



The New England Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 335

AUGUST 1, 1996

NUMBER 5

ORIGINAL ARTICLES

- Changes in Sexual Behavior and a Decline
in HIV Infection among Young Men
in Thailand 297
K.E. NELSON AND OTHERS
- Age-Specific Reference Ranges for Serum
Prostate-Specific Antigen in Black Men 304
T.O. MORGAN AND OTHERS
- Prevention of Jarisch–Herxheimer Reactions
by Treatment with Antibodies
against Tumor Necrosis Factor α 311
D. FEKADE AND OTHERS
- Secular Trends in Coronary Atherosclerosis
— Analysis in Patients with Valvular
Regurgitation 316
M. ENRIQUEZ-SARANO AND OTHERS

IMAGES IN CLINICAL MEDICINE

- Vitamin B₁₂ Deficiency 323
S. MOLL

SPECIAL ARTICLE

- The Use of Medicare Home Health Care
Services 324
H.G. WELCH, D.E. WENBERG, AND W.P. WELCH

REVIEW ARTICLE

- Current Concepts: Evaluation of Dementia 330
D.S. GELDMACHER AND P.J. WHITEHOUSE

MOLECULAR MEDICINE

- Gene Transfer to Hematopoietic Cells 337
M.K. BRENNER

CLINICAL PROBLEM-SOLVING

- The Domino Principle 340
R. JAFFE AND D. ZAHGER

EDITORIALS

- The March of AIDS through Asia 343
B.G. WENIGER AND T. BROWN
- Age-Specific Reference Ranges for Serum PSA ... 345
J.E. OESTERLING
- Tumor Necrosis Factor and the
Jarisch–Herxheimer Reaction 347
B. BEUTLER AND R.S. MUNFORD

CORRESPONDENCE

- Physicians' Experience and Survival in Patients
with AIDS 349
- Human Herpesvirus 8 and Interstitial Pneumonitis
in an HIV-Negative Patient 351
- Late Effects of Treatment for Childhood Hodgkin's
Disease 352
- Cryoglobulinemia after Hepatitis B Vaccination 355
- Traffic Accidents and Daylight Saving Time 355

- BOOK REVIEWS 358
- NOTICES 360

CORRECTIONS

- Direct Cultivation of the Causative Agent of Human
Granulocytic Ehrlichiosis 361
- The Sleepy Sun 361

SPECIAL REPORT

- Columbia/HCA and the Resurgence
of the For-Profit Hospital Business
(First of Two Parts) 362
R. KUTTNER
- INFORMATION FOR AUTHORS 368

Editorials

**THE MARCH OF AIDS
THROUGH ASIA**

IN this issue of the *Journal*, Nelson and colleagues¹ describe a modest victory in what had been a losing battle in northern Thailand to control the most rapid epidemic of sexually transmitted human immunodeficiency virus (HIV) infection ever documented.² Studying large cohorts of randomly selected conscripts in the Royal Thai Army, they report a significant downturn in the prevalence of HIV infection, from a peak of about 13 percent to less than 7 percent, which is also reflected in national trends.³ Although the rate of infection remains serious, this encouraging sign reflects the effect of an enlightened effort in many sectors of society to control the epidemic in Thailand, whose unfortunate experience has presaged that of many neighboring countries.

A decade ago, some health officials believed Asia was immune to HIV and AIDS, safe behind a cultural — if not genetic — Maginot line. The region, along with North Africa and Oceania, was classified epidemiologically in a miscellaneous category known as “pattern III,” meaning that few cases had occurred there.⁴ In reality, chance events had not yet introduced seed virus into the Asian population.

By the late 1980s, HIV type 1 (HIV-1) began invading one Asian country after another, exploiting traditional behavioral patterns and secular trends to spread widely. In 1995 alone, there were an estimated 2.5 million new infections in southeastern Asia (ranging from India through the Indonesian and Philippine archipelagoes), surpassing the combined incidence in sub-Saharan Africa (1.9 million) and the rest of the world (0.3 million).⁵

The beachhead for the AIDS pandemic in Asia was Thailand, where improved disease-control training and infrastructure^{6,7} produced exemplary systems of epidemiologic surveillance to record the arrival and dissemination of HIV-1. In Bangkok the prevalence among injection-drug users rose from 1 percent in late 1987 to over 30 percent eight months later.⁸ Beginning in 1989, routine semiannual province-level surveys tracked steady increases in rates of HIV infection. By mid-1993, the prevalence reached 35 percent among injection-drug users, 29 percent among female sex workers in brothels, 8 percent among male patients with sexually transmitted disease, 4 percent among military conscripts, and 1 percent among pregnant women.⁹ In 1993, six years after the epidemic exploded, roughly three quarters of a million Thais were infected,¹⁰ about as many as in the United States, which has a

population four times as large and an epidemic that has lasted twice as long.

