIV. If doctors treat mothers with AZT and deliver their babies by cesarean section, the chances of the baby being infected can be reduced to a rate of 1 percent.

A study sponsored by NIAID in Uganda found a highly effective and safe drug regimen for preventing transmission of HIV from an infected mother to her newborn that is more affordable and practical than any other examined to date. Interim results from the study show that a single oral dose of the antiretroviral drug nevirapine (NVP) given to an HIV-infected woman in labor and another to her baby within three days of birth reduces the transmission rate by half compared with a similar short course of AZT.

Although researchers have detected HIV in the saliva of infected individuals, no evidence exists that the virus is spread by contact with saliva. Laboratory studies reveal that saliva has natural properties that limit the power of HIV to infect. Research studies of people infected with HIV have found no evidence that the virus is spread to others through saliva such as by kissing. (Know one knows, however, whether so-called "deep" kissing, involving the exchange of large amounts of saliva, or oral intercourse increase the risk of infection). Scientists also have found no evidence that HIV is spread through sweat, tears, urine, or feces.

Studies of families of HIV-infected people have shown clearly that HIV is not spread through casual contact such as the sharing of food utensils, towels and bedding, swimming pools, telephones, or toilet seats. HIV is not spread by biting insects such as mosquitoes or bedbugs.

HIV can infect anyone who practices risky behaviors such as: sharing drug needles or syringes; having sexual contact with an infected person without using a condom or with someone whose HIV status is unknown.

Having a sexually transmitted disease such as syphilis, genital herpes, chlamydial infection, gonorrhea, or bacterial vaginosis appears to make people more susceptible to acquiring HIV infection during sex with infected partners.

**Early Symptoms**

Many people do not develop any symptoms when they first become infected with HIV. Some people, however, have a flu-like illness within a month or two after exposure to the virus. This illness may include fever, headache, tiredness, and enlarged lymph nodes (organs of the immune system easily felt in the neck and groin). These symptoms usually disappear within a week to a month and are often mistaken for those of another viral infection.

More persistent or severe symptoms may not surface for a decade or more after HIV first enters the body in adults, or within two years in children born with HIV infection. This period of "asymptomatic" infection is highly individual. Some people may begin to have symptoms as soon as a few months, while others may be symptom-free for more than 10 years. During the asymptomatic period, however, the virus is actively multiplying, infecting, and killing cells of the immune system. HIV's effect is seen most obviously in a decline in the blood levels of CD4+ T cells (also called T4 cells)—the immune system's key infection fighters. At the beginning of its life in the human body, the virus disables or destroys these cells without causing symptoms.

As the immune system deteriorates, a variety of complications start to take over. For many people, their first sign of infection is large lymph nodes or "swollen glands" that may be enlarged for more than three months. Other symptoms, often experienced months to years before the onset of AIDS, include: lack of energy, weight loss, frequent fevers and sweats, persistent or frequent yeast infections (oral or vaginal), persistent skin rashes or flaky skin, pelvic inflammatory disease in women that does not respond to treatment, or short-term memory loss.

Some people develop frequent and severe herpes infections that cause mouth, genital, or anal sores,

or a painful nerve disease called shingles. Children may grow slowly or often be sick.

**AIDS**

The term AIDS applies to the most advanced stages of HIV infection. Official criteria for the definition of AIDS are developed by CDC in Atlanta, Georgia., which is responsible for tracking the spread of AIDS in the United States.

CDC's definition of AIDS includes all HIV-infected people who have fewer than 200 CD4+ T cells per cubic millimeter of blood. (Healthy adults usually have CD4+ T-cell counts of 1,000 or more.) In addition, the definition includes 26 clinical conditions that affect people with advanced HIV disease. Most of these conditions are opportunistic infections, which rarely cause harm in healthy people. In people with AIDS these infections are often severe and sometimes fatal because the immune system is so ravaged by HIV that the body cannot fight off certain bacteria, viruses, fungi, parasites, and other microbes.

Opportunistic infections common in people with AIDS cause symptoms such as: coughing and shortness of breath, seizures and lack of coordination, difficult or painful swallowing, mental symptoms such as confusion and forgetfulness, severe and persistent diarrhea, vision loss, nausea, abdominal cramps, vomiting, weight loss, extreme fatigue, severe headaches, and coma.

Although children with AIDS may get the same opportunistic infections as adults with the disease, they also experience severe forms of the bacterial infections that all children may get, such as conjunctivitis (pink eye), ear infections, and tonsillitis.

