In this special issue, FOCUS examines the Seventh International Conference on AIDS, held in Florence, Italy, in June. More than a decade into the pandemic, many of the "facts"—about transmission, replication, and pathogenesis—continue to be valid. We emphasize here those aspects that are most quickly evolving and most likely to be of interest to counselors, for example, the changing populations of infected people, vaccine research, combination antiviral therapy, and neurological findings. Interpreting conference presentations is as much an art as a science, requiring knowledge, intuition, and energy. More than 10,000 people attended five days of presentations, including two plenary sessions each morning, sessions emphasizing issues for "Communities Challenging AIDS," and a choice of 500 oral and 3,000 poster presentations divided into four tracks: A-Basic Science; B-Clinical Science and Trials; C-Epidemiology and Prevention; and D-Social and Behavioral Science. In this issue, references to conference abstracts are cited in parentheses within the text: the first part indicating the day, the second indicating the track, and the last indicating the number of the presentation. This month's Clearinghouse (see page four) offers information on how to order conference abstract books and professional publications that provide further commentary.

Epidemiology

The HIV pandemic continues to spread inexorably, especially in the developing world. James Chin, Chief Epidemiologist of the World Health Organization (WHO), predicted that in the industrialized world, where the average duration of time from infection to disease is 10 years, the number of diagnosed AIDS cases will remain high well into the middle of the 1990s, but will level off after that. The infection rate in the developing world, however, will continue to rise.

Millions of new infections are projected in Asia, Latin America, and Africa. Overwhelmingly, new infections throughout the developing world are transmitted through heterosexual contact, although the roles of infected blood supplies and male-to-male transmission are difficult to determine in some countries. While some 10 million people worldwide are currently infected, by the turn of the century the figure is expected to rise to between 25 and 30 million. Yoweri Kaguta Museveni, President of Uganda, stated that by that time, the developing world will account for 90 percent of the diagnosed AIDS cases compared to 50 percent in 1985.

Rates Vary among Drug Users

Some industrialized nations report increased seroprevalence among injection drug users. For example, in London, a study of 534 injection drug users in and out of treatment programs found a seroprevalence rate of 13 percent in 1990 compared to 6 percent in 1989 (M.C.48). In a study of Argentinean injectors in treatment programs, seroprevalence rose from 0 percent in 1986 to 38 percent in 1990 (W.C.3326).

On a more positive note, seroprevalence rates have been stable for one year in Bangkok (34 percent), and for six years in New York (47 percent). Most users in both cities claim to have adopted behavior change consistent with HIV prevention.
Editorial: Towards a New Conference
Robert Marks, Editor

The International AIDS Conference continues to fulfill a valuable role by focusing worldwide attention on the pandemic and by bringing together the international AIDS community. Psychosocial and prevention presentations, in particular, are useful in three ways: they provide an international forum for prevention and social support strategies; they encourage medical and social science professionals to exchange ideas about an epidemic that has blurred lines between these disciplines; and they introduce the media to aspects of HIV disease that may be overlooked in the rush to cover every, and often every insignificant, medical finding.

In the hodgepodge of hundreds of oral and poster presentations, the conference format, designed for the exchange of scientific information, failed to actively facilitate the development of innovative ideas. Most social science and prevention presentations confirmed what has been known for several years, not surprising in the context of a scientific conference where replication is a high art. Many of these presentations were data-based, so that the exchange of ideas was limited even further to concepts that could be tested and proven statistically significant using the scientific method.

Oral presentations offered little opportunity for substantive discussion, rarely extending beyond a recitation of methodology and basic findings. Since the oral presentations in a given session were often only peripherally related to each other, limited discussion never led to useful conclusions about the implications of a body of work. The oral sessions, which this year were fewer and thus more accessible, could have provided opportunities for dialogue and synthesis to guide future research and program development; instead they became little more than talking posters.

A New Approach

It would be wrong to criticize presenters simply because their reports did not contribute to global answers: the enthusiasm and intelligence of HIV workers worldwide is perhaps the most impressive aspect of the conference. Likewise, each year organizers improve on the previous year's model, making information more accessible. It is time, however, to experiment with approaches that go beyond the limitations of the scientific approach.

To do this, there should be greater autonomy between psychosocial and medical aspects. During the first two or three days, the conference could focus on psychosocial, prevention, and public policy issues; for the final two or three days, it could focus on medical and basic science. In between, there could be a one- or two-day session, designed to identify and discuss the most important areas of common interest for attendees of the two larger sections.

