

SIDA: The prognosis for society and the individual

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Since the first cases of AIDS were diagnosed in Los Angeles and New York, HIV infections has been detected in virtually all countries of the globe. It has been estimated that some 30 million persons are infected with 5.8 million new infections occurring each year.⁽¹⁾ There were an estimated 5.8 million people infected in 1997, including 600 thousand children. Parenthetically, HIV infection recently was diagnosed posthumously in a man from Africa who died in 1959, and an analysis of the genome of the causative virus suggests that HIV-1 probably emerged somewhere in Africa in the early 1950s.⁽²⁾ In less than 50 years, HIV has established itself as one of the great plagues of mankind.

It is in Africa that the epidemic has struck the hardest: the UNAIDS report estimated that 7.4% of all persons aged 15 to 49 years are infected with HIV.⁽¹⁾ The rates of infection vary widely, ranging as high as 25 to 30% in adults in Botswana.⁽¹⁾ Even in areas with low rates on past surveys the news is not good. A recently published study of women from a rural province of South Africa attending a prenatal clinic reported an increase in HIV seropositivity from 4.2% in 1992 to 14% in 1995.⁽³⁾

In Asia, although the rates of infection are much lower, the future is alarming as the epidemic is gaining speed. India has an estimated 3 to 4 million persons with HIV. Southeast Asia (Thailand, Cambodia, Viet Nam, Myanmar) has variable rates of infection, but rapid rises in the prevalence rate of seropositivity in selected populations (sex workers, drug users) indicate a bleak future.

In the countries of Central and South America and the Caribbean the epidemic is spreading from the homosexual men and drug users into the lower socio-economic strata and is threatening to overwhelm the resources of already strained health care systems.

Is there reason for optimism in the face of these daunting figures? AIDS surveillance in the United States showed the first yearly drop in AIDS cases and AIDS-associated deaths in 1996,⁽⁴⁾ and the trend is continuing for 1997. Similar trends are evident in western Europe. Even though surveillance of AIDS cases does not tell the true story of the HIV epidemic in the United States, (and we know that transmission is continuing!) the news is encouraging. There is clear evidence that prevention programs work. From San Francisco to Thailand, prevention programs have had significant impact on the incidence of HIV.^(5,6) In San Francisco, for example, the sero-incidence of HIV infections among gay and bisexual men peaked in 1982 and then fell dramatically in 1985 as aggressive prevention programs

became active.⁽⁵⁾ Focused, intense educational efforts directed at a particular “at risk” group can change behavior.⁽⁷⁾ In Thailand, all elements of society were mobilized in an all out effort to stem an explosive outbreak of HIV in the heterosexual population. By involving all segments –with special emphasis on personal responsibility– the country claims to have dramatically stemmed the epidemic.⁽⁶⁾

Prenatal screening and administration of antiretroviral drugs to the HIV-1 infected woman and the newborn has cut the rate of vertical transmission in the United States and Europe.⁽⁸⁾ Studies are underway to determine how to avail preventive therapy to pregnant women in countries with limited resources.

The WHO and governmental agencies around the globe are mobilizing resources for prevention activities. Industrialized countries with large research budgets are increasing funding for vaccine development. In spite of initial failures, vaccine research continues. In the “here and now” of the real world, while we await an HIV vaccine, reduction in HIV infection and AIDS must come from prevention. Throughout the world, it is the public health organizations which are tasked with disease prevention and control, but physicians, nurses and ancillary care givers must play a critical role. Attendees at this conference must be aware of their responsibilities. Care givers are respected and trusted: this trust must be exploited to change individual behavior by equipping the individual about personal safety. Discussions of sexual matters cannot be relegated to the gynecologist or STD (sexually transmitted diseases) specialist – sexuality is an important issue for virtually everyone (we may except the newborn and very young) and must be addressed to equip patients to live safely in the world with AIDS.

What is in store for the individual with HIV infection? HIV remains a killer. In the United States it remains the leading cause of death for young men and women⁽⁴⁾. On the other hand, real progress has been made and the prognosis for the person with HIV-1 infection is much brighter than what it was a few years ago. First came the improvement in management of opportunistic infections and the use of prophylaxis to prevent the common OIs. Then in quick succession came: A) assays of HIV-1 RNA copies which enhanced our prognostic capability for the individual patient, and, especially, our ability to monitor therapy; B) new potent classes of antiretroviral drugs (non-nucleoside reverse transcriptase inhibitors and protease inhibitors); C) a better understanding of the pathogenesis of HIV-1 disease; and D) the move to combination therapy which dramatically improved our ability to control HIV-1 replication with concomitant restoration (or prevent deterioration of) immune function. Other lectures during this conference deal with these advances in detail.