People with AIDS are particularly prone to developing various cancers, especially those caused by viruses such as Kaposi's sarcoma and cervical cancer, or cancers of the immune system known as lymphomas. These cancers are usually more aggressive and difficult to treat in people with AIDS. Signs of Kaposi's sarcoma in light-skinned people are round brown, reddish, or purple spots that develop in the skin or in the mouth. In dark-skinned people, the spots are more pigmented.

Many people are so debilitated by the symptoms of AIDS that they cannot hold steady employment or do household chores. Other people with AIDS may experience phases of intense life-threatening illness followed by phases in which they function normally.

A small number of people (fewer than 50) initially infected with HIV ten or more years ago have not developed symptoms of AIDS. Scientists are trying to determine what factors may account for their lack of progression to AIDS, such as particular characteristics of their immune systems or whether they were infected with a less aggressive strain of the virus or if their genes may protect them from the effects of HIV. Scientists hope that understanding the body's natural method of control may lead to ideas for protective HIV vaccines and use of vaccines to prevent the disease from progressing.

**Diagnosis**

Because early HIV infection often causes no symptoms, a doctor or other health care worker usually can diagnose it by testing a person's blood for the presence of antibodies (disease-fighting proteins) to HIV. HIV antibodies generally do not reach levels in the blood that the doctor can see until one to three months following infection, and it may take the antibodies as long as six months to be produced in quantities large enough to show up in standard blood tests.

People exposed to the virus should get an HIV test as soon as they are likely to develop antibodies to the virus. By getting tested early, they can get the right treatment at a time when their immune systems are most able to combat HIV and thus prevent the emergence of certain opportunistic infections (see **Treatment** below). Early testing also alerts HIV-infected people to avoid high-risk behaviors that could spread the virus to others.

Doctors diagnose HIV infection by using two different types of antibody tests, ELISA and Western Blot. If a person is highly likely to be infected with HIV and yet both tests are negative, a doctor may look for HIV itself in the blood. The person also may be told to repeat antibody testing at a later date, when antibodies to HIV are more likely to have developed.

Babies born to mothers infected with HIV may or may not be infected with the virus, but all carry their mothers' antibodies to HIV for several months. If these babies lack symptoms, a definitive diagnosis of HIV infection using standard antibody tests cannot be made until after 15 months of age. By then, babies are unlikely to still carry their mothers' antibodies and will have produced their own, if they are infected. New technologies to detect HIV itself are being used to more accurately determine HIV infection in infants between ages 3 months and 15 months. A number of blood tests are being evaluated to determine if they can diagnose HIV infection in babies younger than 3 months.

**Treatment**

When AIDS first surfaced in the United States, no medicines were available to combat the underlying immune deficiency and few treatments existed for the opportunistic diseases that resulted. Over the past 10 years, however, researchers have developed treatments to fight both HIV infection and its associated infections and cancers.

The Food and Drug Administration has approved a number of drugs for treating HIV infection. The first group of drugs used to treat HIV infection, called nucleoside reverse transcriptase (RT) inhibitors, interrupt an early stage of the virus making copies of itself. Included in this class of drugs (called nucleoside analogs) are AZT (also known as zidovudine or ZDV), ddC (zalcitabine), ddI (dideoxyinosine), d4T (stavudine), and 3TC (lamivudine). These drugs may slow the spread of HIV in the body and delay the onset of opportunistic infections.

More recently, a second class of drugs has been approved for treating HIV infection. These drugs, called protease inhibitors, interrupt virus replication at a later step in its life cycle. They include ritonavir (Norvir), saquinivir (Invirase), indinavir (Crixivan), amprenivir (Agenerase), and nelfinavir (Viracept). Because HIV can become resistant to both classes of drugs, combination treatment using both is necessary to effectively suppress the virus.

The risk of HIV transmission from a pregnant woman to her baby is significantly reduced if she takes AZT during pregnancy, labor, and delivery, and her baby takes it for the first six weeks of life. Currently available antiretroviral drugs do not cure people of HIV infection or AIDS, however, and they all have side effects that can be severe. Some of the nucleoside RT inhibitors may cause a depletion of red or white blood cells, especially when taken in the later stages of the disease. Some may also cause an inflammation of the pancreas and painful nerve damage. Other complications, including lactic acidosis and severe hepatomegaly (enlarged liver) with steatosis (fatty liver) that may result in liver failure and death have also been reported with the use of antiretroviral nucleoside analogs alone or in combination, including AZT, ddI, ddC, 3TC, and abacavir.