The new format should be matched by a new approach. Using this approach, organizers would define the key HIV-related social science, prevention, and public policy topics. They would write position papers—defining the state of current knowledge and research—about these topics and would suggest a range of unresolved questions that presentations could address. Panel participants, chosen on the basis of their responses, would be those who organizers believed were the best equipped to challenge the limits of current knowledge through their presentations and discussion.

Sessions should include a healthy amount of audience participation and culminate in the development of a statement detailing points of agreement, and suggestions for future discussion. The product of the conference, the compiled statements from each session, would form a coherent guide for future research and program development.

guidelines and, consistent with these data, new seroconversions tended to cluster among those who are new injectors. (M.C.I). WHO has undertaken a five-year seroprevalence study of drug use in 11 major cities throughout the world, and this data should provide an assessment of the success of behavior change programs.

Women and Young Gay Men Vulnerable

The numbers of women infected with HIV is rapidly growing in Western industrialized countries. In a comprehensive study of Centers for Disease Control (CDC) case reports, researchers found women to comprise 55 percent of all U.S. cases reported since January 1989 (W.C.I). While 51 percent of these cases occurred among injection drug users, in 1990, 31 percent were the result of heterosexual contact, and this category has had the highest rate of increase.

An ongoing observational study of HIV-infected women in 18 U.S. cities reported that, of the first 222 women enrolled, the average age of participants was 35; 65
percent were African-American, 21 percent were Latino/Hispanic; and the most often reported risk exposures were injection drug use and heterosexual contact (M.B.2442). Fifty-nine (27 percent) had a history of vaginal candidiasis.

One of the most disturbing epidemiologic reports came from the San Francisco area, where a survey of six sexually transmitted disease (STD) clinics assessed HIV seroprevalence among 1,688 young gay and bisexual men. Overall, 27 percent of White men, 54 percent of Black men, and 11 percent of Latino men were antibody positive. In San Francisco County alone, 49 percent of this group of young men were infected (W.C.3010).

Natural History

From early in the epidemic, researchers have studied the natural history—the development over time—of HIV infection in hopes of defining routes of transmission, recognizing cofactors that facilitate disease progression, identifying biological markers that indicate or predict disease progression, and distinguishing disease progression among groups of people.

Cofactors: Age, Stress, and Unsafe Sex

Researchers have considered everything from diet to popper use as cofactors for progression to AIDS. But, while many of these seem intuitively related to health and the body's ability to fight disease, none have been shown to have a direct relationship to disease course. The only consistent conference finding regarding the role of cofactors was age at time of infection. Numerous studies agreed that those who become infected later in life, especially after 35, tend to progress more rapidly to AIDS and showed that this effect existed in various populations.

Other possible cofactors, however, continue to be investigated. Findings from the U.S. Multicenter AIDS Cohort Study (MACS) suggested that more rapid progression to AIDS is related to repeated exposure to multiple and perhaps more virulent strains of HIV, or to some other sexually transmitted factor (M.C.95). Researchers studied 32 men who progressed to AIDS within five years of seroconversion and seropositive controls who had not progressed to AIDS. Those with AIDS reported more frequent bouts of STDs prior to seroconversion, and receptive anal intercourse with more partners before and after seroconversion.

Other studies found that stress may reduce T-killer cell levels (TH.B.91), and that continuing heroin injection does not accelerate disease progression. (TH.C.48).

Progression Similar in All Groups

The standard data about progression from HIV infection to AIDS comes from four large San Francisco cohorts of gay White men, which have found that less than 3 percent progress to AIDS during the first few years, but 6 or 7 percent progress annually during subsequent years. This results in an infection rate exceeding 50 percent by the end of the 10th year. The United Kingdom Hemophilia Cohort and the Italian Hemophilia Group, both large studies of seropositive people followed for five and six years, found nearly identical rates of progression (M.C.3131). Surprisingly similar findings were reported among injection drug users. One large Italian study assessed the rate of progression of disease among 539 injectors, plotted initial five year results, and found the "natural history of HIV infection in injection drug users does not seem to differ from that of gay men in the U.S." (W.C.3354). A second study of 358 injectors in Rome replicated the AIDS Clinical Trials Group (ACTG) 019 study that assessed the use of zidovudine (ZDV; AZT) in gay men with T-helper cell counts of less than 500. Progression to AIDS and advanced symptomatic disease was "similar to that reported for gay men in ACTG 019" (M.C.3183). Of particular interest was that progression rates for men and women were essentially equal. A third study from Baltimore, Maryland, demonstrated that while a rapid decline in T-helper cells follows seroconversion among injection drug users, after a plateau is achieved, the decline continues slowly and "resembles that seen in other risk groups" (TU.C.44).

