Slowing the Spread of HIV: Agenda for the 1990s

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Today, 12 years after the first description of AIDS (acquired immunodeficiency syndrome), the pandemic continues to expand. Yet, we know more about the causal microorganism, the human immunodeficiency virus (HIV), than about any other virus, and we have methods of proven efficacy for preventing transmission. Should our prevention agenda for the 1990s call simply for "more of the same"—application of the same interventions, but on a far wider scale? Or do we need to explore new avenues altogether? What are the major challenges for the scientific community in the decade ahead?

Our Starting Point

If we can slow the sexual transmission of HIV, we can curb the AIDS pandemic. This is because AIDS is essentially a sexually transmitted disease (STD) that, like some of the conventional STDs (all STDs excluding HIV infection), can also be transmitted through blood and perinatally. The presence of a conventional STD such as syphilis or chancroid increases the risk of sexual HIV transmission considerably, perhaps by as much as 10- to 100-fold for a single act of intercourse.

The World Health Organization (WHO) estimates (*1*) that as of mid-1993, over 13 million young people and adults have become infected with HIV since the start of the pandemic (Fig. 1), the majority through heterosexual intercourse, and that about 1 million children have been infected perinatally. Of the cumulative infections in adults, more than 8 million have occurred in sub-Saharan Africa, and over 1.5 million in North America and western Europe, where the HIV pandemic is oldest. For reasons that need elucidation, prevalence in some African cities seems to have stabilized at different levels.

Infections are on the rise in Latin America and the Caribbean (1.5 million cumulative adult infections), North Africa and the Middle East (75,000), and eastern Europe and central Asia (50,000). The steepest rises now being seen, however, are those in Asia, particularly south and southeast Asia (over 1.5 million adult infections). For example, among men seeking care for a conventional STD, national HIV prevalence rates in Thailand rose from zero in mid-1989 to 6% in mid-1992, and in Myanmar, from 2 to 9% between 1990 and 1991. By the end of 1992, HIV seroprevalence in the general population had reached as high as 4% in northern Thailand and 7% in southern Myanmar. Given its population, Asia's epidemic may ultimately dwarf all others in scope and impact.

To date, over 2 million HIV-infected adults have developed AIDS, and most of them have died (*1*). The cost, in terms of personal suffering, family disruption, and impact on the community, has already been horrific. In high-prevalence cities of Africa, as many as one out of every three adults is infected. In some cities, up to 80% of adult hospital beds are occupied by AIDS patients, about half of whom also suffer from tuberculosis. How to provide and pay for their care is a growing dilemma. But these direct costs are dwarfed by the pandemic's colossal indirect costs in the form of lost income and decreased workforce output as millions of people in society's most productive age group fall sick and die. To take just one example, the government of Thailand estimates that the direct and indirect costs of AIDS in that country will total some $9 billion by the year 2000 (*2*).

Thus, while we step up the search for better ways of keeping people with HIV infection alive and well, we must intensify efforts to prevent any further spread of the virus. The ultimate cost of failure to prevent new infections does not need to be imagined: it is already visible in the hardest hit parts of Africa described above. Prevention is the key to curtailing the ultimate impact of AIDS.

Prevention Through Vaccines

There has been considerable publicity about AIDS vaccines. Immunization may some day contribute to the prevention of AIDS, but there are many hurdles ahead.

A major hurdle is our inadequate understanding of HIV pathogenesis and the host's immune response to this virus. What exactly happens during the first few hours or days after infection? Why do some individuals fail to become infected despite repeated exposure? Perhaps the establishment of chronic infection might be aborted by as yet poorly understood immune responses, possibly involving cell-mediated immunity. Dose-response factors and genetic variability in human susceptibility to HIV may also be involved.