The most common side effects associated with protease inhibitors include nausea, diarrhea, and other gastrointestinal symptoms. In addition, protease inhibitors can interact with other drugs resulting in serious side effects.

Researchers have credited highly active antiretroviral therapy, or HAART, as being a major factor in reducing the number of deaths from AIDS in the United States. by 47 percent in 1997. HAART is a combination of several drugs to treat patients. These drugs include reverse transcriptase inhibitors and protease inhibitors. Patients who are newly infected with HIV as well as AIDS patients can take the combination.

HAART is not a cure. The health of HIV and AIDS patients has benefited dramatically by combining protease inhibitors with other AIDS drugs, but there are drawbacks. Also, though HIV may not be found in the patients successfully treated with HAART, researchers know that it is still present, lurking in hiding places such as the lymph nodes, the brain, testes, and the retina of the eye.

A number of drugs are available to help treat opportunistic infections to which people with HIV are especially prone. These drugs include foscarnet and ganciclovir, used to treat cytomegalovirus eye infections, fluconazole to treat yeast and other fungal infections, and rimethopim/sulfamethoxazole (TMP/SMX) or pentamidine to treat *Pneumocystis carinii* pneumeonia (PCP).

In addition to antiretroviral therapy, adults with HIV whose CD4+ T-cell counts drop below 200 are given treatment to prevent the occurrence of PCP, which is one of the most common and deadly opportunistic infections associated with HIV.

**Prevention**

Because no vaccine for HIV is available, the only way to prevent infection by the virus is to avoid behaviors that put a person at risk of infection, such as sharing needles and having unprotected sex.

Many people infected with HIV have no symptoms. Therefore, there is no way of knowing with certainty whether a sexual partner is infected unless he or she has repeatedly tested negative for the virus and—has not engaged in any risky behavior.

People should either abstain from having sex or use latex condoms, which may offer partial protection, during oral, anal, or vaginal sex. Only condoms made of latex should be used, and water-based lubricants should be used with latex condoms.

Although some laboratory evidence shows that spermicides can kill HIV, researchers have not found that these products can prevent a person from getting HIV.

**Research**

NIAID-supported investigators are conducting an abundance of research on HIV infection, including the development and testing of HIV vaccines and new therapies for the disease and some of its associated conditions. Twenty-eight HIV vaccines are being tested in people, and many drugs for HIV infection or AIDS-associated opportunistic infections are either being developed or being tested. Researchers also are investigating exactly how HIV damages the immune system. This research is suggesting new and more effective targets for drugs and vaccines. NIAID-supported investigators also continue to trace how the disease progresses in different people.

Scientists are investigating and testing chemical barriers, such as topical microbicides, that people can use in the vagina or in the rectum during sex to prevent HIV transmission. They also are looking at other ways to prevent transmission such as controlling sexually transmitted diseases and modifying people's behavior as well as ways to prevent transmission from mother to child.

Further information is available at http://www.niaid.nih.gov/

# The Evidence Linking HIV to AIDS

*The following fact sheet, prepared by the U.S National Institute of Allergy and Infectious Diseases(NIAID), a component of the National Institutes of Health, refutes many of the myths surrounding the AIDS epidemic.*

**MYTH:** HIV antibody testing is unreliable.

**FACT:** Diagnosis of infection using antibody testing is one of the best-established concepts in medicine. HIV antibody tests exceed the performance of most other infectious disease tests in both sensitivity (the ability of the screening test to give a positive finding when the person tested truly has the disease) and specificity (the ability of the test to give a negative finding when the subjects tested are free of the disease under study). Current HIV antibody tests have sensitivity and specificity in excess of 98 percent and are therefore extremely reliable (WHO 1998; Sloand et al. JAMA 1991;266: 2861).

Progress in testing methodology has also enabled detection of viral genetic material, antigens, and the virus itself in body fluids and cells. While not widely used for routine testing due to high cost and requirements in laboratory equipment, these direct testing techniques have confirmed the validity of the antibody tests (Jackson et al. J Clin Microbiol 1990;28:16; Busch et al. NEJM 1991;325:1; Silvester et al. J Acquir Immune Defic Syndr Hum Retrovirol 1995;8:411; Urassa et al. J Clin Virol 1999;14:25; Nkengasong et al. AIDS 1999;13:109; Samdal et al. Clin Diagn Virol 1996;7:55).