As more and more women become infected, there is greater interest in the effect of pregnancy on disease progression. French researchers studied seropositive pregnant women, none of whom had AIDS, to see if there was a difference in disease progression between those who carried their babies to term and those who aborted in the first or second trimester (W.B.2046). Interestingly, they found no difference between the two groups in terms of T-helper cell levels.

50 T-Helper Cell Threshold

Finding surrogate markers that predict or indicate disease progression has been a research priority since early in the epi-
The U.S. National Cancer Institute (NIH) reviewed the records of patients who had participated in antiviral therapy studies and found that only one of 51 patients who died of AIDS had a T-helper cell count of more than 50. The study also found that the median survival time of patients after their counts had fallen below 50 was only 9 months (M.B.37). The researchers concluded that a count of 50 may be an important benchmark for defining stage of illness, and Samuel Broder, Director of NIH, suggested at the conference's closing that keeping counts above 50 may be the goal of therapy.

Treatment

Conference data continued to support the efficacy of early antiviral treatment and offered new evidence about the use of combination therapy as disease progresses. Researchers presented evidence that ZDV was well tolerated in early use and that the development of anemia, which was often seen at the previously recommended doses of 1,500 milligrams per day, was a rare complication at doses less than 500 milligrams per day. Furthermore, they found that if patients had not developed anemia within the first six months of treatment, it was unlikely that they would.

ZDV Comparable in Women and Men

The number of presentations on the treatment of women—not including the many studies on vertical transmission of HIV to the fetus—could be tallied on a hand or two. Studies that were reported, however, begin to define the differences between manifestations and treatment of HIV disease among women. Two studies, both from Canada, examined ZDV use in women. The first, comprised of 58 subjects followed for a mean of 45 weeks, found that the low rate of progression to AIDS—6.1 percent for the sample—was comparable with predominantly male samples treated with higher doses (W.B.2068). Anemia and leukopenia (depressed white blood cell count) seemed more prevalent in this sample, particularly for women receiving more than 600 milligrams per day, than in male samples. The second study found that, of the 289 female subjects, 89 percent survived after 12 months and anemia was the most common side effect (W.B.2085).

Combination Therapy Reduces Toxicity

Combining ZDV with other drugs to enhance efficacy, and to reduce toxicity and the development of resistance, is an area of continuing research. Strategies include using ZDV with drugs that interfere with different aspects of the HIV life cycle, for example, alpha interferon (TH.B.35), as well as using drugs from the same chemical family, for example, dideoxycytidine (ddC) and dideoxyinosine (ddI). In the laboratory, ddC and ddl have shown additive effects against HIV when combined with ZDV (W.B.2110), and several studies supported this strategy.

2. Results confirming the positive effects of early treatment with ZDV were reflected in a number of presentations (W.B.2001, W.B.2125, W.C.41).

Clearinghouse: AIDS Conference

We surveyed 30 professional journals and newsletters to find out in which would appear summaries of the Seventh International AIDS Conference. The following is a compilation of those offering special coverage. We have tried to include ordering information and pricing when this was available.

Conference-Specific Publications

Official conference abstract books are expected to be available for purchase. To receive more information, write: Seventh International AIDS Conference, General Secretariat, Laboratory of Virology, Instituto Superiore di Sanita, Viale Regina Elena, 299, 00161 Rome, Italy.

Audiotapes of conference presentations are available for $8.00 each from InfoMedix. To receive a list of presentations or to order, call: (800) 367-9286.

Journals and Newsletters

AIDS, a monthly journal, plans to publish a special edition focusing on the Florence conference and reviewing 1991's HIV-related medical and psychosocial advances. To order the hardbound edition, to be released at the end of 1991, write: Current Science, Philadelphia Sciences Group, Order Fulfillment Department, 12908 Acorn Hill Court, Midlothian, VA, 23112, or call (804) 744-5233.

AIDS 91 Florence Summary, abstracts the conference findings. Send $64.75 before December 1, or $90.75 after this date to: Philadelphia Sciences Group, Order Fulfillment Department, 12908 Acorn Hill Court, Midlothian, VA, 23112, or call (804) 744-5233.
The Vaccine Solution

Following the disappointments of last year's conference, when advancing research served only to emphasize the challenges facing vaccine development, this year's conference offered evidence that those challenges might be overcome. Thirteen vaccines are in human safety trials and, within the next three years, should enter efficacy trials. While research is moving rapidly, none of the vaccines presented meets two of the key criteria for a successful model: that is, the ability to raise antibodies that will kill free-floating HIV and to induce a T-killer cell response that will eliminate cells that are already infected. However, even data that demonstrated failed attempts suggested that these criteria can and will be met during what Dani Bolognesi, a leading researcher from Duke University, dubbed the "Decade of the Vaccine."