Several points bear emphasis here. Adherence to combination drug regimens is not easy, and a regimen taken erratically is worse than no treatment as it selects for mutants resistant to the drugs. There is significant potential for drug interaction, especially with the protease inhibitors. Monitoring of therapy with Quantitative assays has been compared to the monitoring of blood glucose for monitoring insulin management of diabetes, but the assays are extremely expensive and not yet available to all patients. We still do not know the optimal time to initiate therapy, nor which regimen is superior to another, nor what to

substitute when a patient fails one regimen. The extent to which a person with AIDS can achieve restoration of immune function is unknown: the expansion in CD4 cell counts does not equate with restored function. All this said, combination therapy has dramatically changed the prognosis of the person with HIV-1 disease lucky enough to obtain and tolerate it.

In summary, the HIV-1 epidemic continues to take its toll and promises to become worse on the global scene even as we begin to make progress in some areas. One cannot stress sufficiently the need to educate the public about HIV-1 infection and to encourage anyone at risk –especially young people– to take personal precautions. This includes widespread HIV testing. There is much that can be done for persons with infection –even for those for whom antiretroviral therapy is unattainable– that early diagnosis should be a goal of all physicians. Moreover, the knowledge that one is infected with HIV-1 is a strong inducement for more responsible sexual behavior and thereby preventing further transmission. We are seeing genuine progress in therapy. Hopefully the therapeutic successes will continue as we await the development of an effective vaccine.

References

1. UNAIDS Presse Release, Paris, 26 Nov. 1997. (<http://www.us.unaids.org/highband/press/wadrelease.html>)
2. Zhu T., Korber B.T., Nahmias A.J., Hooper E., Sharp P.M., Ho D.D. An African HIV-1 sequence from 1959 and implications for the origin of the epidemic. *Nature* 1998; 391:595.
3. Coleman R.L., Wilkinson D. Increasing HIV prevalence in a rural district of South Africa from 1992 through 1995, *J AIDS*. 1997; 16:50-53.
4. Centers for Disease Control and Prevention. Update: trends in AIDS incidence. *MMWR*. 1997; 46:165-173.
5. Lemp G.F., Porco T.C., Hirozawa A.M. *et al.* Projected incidence of AIDS in San Francisco: the peak and decline of the epidemic. *J. AIDS*. 1997; 16:182-189.
6. Phoolchareon W. Prevention successes in Thailand, 5th Conference on Retroviruses and Opportunistic Infections. 1998, Chicago, IL. Abst. S14.
7. Coates T.J. and The Voluntary Counseling and Testing Efficacy Study Group. The efficacy of counseling and testing in reducing HIV risk in developing countries: a three-country randomized controlled trial. 5th Conference on Retroviruses and Opportunistic Infections. 1998, Chicago, IL. Abst. 16
8. Mofenson L. Prevention of perinatal HIV transmission. 5th Conference on Retroviruses and Opportunistic Infections. 1998, Chicago, IL. Abst. S11.

Additional recommended references

Carpenter CCJ, Fischl M.A., Hammer S.M., *et al*, for the International AIDS Society-USA. Antiretroviral therapy for HIV infection in 1997: recommendations of the international panel. JAMA. 1997; 277:1962-1969.

Carr A., Marriot D., Field A., Vasak E., Cooper D.A. Treatment of HIV-1 associated microsporidiosis and cryptosporidiosis with combination antiretroviral therapy. Lancet 1998; 351:256-61.

Fauci A.S., Host factors and the pathogenesis of HIV-induced disease. Nature. 1996; 384:529-534.

Finzi D., Hermankova M., Pierson T., *et al*, for Identification of a Reservoir for HIV-1 in patients on highly active Antiretroviral Therapy. Science. 1997; 278:1295-1300.

Gulick R.M., Mellors J.W., Havlir, D. *et al*, Treatment with Indinavir, Zidovudine, and Lamivudine in Adults with Human Immunodeficiency Virus infection and prior Antiretroviral Therapy. N Engl J Med. 1997; 337:734-739.

Hammer S.M., Squires K.E., Hughes M.D., *et al*, A Controlled Trial of two Nucleoside Analogues plus Indinavir in persons with Human Immunodeficiency Virus Infection and CD4 Cell counts of 200 per cubic millimeter or less. N Engl J Med. 1997; 337:725-733.

Musey L., Hughes J., Schacker T., *et al*, Cytotoxic-T-Cell Responses, Viral Load, and Disease Progression in early HIV-1 Infection. N Engl J Med. 1997; 337:1267-1274.

Verheugt FWA, Effect of HAART on natural history of AIDS-related opportunistic disorders. Lancet. 1998; 351:228-230.