**MYTH:** There is no AIDS in Africa. AIDS is nothing more than a new name for old diseases.

**FACT:** The diseases that have come to be associated with AIDS in Africa—such as wasting syndrome, diarrheal diseases, and tuberculosis (TB)—have long been severe burdens there. However, high rates of mortality from these diseases, formerly confined to the elderly and malnourished, are now common among HIV-infected young and middle-aged people (UNAIDS, 1999).

For example, in a study in Cote d'Ivoire, HIV-seropositive individuals with pulmonary TB were 17 times more likely to die within six months than HIV-seronegative individuals with pulmonary TB (Ackah et al. Lancet 1995; 345:607). In Malawi, mortality over three years among children who had received recommended childhood immunizations and who survived the first year of life was 9.5 times higher among HIV-seropositive children than among HIV-seronegative children. The leading causes of death were wasting and respiratory conditions (Taha et al. Pediatr Infect Dis J 1999;18:689). Elsewhere in Africa, findings are similar.

**MYTH:** HIV cannot be the cause of AIDS because researchers are unable to explain precisely how HIV destroys the immune system.

**FACT:** A great deal is known about the pathogenesis of HIV disease, even though important details remain to be elucidated. However, a complete understanding of the pathogenesis of a disease is not a prerequisite to

knowing its cause. Most infectious agents have been associated with the disease they cause long before their pathogenic mechanisms have been discovered. Because research in pathogenesis is difficult when precise animal models are unavailable, the disease-causing mechanisms in many diseases, including tuberculosis and hepatitis B, are poorly understood. The critics' reasoning would lead to the conclusion that *M. tuberculosis* is not the cause of tuberculosis or that hepatitis B virus is not a cause of liver disease (Evans. Yale J Biol Med 1982;55:193).

**MYTH:** AZT and other antiretroviral drugs, not HIV, cause AIDS.

**FACT:** The vast majority of people with AIDS never received antiretroviral drugs, including those in developed countries prior to the licensure of AZT in 1987, and people in developing countries today where very few individuals have access to these medications (UNAIDS, 1999).

As with medications for any serious diseases, antiretroviral drugs can have toxic side effects. However, there is no evidence that antiretroviral drugs cause the severe immunosuppression that typifies AIDS, and abundant evidence that antiretroviral therapy, when used according to established guidelines, can improve the length and quality of life of HIV-infected individuals (Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents, 2000).

In the 1980s, clinical trials enrolling patients with AIDS found that AZT given as single-drug therapy conferred a modest (and short-lived) survival advantage compared to placebo. Among HIV-infected patients who had not yet developed AIDS, placebo-controlled trials found that AZT given as single-drug therapy delayed, for a year or two, the onset of AIDS-related illnesses. Significantly, long-term follow-up of these trials did not show a prolonged benefit of AZT, but also never indicated that the drug increased disease progression or mortality. The lack of excess AIDS cases and death in the AZT arms of these placebo-controlled trials effectively counters the argument that AZT causes AIDS (NIAID, 1995).

Subsequent clinical trials found that patients receiving two-drug combinations had up to 50 percent increases in time to progression to AIDS and in survival when compared to people receiving single-drug therapy. In more recent years, three-drug combination therapies have produced another 50 percent to 80 percent improvement in progression to AIDS and in survival when compared to two-drug regimens in clinical trials (Deeks, Volberding, 1999). Use of potent anti-HIV combination therapies has contributed to dramatic reductions in the incidence of AIDS and AIDS-related deaths in populations where these drugs are widely available, an effect which clearly would not be seen if antiretroviral drugs caused AIDS (Figure 1; CDC. HIV AIDS Surveillance Report 1999;11[2]:1; CDC MMWR 1999;48:1; Palella et al. NEJM 1998;338:853; Mocroft et al. Lancet 1998;352:1725; Vittinghoff et al. J Infect Dis 1999;179:717; Detels et al. JAMA 1998;280:1497).

**MYTH:** Behavioral factors such as recreational drug use and multiple sexual partners account for AIDS.

**FACT:** The proposed behavioral causes of AIDS, such as multiple sexual partners and long-term recreational drug use, have existed for many years. The epidemic of AIDS, characterized by the occurrence of formerly rare opportunistic infections such as Pneumocystis carinii pneumonia (PCP), did not occur in the United States until a previously unknown human retrovirus—HIV—spread through certain communities (NIAID, 1995a; NIAID, 1995b).