"Post-exposure" vaccines, those that stimulate the immune system to overcome HIV after it has infected the body, generated the greatest enthusiasm among conference participants. Dr. Bolognesi noted that the array of post-exposure vaccine findings shared similar results: stabilization of T-helper cell levels, stabilization of weight loss, reduction in opportunistic infections, and increased survival. The relatively uniform success of these approaches is expected to lead to rapid and greatly expanded trials.

Opportunistic Conditions

Conference presentations reported on a range of treatment developments for opportunistic conditions. According to AIDS Treatment News, "Most of the clinical information [on opportunistic conditions] came from relatively small confirmatory
Long-term survivors are 'superb medical consumers'; optimistic, tenacious, and determined; and use denial only minimally to cope with illness.

Conference reports offered few new insights into psychosocial issues. Some interesting studies, however, reaffirmed the clinical experiences of mental health providers. The importance of social support for people with HIV disease was shown in studies of hemophiliacs (W.B.2399), injection drug users (W.D.4026), gay men (W.D.4212), and both gay men and injection drug users (W.B.2385). Most notably, in a study from a semi-rural setting in the U.S., fewer social supports predicted the development of major depression in a group of 75 people with HIV disease (W.D.4276).

A San Francisco study presented data on multiple loss, grief, and depression (W.D.2). Responses from 430 gay men revealed significant increases in depression as AIDS deaths or diagnoses of friends or acquaintances increased from a median of one in 1984, to three in 1986, to seven in 1988. Seropositive subjects showed significantly higher levels of depression in response to losses.

A study of long-term survivors in New York attempted to determine the psychological consequences of prolonged illness, and to identify factors associated with the maintenance of hope and quality of life (TU.D.105 and M.D.105). "Long-term" was defined as having an AIDS diagnosis for 36 months, twice as long as the CDC survey's 1990 median survival time.

Participants were generally pragmatic and realistic about their illnesses. They were highly informed about their disease and "superb medical consumers" who worked in partnership with their physicians and reported high satisfaction with their doctors. They were optimistic, tenacious, and determined, and most reported a sense of accomplishment about their lives. They used denial as a coping mechanism only minimally; while these men were acutely aware of their foreshortened lives, they did not believe they would "beat" their illness.

Women and the Politics of Sexuality

Attention to issues affecting women with HIV disease was more noticeable this year than in the past, but research progress was limited. Much of the psychosocial discussion emphasized the shortcomings of the CDC AIDS case definition, which does not include gynecological manifestations of HIV infection, the failure of sexual behavior change programs to target men in heterosexual relationships, the lack of research on safer sex methods that, unlike condoms, women can control, and the poor, although improving, access of women to clinical trials.

At a community session on women, Columbia University researcher Zena Stein noted that only a handful of conference presentations addressed safer sex methods over which women have control, for example, a vaginal virucide or the female condom. There was agreement among participants that energy must focus on changing sexual power relationships throughout the world, and research must seek safer sex alternatives that compensate for this imbalance.

A study of women's participation in clinical trials found that the recruitment of women in ACTG trials has increased over time but is leveling off. Women have accounted for a total of 6.7 percent of all ACTG subjects (TU.D.114). In addition, women in trials are not necessarily representative of the bulk of women with HIV: women of color comprise 73 percent of women with AIDS but only 52 percent of trial participants; women injection drug users comprise 51 percent of women with AIDS but only 23 percent of participants.

Approaches to Prevention

Reports on prevention programs generally fell into two categories: the first...
represents the application of basic prevention activities in communities around the world. These reports indicated the huge effort underway to implement such programs, but failed to provide new insights for most other programs.

The second category involves a more thoughtful approach to the fundamental challenges of human behavior change. Researchers in a few sites applied basic theories of behavior change to program development. Thus, some new studies attempted to create social norms to influence behavior while others focused on perceived personal efficacy as a primary factor for risk reduction. Other studies relied heavily on the principles of commercial marketing to develop the most effective messages for specific target populations. The variety of approaches in this second category reflects the fact that there is no clear agenda for behavior change research or programming. Without this agenda to serve as a context for interpretation, valuable lessons from the field get lost in the thousands of repetitive studies conducted each year.