Several other Asian nations are in various stages of this “pattern IV” sequence of explosive increase in HIV-1 infection among injection-drug users and female sex workers, who pass the virus to their male clients, who in turn infect their wives and thus newborns.^{8,11} As early as 1990, prevalence rates greater than 60 percent had been found among injection-drug users in some sites in Myanmar (Burma), India, and China. By 1993, the rates among injection-drug users exceeded 30 percent in parts of Malaysia and Vietnam. Surveys of sex workers between 1992 and 1994–1995 showed rates rising from 40 percent to 51 percent in Bombay, India; from 9 percent to 38 percent in Vietnam; from 4 percent to 18 percent in Myanmar; and from 2 percent to 10 percent in Cambodia. In Thailand, Bombay, Myanmar, and Cambodia over 2 percent of pregnant women are now infected with HIV.

The principal determinant driving the Asian epidemics is a traditional double standard in sexual behavior.^{8,11} Substantial proportions of Asian men engage in sex with a relatively small population of female sex workers, whereas most women are abstinent before marriage and monogamous afterward. Because of their numerous encounters, sex workers quickly acquire HIV and other sexually transmitted diseases from infected clients, raising the statistical probability of exposure to HIV among uninfected clients. Mathematical modeling¹² explains how an epidemic can be accelerated by such a small core group of sex workers, in comparison with larger proportions of women who participate in premarital and extramarital sex, as in the pattern II countries⁴ of sub-Saharan Africa and the Caribbean. In Asia, homosexual men represent a very small proportion of cases, in contrast with the pattern I countries of the Americas, Western Europe, and Australia, where they are the predominant group.

Some secular trends in Asia also contribute to the pandemic. Increasingly effective suppression of the narcotics trade that originates in the Golden Triangle, where Laos, Myanmar, and Thailand meet, has caused opiate refineries to move closer to the remote poppy fields to avoid detection. More and more, drug users inject the heroin that is now available along smuggling routes, instead of smoking opium. Widespread industrialization is attracting young men and women from rural areas to work in factory towns, delaying marriage and increasing the rate of premarital sex away from the normative influences of family and village. Economic liberalization in China, Vietnam, and Cambodia has revived an entrepreneurial capitalism in which commercial sex is flourishing, along with sexually transmitted diseases, after being suppressed for decades under communism.

An enigma in the Asian pandemic is that rapid

sexual transmission has not occurred in some places, confounding predictions, even though the virus has been there for several years and commercial sex is common — for example, in Bangladesh, Indonesia, and the Philippines. One contributing reason may be the high proportion of men in these Muslim and Catholic societies who are circumcised, a factor that has been shown elsewhere to reduce the rate of female-to-male transmission.¹³ In most Asian areas with rapid sexual spread of HIV-1, circumcision is rare.

One surprise was the discovery that two distinct strains of HIV-1 were circulating in segregated patterns in Thailand, where 75 percent of injection-drug users had subtype B of the *env* gene, whereas over 90 percent of sexually infected persons had subtype E,¹⁴ invalidating a presumption that the former were the source of virus for the latter. In India, moreover, subtype C predominates. These findings might result from genetic founder effects, but preliminary data from Thailand also suggest biologic differences between HIV-1 subtypes in transmissibility and immune impairment. Some have postulated from *in vitro* work that subtypes E and C are transmitted with greater efficiency through heterosexual sex than other subtypes, thereby accounting for the rapid spread of the epidemic in Asia.¹⁵ But there is as yet no epidemiologic evidence that such differences between strains would outweigh other factors contributing to rapid transmission, such as frequent sexual relations, the involvement of core groups, the presence of other sexually transmitted diseases, and the absence of circumcision. In fact, subtype B, which is predominant in the Americas and Europe, has caused serious epidemics of heterosexually transmitted infection in Honduras and elsewhere in the Caribbean.

Nelson et al.¹ attribute the decline in the prevalence of HIV among young men in Thailand to the innovative "100 percent condom campaign" that encourages brothel owners and sex workers to insist that clients use condoms. But theirs was not a controlled study of this intervention; other potential influences on sexual behavior included efforts in the broadcast media, school curriculums, the workplace, and health centers to educate people about AIDS and build personal decision-making skills. By the mid-1990s, when large numbers of HIV-infected persons finally became ill, the men in the study may also have been affected by knowing sick or dying relatives or acquaintances. In contrast, in the early 1990s, when the epidemic was young, conscripts knew a lot about AIDS, but few knew anyone with the disease.¹⁶ Because of this, they may have been slow to acquire the perception of risk that is essential for behavior to change.