Compelling evidence against the hypothesis that behavioral factors cause AIDS comes from recent studies that have followed cohorts of homosexual men for long periods of time and found that only HIV-seropositive men develop AIDS.

In a prospectively studied cohort in Vancouver, 715 homosexual men were followed for a median of 8.6 years. Among 365 HIV-positive individuals, 136 developed AIDS. No AIDS-defining illnesses occurred among 350 seronegative men despite the fact that these men reported appreciable use of inhalable nitrites ("poppers") and other recreational drugs, and frequent receptive anal intercourse (Schechter et al. Lancet 1993;341:658).

Other studies show that among homosexual men and injection-drug users, the specific immune deficit that leads to AIDS—a progressive and sustained loss of CD4+ T cells—is extremely rare in the absence of other immunosuppressive conditions. For example, in the Multicenter AIDS Cohort Study, more than 22,000 T-cell determinations in 2,713 HIV-seronegative homosexual men revealed only one individual with a CD4+ T-cell count persistently lower than 300 cells per cubic millimeter (mm3) of blood, and this individual was receiving immunosuppressive therapy (Vermund et al. NEJM 1993;328:442).

In a survey of 229 HIV-seronegative injection-drug users in New York City, mean CD4+ T-cell counts of the group were consistently more than 1000 cells/mm3 of blood. Only two individuals had two CD4+ T-cell measurements of less than 300/mm3 of blood, one of whom died with cardiac disease and non-Hodgkin's lymphoma listed as the cause of death (Des Jarlais et al. J Acquir Immune Defic Syndr 1993;6:820).

**MYTH:** AIDS among transfusion recipients is due to underlying diseases that necessitated the transfusion, rather than to HIV.

**FACT:** This notion is contradicted by a report by the U.S. Transfusion Safety Study Group (TSSG), which compared HIV-negative and HIV-positive blood recipients who had been given transfusions for similar diseases. Approximately three years after the transfusion, the mean CD4+ T-cell count in 64 HIV-negative recipients was 850/mm3 of blood, while 111 HIV-seropositive individuals had average CD4+ T-cell counts of 375/mm3 of blood. By 1993, there were 37 cases of AIDS in the HIV-infected group, but not a single AIDS-defining illness in the HIV-seronegative transfusion recipients (Donegan et al. Ann Intern Med 1990;113:733; Cohen. Science 1994;266:1645).

**MYTH:** High usage of clotting factor concentrate, not HIV, leads to CD4+ T-cell depletion and AIDS in hemophiliacs.

**FACT:** This view is contradicted by many studies. For example, among HIV-seronegative patients with hemophilia A enrolled in the Transfusion Safety Study, no significant differences in CD4+ T-cell counts were noted between 79 patients with no or minimal factor treatment and 52 with the largest amount of lifetime treatments. Patients in both groups had CD4+ T cell-counts within the normal range (Hasset et al. Blood 1993;82:1351). In another report from the Transfusion Safety Study, no instances of AIDS-defining illnesses were seen among 402 HIV-seronegative hemophiliacs who had received factor therapy (Aledort et al. NEJM 1993;328:1128).

In a cohort in the United Kingdom, researchers matched 17 HIV-seropositive hemophiliacs with 17 HIV-seronegative hemophiliacs with regard to clotting factor concentrate usage over a 10-year period. During this time, 16 AIDS-defining clinical events occurred in nine patients, all of whom were HIV-seropositive. No AIDS-defining illnesses occurred among the HIV-negative patients. In each pair, the mean CD4+ T cell count during follow-up was, on average, 500 cells/mm3 lower in the HIV-seropositive patient (Sabin et al. BMJ 1996;312:207).

Among HIV-infected hemophiliacs, Transfusion Safety Study investigators found that neither the purity nor the amount of Factor VIII therapy had a deleterious effect on CD4+ T cell counts (Gjerset et al., Blood 1994;84:1666). Similarly, the Multicenter Hemophilia Cohort Study found no association between the cumulative dose of plasma concentrate and incidence of AIDS among HIV-infected hemophiliacs (Goedert et al. NEJM 1989;321:1141).

**MYTH:** The distribution of AIDS cases casts doubt on HIV as the cause. Viruses are not gender-specific, yet only a small proportion of AIDS cases are among women.

**FACT:** The distribution of AIDS cases, whether in the United States or elsewhere in the world, invariably mirrors the prevalence of HIV in a population. In the United States, HIV first appeared in populations of homosexual men and injection-drug users, a majority of whom are male. Because HIV is spread primarily through sex or by the exchange of HIV-contaminated needles during injection-drug use, it is not surprising that a majority of U.S. AIDS cases have occurred in men (U.S. Census Bureau, 1999; UNAIDS, 1999).