The subsequent pathogenesis is likewise obscure. Why, for example, do some HIV-infected people progress rapidly, whereas others deteriorate suddenly after doing well for a long time? Why is it that some people infected with HIV 15 years ago have still not developed AIDS? And why do some people live in relatively good health for more than 5 years after being diagnosed with AIDS? Again, the possible host and viral factors involved need urgent investigation: for instance, the observed correlation between syncytium-inducing virus and rapid disease progression.

Despite these gaps in knowledge, some candidate vaccines have been developed that show promise in initial tests. However, only large-scale efficacy trials will tell us if they are truly protective against HIV infection (preventive vaccines) or against the development of AIDS in HIV-infected people (therapeutic vaccines, or immunotherapy). Even if such trials are launched quickly, a preventive vaccine of proven efficacy cannot realistically be on the market before the end of this decade.

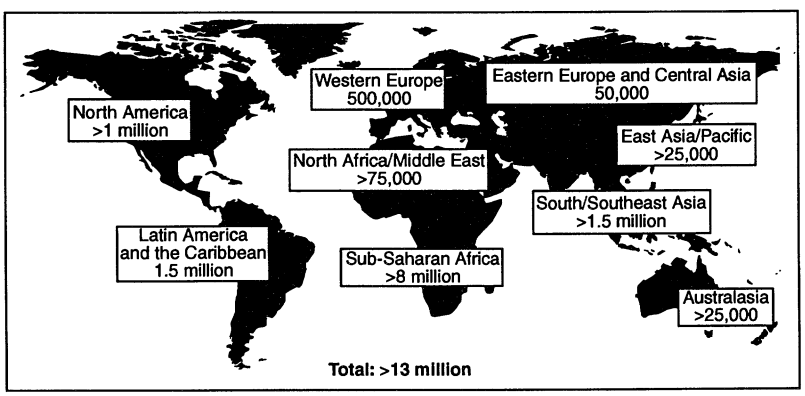

Fig. 1. Estimated distribution of cumulative HIV infections in adults, by continent or region, as of mid-1993.

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But no preventive vaccine will have a significant impact on the HIV pandemic unless it is appropriate for use in developing countries; WHO projects that 90% of all new HIV infections by the year 2000 will occur in these countries (*1*). According to WHO estimates, an initial mass immunization campaign in high-prevalence countries will need to reach over 300 million people during the first 5 years alone (*3*). Cost is thus a critical factor. So is ease of transport and storage. Above all, a vaccine will have to induce long-lasting immunity with few doses and protect against the antigenically different HIV strains present around the world. It makes sense to build these requirements, especially the latter two, into the process of research and development rather than take an already developed vaccine and try to adapt it after the fact.

Unfortunately, not enough is being done in this regard. I believe it is urgent to expand our vaccine development agenda beyond the current candidates to maximize our chances of finding a vaccine that will protect against virus strains found in developing countries and will induce immunity with few doses. Given our relative ignorance about what the best avenues really are, we need to explore all scientifically reasonable options and find ways of addressing safety and potential liability concerns. This includes looking into the development of live vectored vaccines and even live attenuated virus vaccines.

Whatever the candidate vaccine, trials will need to conform to the highest scientific and ethical standards, respecting the individual rights and community traditions of volunteers. They will also have to be conducted in the developing world, not only in the industrialized countries. Steps are now being taken by WHO to ensure that at least four trial sites—in Brazil, Rwanda, Thailand, and Uganda—will be ready to begin large-scale trials as soon as appropriate candidate vaccines are available (*4*).

Without prejudging the outcome of our search for an appropriate vaccine, one thing is clear: at best, a preventive vaccine can only complement, not replace, other prevention methods. No vaccine is likely to have 100% efficacy, and as we know from decades of experience with childhood immunization programs, total population coverage is extremely difficult to achieve. Unlike condom use and other forms of safer sex, an HIV vaccine cannot protect against other sexually transmitted pathogens that are now endemic or may become epidemic, as HIV has done. The prevention agenda for the 1990s and beyond thus calls for continued reliance on our ability to convince and enable people to avoid risky sexual behavior and to ensure that they are treated promptly and effectively for conventional STDs.