Two key elements underlie the reduction in risky sexual behavior achieved in Thailand. One is the rec-

ognition, after initial complacency and denial,¹⁷ that AIDS threatens the nation and that studying the extent of the epidemic and publishing the information help marshal resources and target defenses against it. The other is the acknowledgment that prostitution cannot be eradicated and that it is necessary to work with those involved in an overt, nonjudgmental way to reduce the role of commercial sex in HIV transmission. With infection in China still limited mostly to injection-drug users, sex workers, and their sexual partners in rural border regions of Yunnan province, the next battleground of the pandemic will be the vast population of the Middle Kingdom. The wisdom 2500 years ago of Sun-tzu, the great Chinese military strategist, applies to the challenge presented by AIDS today:

If you know the enemy and know yourself, you need not fear the result of a hundred battles. If you know yourself but not the enemy, for every victory gained you will also suffer a defeat. If you know neither the enemy nor yourself, you will succumb in every battle.

BRUCE G. WENIGER, M.D., M.P.H.

Centers for Disease Control and Prevention
Atlanta, GA 30333

TIM BROWN, PH.D.

East-West Center
Honolulu, HI 96848

REFERENCES

1. Nelson KE, Celentano DD, Eiumtrakol S, et al. Changes in sexual behavior and a decline in HIV infection among young men in Thailand. *N Engl J Med* 1996;335:297-303.
2. Weniger BG. Experience from HIV incidence cohorts in Thailand: implications for HIV vaccine efficacy trials. *AIDS* 1994;8:1007-10.
3. Mason CJ, Markowitz LE, Kitsiripornchai S, et al. Declining prevalence of HIV-1 infection in young Thai men. *AIDS* 1995;9:1061-5.
4. Piot P, Plummer FA, Mhalu PS, Lamboray J-L, Chin J, Mann JM. AIDS: an international perspective. *Science* 1988;239:573-9.
5. The Global AIDS Policy Coalition, Mann J, Tarantola D, eds. *AIDS in the world*. Vol. 2. Oxford, England: Oxford University Press, 1996.
6. Brandling-Bennett AD, Jatanasen S, Matusosapas W, Kunasol P, Brachman PS. A practical way to train epidemiologists. *World Health Forum* 1983;4:344-7.
7. World Health Organization. Field epidemiology training programme: annual report 1984-1985 (Thailand). *Wkly Epidemiol Rec* 1986;61(20): 149-51.
8. Weniger BG, Limpakarnjanarat K, Ungchusak K, et al. The epidemiology of HIV infection and AIDS in Thailand. *AIDS* 1991;5:Suppl 2:S71-S85. [Erratum, *AIDS* 1993;7:following 147.]
9. Brown T, Sittitrai W, Vanichseni S, Thisyakorn U. The recent epidemiology of HIV and AIDS in Thailand. *AIDS* 1994;8:Suppl 2:S131-S141.
10. Brown T, Sittitrai W. Estimates of recent HIV infection levels in Thailand. Bangkok, Thailand: Program on AIDS, Thai Red Cross Society, 1993. (Research report no. 9.)
11. Brown T, Xenos P. AIDS in Asia: the gathering storm. *Asia Pacific Issues: Analysis from the East-West Center*. No. 16. August 1994:1-15.
12. Garnett GP, Anderson RM. Balancing sexual partnerships in an age and activity stratified model of HIV transmission in heterosexual populations. *IMA J Math Appl Med Biol* 1994;11:161-92.
13. Moses S, Plummer FA, Bradley JE, Ndinya-Achola JO, Nagelkerke NJ, Ronald AR. The association between lack of male circumcision and risk for HIV infection: a review of the epidemiological data. *Sex Transm Dis* 1994; 21:201-10.

14. Weniger BG, Takebe Y, Ou C-Y, Yamazaki S. The molecular epidemiology of HIV in Asia. *AIDS* 1994;8:Suppl 2:S13-S28.
15. Soto-Ramirez LE, Renjifo B, McLane MF, et al. HIV-1 Langerhans' cell tropism associated with heterosexual transmission of HIV. *Science* 1996;271:1291-3.
16. Sweat MD, Nopkesorn T, Mastro TD, et al. AIDS awareness among a cohort of young Thai men: exposure to information, level of knowledge, and perception of risk. *AIDS Care* 1995;7:573-91.
17. Tarantola D, Mann J, Viravaidya M, Moodie R, Sundararaman S. Governments of Asia and the Pacific responding to the HIV/AIDS pandemic. *AIDS* 1994;8:Suppl 2:S183-S198.

©1996, Massachusetts Medical Society.

©Copyright, 1996, by the Massachusetts Medical Society
Printed in the U.S.A.