Increasingly, however, women in the United States are becoming HIV-infected, usually through the exchange of HIV-contaminated needles or sex with an HIV-infected male. The Centers for Disease Control (CDC) estimates that 30 percent of new HIV infections in the United States in 1998 were in women. As the number of HIV-infected women has risen, so too has the number of female AIDS patients in the United States. Approximately 23 percent of U.S. adult/adolescent AIDS cases reported to the CDC in 1998 were among women. In 1998, AIDS was the fifth leading cause of death among women aged 25 to 44 in the United States, and the third leading cause of death among African-American women in that age group (NIAID Fact Sheet: HIV/AIDS Statistics).

In Africa, HIV was first recognized in sexually active heterosexuals, and AIDS cases in Africa have occurred at least as frequently in women as in men. Overall, the worldwide distribution of HIV infection and AIDS between men and women is approximately one to one (U.S. Census Bureau, 1999; UNAIDS, 1999).

**MYTH:** HIV cannot be the cause of AIDS because the body develops a vigorous antibody response to the virus.

**FACT:** This reasoning ignores numerous examples of viruses other than HIV that can be pathogenic after evidence of immunity appears. Measles virus may persist for years in brain cells, eventually causing a chronic neurologic disease despite the presence of antibodies. Viruses such as cytomegalovirus, herpes simplex, and varicella zoster may be activated after years of latency even in the presence of abundant antibodies. In animals, viral relatives of HIV with long and variable latency periods, such as visna virus in sheep, cause central nervous system damage even after the production of antibodies (NIAID, 1995).

Also, HIV is well recognized as being able to mutate to avoid the ongoing immune response of the host (Levy. Microbiol Rev 1993;57:183).

**MYTH:** Only a small number of CD4+ T cells are infected by HIV, not enough to damage the immune system.

**FACT:** New techniques such as the polymerase chain reaction (PCR) have enabled scientists to demonstrate that a much larger proportion of CD4+ T cells are infected than previously realized, particularly in lymphoid tissues. Macrophages and other cell types are also infected with HIV and serve as reservoirs for the virus. Although the fraction of CD4+ T cells that is infected with HIV at any given time is never extremely high (only a small subset of activated cells serve as ideal targets of infection), several groups have shown that rapid cycles of death of infected cells and infection of new target cells occur throughout the course of disease (Richman J Clin Invest 2000;105:565).

**MYTH:** HIV is not the cause of AIDS because many individuals with HIV have not developed AIDS.

**FACT:** HIV disease has a prolonged and variable course. The median period of time between infection with HIV and the onset of clinically apparent disease is approximately 10 years in industrialized countries, according to prospective studies of homosexual men in which dates of seroconversion are known. Similar estimates of asymptomatic periods have been made for HIV-infected blood-transfusion recipients, injection-drug users, and adult hemophiliacs (Alcabes et al. Epidemiol Rev 1993;15:303).

As with many diseases, a number of factors can influence the course of HIV disease. Factors such as age or genetic differences between individuals, the level of virulence of the individual strain of virus, as well as exogenous influences such as co-infection with other microbes may determine the rate and severity of HIV disease expression. Similarly, some people infected with hepatitis B, for example, show no symptoms or only jaundice and clear their infection, while others suffer disease ranging from chronic liver inflammation to cirrhosis and hepatocellular carcinoma. Co-factors probably also determine why some smokers develop lung cancer while others do not (Evans. Yale J Biol Med 1982;55:193; Levy. Microbiol Rev 1993;57:183; Fauci. Nature 1996;384:529).

**MYTH:** Some people have many symptoms associated with AIDS but do not have HIV infection.

**FACT:** Most AIDS symptoms result from the development of opportunistic infections and cancers associated with severe immunosuppression secondary to HIV.

However, immunosuppression has many other potential causes. Individuals who take glucocorticoids and/or immunosuppressive drugs to prevent transplant rejection or for autoimmune diseases can have increased susceptibility to unusual infections, as do individuals with certain genetic conditions, severe malnutrition, and certain kinds of cancers. There is no evidence suggesting that the numbers of such cases have risen, while abundant epidemiologic evidence shows a staggering rise in cases of immunosuppression among individuals who share one characteristic: HIV infection (NIAID, 1995; UNAIDS, 1999).