Sexual Behavior Change

Perhaps the main lesson learned so far during this pandemic is that sexual behavior change is an achievable goal. There is growing evidence that people from a striking diversity of cultures, on different continents, have managed to adopt safer behavior, including having fewer sex partners, choosing nonpenetrative forms of sex, and, the best documented change, using condoms.

The behavioral interventions that have been successful in helping people move through these steps tend to have several components (*5*): (i) repeated messages about AIDS through the mass and other media; (ii) person-to-person contacts in which individuals are educated about risks, and messages about risk reduction are reinforced, usually by a trusted member of their community or a peer; (iii) good condom promotion and availability; and (iv) a favorable "policy climate" characterized by a willingness to confront the problem of AIDS, frankness about sexuality, and a nonstigmatizing approach to groups who often face discrimination (such as homosexual and bisexual men).

It is useful, particularly when an HIV epidemic is at an early stage, to aim educational interventions at specially vulnerable groups, such as young people, homosexual and bisexual men, and prostitutes and their clients. At the same time, because many people at risk for HIV infection will not be discernible or reachable as part of an identified "target group," carefully crafted prevention messages need to reach the general public as well so as to ensure truly universal education about AIDS.

Until now, except in a handful of countries, these behavioral interventions have been implemented on far too limited a scale to make a real impact on the pandemic. Our agenda for the 1990s should therefore call for the expansion of their application worldwide.

Mere application of "more of the same" will not suffice, however, particularly for a reduction in heterosexual transmission. Experience has confirmed what women have been saying all along: they are less able than men to protect themselves from HIV infection by a simple act of will. Wherever women are culturally and economically subordinate to men, they cannot control or even readily negotiate safer sex, including condom use and lifelong mutual fidelity.

This fact needs to dictate our prevention approaches. Men need to be convinced to stick to safer sex, for their own sake and that of their partners and children. For women, the agenda is to change the circumstances in which sex takes place. Over the long term, this needs to be done through the improvement of their educational, legal, and economic status, and in the short term, through stratagems for circumventing their subordination. For example, prostitutes have been organized to raise their prices simultaneously so they can afford to turn away clients who refuse condom use (*5*); this is a particularly useful stratagem because it enhances women's agency and control rather than leaving them passive.

The best short-term stratagem would be the use of a safe and effective barrier to HIV transmission under the control of women—one that they could apply, if necessary, without their partner's knowledge. It is disturbing, even shocking, that what appears today to be a top priority on the AIDS research agenda has been widely neglected—perhaps because too few women have been involved in setting the agenda, heterosexual transmission has received insufficient attention, and the pharmaceutical industry has been fearful of liability problems. We urgently need to study the safety and protective efficacy of existing spermicides that are known to be effective in vitro against HIV. At the same time, we need to develop new, nonirritating virucidal agents—preferably with antibacterial properties as well, so that they would protect against conventional STDs, too—and further explore the acceptability and protective efficacy of the female condom, the diaphragm, and the cervical cap, alone or in combination with a microbicide. It is likely that, as for contraception, women will always need an array of HIV barrier methods to choose from.

Let us recognize that these methods alone will not "empower" women any more than a vaccine would. However, barrier methods may be able to keep women alive long enough for them to acquire other kinds of control over their lives.

STD Care

Given the enormous magnifying effect of conventional STDs on HIV transmission, effective STD care must be a priority throughout this decade and into the next century. The immediate agenda is to apply widely and systematically the case management approaches that have proven effective under real field conditions. Fortunately, the common STDs can be detected with the aid of simple algorithms based on syndromes (*6*) without the need for laboratory tests, which are so often unavailable in the communities of developing countries. The same algorithms then guide the health worker in

deciding on the right treatment.

All this, of course, presupposes the availability of the right drugs and a functioning health system, an enormous challenge in many developing countries. It also presupposes that people have been made aware of the need to seek prompt help for genital infections. As with education for safer sex, STD awareness campaigns need to be aimed at specially vulnerable groups as well as, more generally, the whole population.

Case management of STDs must include primary prevention through education on safer sex and the provision of condoms, the same intervention as for AIDS prevention, which argues for an integrated approach. This is all the more important as individuals with a conventional STD have, by definition, been at risk of HIV infection and are thus an ideal "captive audience" for AIDS prevention messages. Such people may not be easily reachable in any other locale.

The other side of the coin, however, is that STD care urgently needs to be lifted out of its traditional coercive context, particularly if it is to be integrated with AIDS prevention. Even where there is no formal coercion, many STD clinics humiliate or act condescendingly toward patients instead of providing sympathetic care that would encourage people to seek early diagnosis and care. Although efforts must be made to change this state of affairs, attendance at specialized STD facilities is likely to remain stigmatizing for some time to come.

For women, a possibility to be explored is the integration of HIV and STD care into maternal and child health care and family-planning services. This solution would have the added benefit of bringing the many asymptomatic women into contact with health workers.

The Challenge for Science

If we are to act on this expanded research and intervention agenda, we will have to confront the denial, stigma, and taboo connected with AIDS. Few people are as well placed as scientists when it comes to fighting these reactions, which are not only irrational but profoundly inimical to prevention. I see four challenges for the scientific community:

1) Scientists have the necessary knowledge to understand and explain to others why complacency in the face of the expanding AIDS pandemic is so dangerous. According to WHO's conservative estimates, as many as 40 million people worldwide will have been infected by the year 2000 (*1*). By the same token, scientists can use their prestige and influence to press for decisive action at home and abroad. The resources available for prevention programs are dangerously inadequate. This is especially so in the developing countries, where currently $120 million a year is spent, compared with the $1.5 to $2.9 billion that WHO calculates is needed to implement a basic prevention package (*7*).

2) Scientific discourse needs to permeate our whole approach to prevention. For a scientist, facing the facts with objectivity is the standard first step in problem solving. Objectively, the first step in AIDS prevention is acknowledgment of the existence of risk behaviors, such as sex among young people, as indicated by the worldwide decrease in median age at first sexual intercourse.

The next step is to apply the most effective measures for the reduction of the potential of these behaviors for HIV transmission. To take the example of youth, we can by all means encourage abstinence, but let us not delude ourselves into believing that this is a realistic option for all young people. We therefore need to let them know that nonpenetrative forms of sex do not transmit HIV and that condoms significantly reduce the infection risk. Exactly how to convey these messages can be debated; what counts is getting the information across.

3) The study of AIDS is a field of such intellectual and technological importance that it is tempting to try to push back all the frontiers of knowledge. But if we are to bring this pandemic under control, the scientific community will have to focus on priority prevention research. At the top of the list are a vaginal microbicide, greater understanding of HIV pathogenesis and immune response, a vaccine appropriate for developing countries, improved approaches to STD care, and better ways of helping people adopt and sustain what is for them an appropriate form of low-risk behavior.

4) To ensure that AIDS research explores the issues that really matter, it must be guided and carried out by those who are best placed to know what the key issues are. Research agendas must therefore be set by scientists from developing countries as well as researchers from the developed countries, by behavioral as well as biomedical researchers, by women as well as men, and by people with HIV infection and AIDS as well as uninfected people. Research that is planned and conducted by all of these parties also stands the best chance of conforming to the highest ethical standards.

If the scientific community worldwide rises to these four challenges, we will have a historic opportunity—the opportunity to scale up application of what we already know works to slow the spread of HIV and to give even greater emphasis than in the past to new avenues for prevention. If we implement this prevention agenda wisely during the 1990s, it is within our power to avert millions of deaths in the decades beyond.

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