**MYTH:** The spectrum of AIDS-related infections seen in different populations proves that AIDS is actually many diseases not caused by HIV.

**FACT:** The diseases associated with AIDS, such as PCP and Mycobacterium avium complex (MAC), are not caused by HIV but rather result from the immunosuppression caused by HIV disease. As the immune system of an HIV-infected individual weakens, he or she becomes susceptible to the particular viral, fungal, and bacterial infections common in the community. For example, HIV-infected people in certain Midwestern and mid-Atlantic regions are much more likely than people in New York City to develop histoplasmosis, which is caused by a fungus. A person in Africa is exposed to different pathogens than is an individual in an American city. Children may be exposed to different infectious agents than adults (AIDS Knowledge Base, 1999a; 1999b).

An expanded version of this fact sheet is available on the NIAID website www.niaid.nih.gov/factsheets/evidhiv.htm

*NIAID, a component of the National Institutes of Health (NIH), supports research on AIDS, tuberculosis, malaria, and other infectious diseases, as well as allergies and immunology. NIH is an agency of the U.S. Department of Health and Human Services.*

# additional resources

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# Selected Internet Resources

**XIII International AIDS Conference**
July 9-July 14, 2000, Durban, South Africa.
*http://www.aids2000.com/*

**AIDS Education Global Information System**
The AIDS Education Global Information System (AEGIS) offers news, clinical information, a law library, and other features. Maintained by the Sisters of Saint Elizabeth of Hungary.
*http://www.aegis.com/*

**AIDS Knowledge Base**
This 1999 textbook on HIV disease in adults is from the University of California, San Francisco, and the San Francisco General Hospital.
*http://hivinsite.ucsf.edu/akb/1997/about.html*

**Best of the Net**
Links to HIV/AIDS programs and organizations in various countries selected by editorial reviewers from "Best of the Net" section of the "Journal of the American Medical Association," HIV/AIDS Information Center.
*http://www.ama-assn.org/special/hiv/bestonet/global.htm*

**The Body: An AIDS and HIV Information Resource**
This service of the Body Health Resources Corporation is sponsored in part by several pharmaceutical companies, and provides information in over 250 topical areas.
*http://www.thebody.com/*

**CDC Network**
The National Prevention Information Network (NPIN) is a reference, referral, and distribution service for information on HIV/AIDS, sexually transmitted diseases, and tuberculosis, sponsored by the U.S. Centers for Disease Control and Prevention.
*http://www.cdcnpin.org/*

**The Deadliest Epidemic: AIDS in Africa**
A collection of news articles and links compiled by the Washington Post.
*http://www.washingtonpost.com/wp-dyn/world/issues/aidsinafrica/*

**Guide to NIH HIV/AIDS Information Services**
Prepared by the National Library of Medicine, this is a guide to the many HIV/AIDS programs of the National Institutes of Health, with selected public health service activities.
*http://www.sis.nlm.nih.gov/aids/*

**HIV/AIDS**
Information about development programs to combat HIV/AIDS and infectious diseases from the U.S. Agency for International Development (USAID).
*http://www.info.usaid.gov/pop_health/aids/*

**HIV/AIDS**
The World Health Organization (W.H.O.) provides information on its work combating HIV/AIDS and sexually transmitted infections.
*http://www.who.int/health-topics/hiv.htm*

**HIV/AIDS—A Guide to Resources**
Policy texts and annotated links to U.S. and international resources concerning AIDS and other infectious diseases. From the Office of International Information Programs, U.S. Department of State.
*http://usinfo.state.gov/topical/global/hiv/*

**HIV/AIDS Treatment Information Service (ATIS)**
Coordinated by the U.S. Department of Health and Human Services, ATIS provides information in English and Spanish about federally approved treatment guidelines for HIV and AIDS.
http://www.hivatis.org/

**HIV/AIDS and the World of Work**
Information on the impact of HIV/AIDS on work, productivity, employment, and development. Maintained by the International Labor Organization.
*http://www.ilo.org/public/english/protection/trav/aids/*

**National Institute of Allergy and Infectious Diseases**
The Division of Acquired Immunodeficiency Syndrome (DAIDS) provides information on AIDS vaccine research, clinical trials, and DAIDS-supported programs.
*http://www.niaid.nih.gov/research/Daids.htm*

**Report on the Global HIV/AIDS Epidemic**
Released by the Joint United Nations Programme on HIV/AIDS (UNAIDS) in June, 2000. Available in English, French, and Spanish.
*http://www.unaids.org/epidemic_update/report/*

**UNAIDS**
The homepage of the Joint United Nations Programme on HIV/AIDS provides documents on the World AIDS Campaign, and information on international conferences on AIDS.
*http://www.unaids.org/*

**White House Office of National AIDS Policy**
Information on efforts by the Clinton/Gore administration to address the national and international AIDS pandemic. Provides links to government and non-government sites.
*http://www.whitehouse.gov/ONAP/*

# global issues

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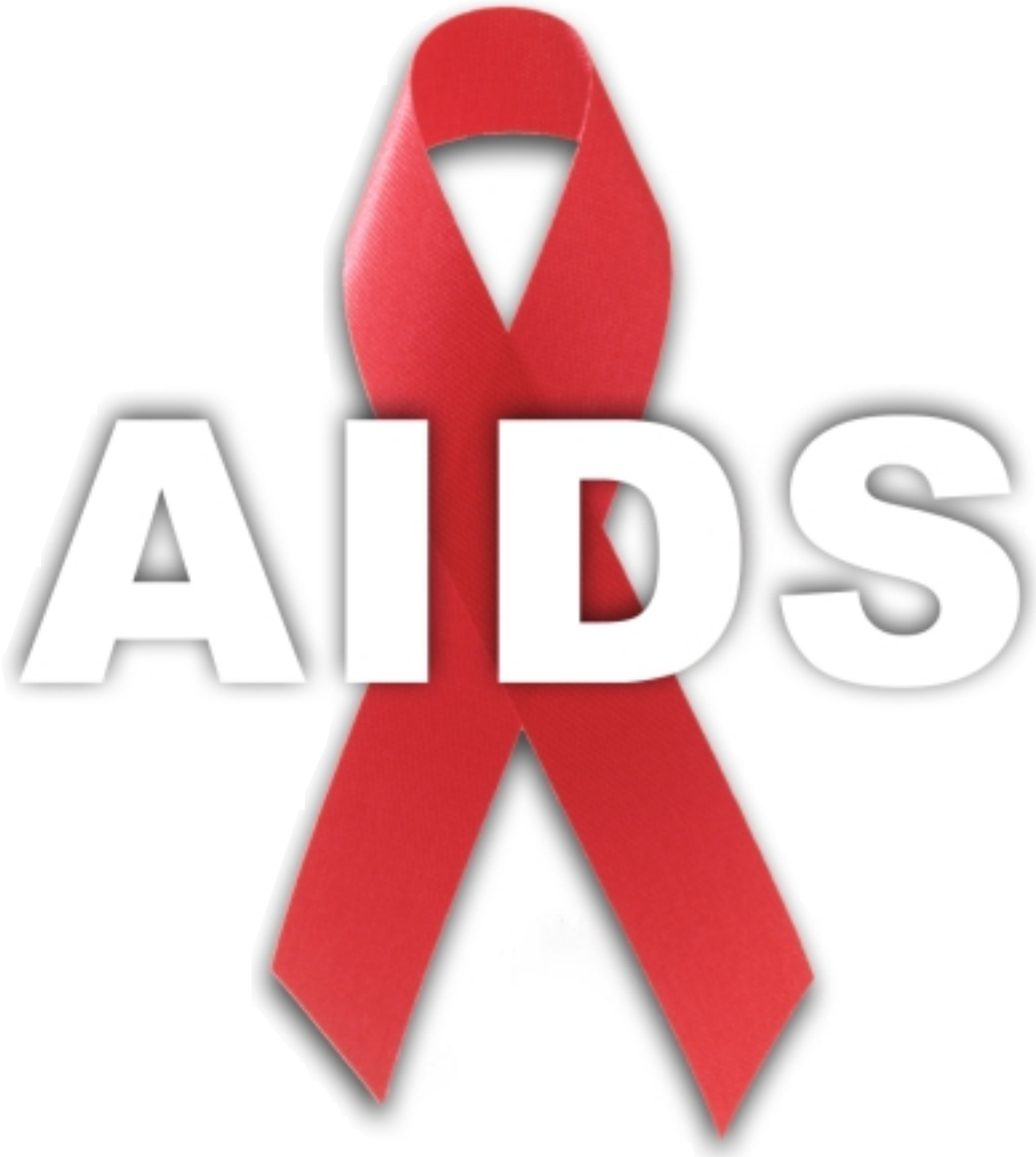


## The Threat to World Security