The fact that behavior change researchers are seeking to identify factors that move people from "being aware" to "willing to try new behaviors" or from early adoption of behavior to sustained behavior changes reveals that many researchers and programmers recognize that the "easy" part of AIDS education is over. The worldwide public is, for the most part, knowledgeable about HIV disease. The challenges in AIDS prevention now are to define an effective prevention theory, to establish priorities and an agenda, and to obtain the resources necessary to implement comprehensive programs for behavior change.

Neuropsychiatric Aspects

In what is perhaps the most important neurological report since the beginning of the epidemic, Leon Epstein of the University of Rochester in New York announced the successful development of an animal model for studying HIV infection in the brain. Epstein made the presentation in Padua, Italy, at the Neuroscience Satellite Symposium, which preceded the International Conference. The process involves grafting human fetal tissue into the anterior chamber of an adult rat's eye, which, since it is free from normal immune system response, does not reject the implant. The fetal tissue grows normally, develops a blood-brain barrier, and differentiates into specific human nerve cells. Dr. Epstein and his colleagues are currently attempting to infect the graft with HIV to study the process of primary infection. Other studies may include examining effects of other organisms on brain function.

Also at the symposium, Steven Wolinsky of Northwestern University in Chicago reported that HIV "env" gene sequences vary by as much as 11 percent in the blood and brain of a single individual. These differences may be responsible for producing in the same person strains of HIV that are more effective at infecting either nervous tissue cells or systemic immune cells, and may arise because of differences in pressure on either side of the blood-brain barrier.

Neurological Impairment

At the International Conference, reports from a variety of countries continued the debate on whether asymptomatic seropositives are subject to cognitive impairment. The majority of the evidence continues to suggest that asymptomatic individuals are not significantly more likely than uninfected controls to be impaired.

Several presentations, however, did suggest that seropositives had slower "central conduction times," that is, their brains processed electrical impulses more slowly than the brains of seronegative controls (M.B.2070, M.B.2118, M.B.2086). This finding is consistent with the accepted fact that HIV infection of the brain and spinal cord occurs early in the course of the illness and that this infection can and at times does lead to problems in thinking. However, infection does not seem to lead consistently to poor test results on formal neuropsychological examinations.

Other neuropsychiatric conference presentations included:

- a case report of mania in two people with AIDS being treated with a daily dose of 750 milligrams of ddI (M.B.2031). The patients had no history of mania, and the episodes resolved within 10 days of stopping treatment.
- a study of 64 children whose cognitive impairment improved six to 12 months after treatment with ddI (W.B.2051). There was no additional improvement after 12 months.
- a study of 350 consecutive psychiatric admissions to an acute inpatient ward in New York showing a 7 percent sero-prevalence rate, much higher than in the general population (M.B.2114).
Summary

Epidemiology. In industrialized nations, the populations affected by the epidemic continue to broaden from gay White men to women, people of color, and injection drug users, and professionals who wish to continue to respond will need to know more about these populations in order to address their needs. In the near term, gay men will remain dominant in the statistics, and the need for support for gay men with HIV infection will be matched by the need for support for gay communities dealing with years of cumulative, long-term loss.

Natural History. Research continues to fail to discover a magic cofactor that people with HIV disease can avoid or embrace to remain healthy. In fact, the emerging correlation between progression, STDs, and HIV reinfection supports the stance, disappointing to some, that safer sex is as central to HIV treatment after infection as it is to HIV prevention before infection.

Conference data suggest that the course of disease is far more similar across transmission categories than it is different. The identification of a 50 T-helper cell threshold strengthens arguments for antiviral treatments, which may be valuable in extending life even if they fail to restore full immune function. Armed with information that may give people with HIV disease the sense that they have more time available to adjust and to make decisions, counselors can help clients deal with the overwhelming demands of infection in a more deliberate way. At the same time, counselors should be prepared to deal with the heightened concerns of people whose T-helper cell counts fall below 50 and who interpret these results as a death sentence.

Treatment. Treatment decisions for most medical conditions are usually confined to the physician's office, but for HIV disease, mental health practitioners frequently work with their clients to sort out these questions. While it is disappointing that ZDV and its analogs, ddC and ddI, remain the only real choices for treatment, the emergence of the TIBO derivatives and the post-exposure vaccine promise potent alternatives. Conference data suggest that lower doses and combinations of antivirals may lead to fewer and less toxic side effects, and may make treatment choices less intimidating.

Who would have thought, after last year's gloomy outlook, that vaccine research success would have dominated the Florence conference? An effective vaccine could fulfill four goals: protection for the uninfected; treatment for those already infected; a potentially affordable treatment for developing nations where poverty has made even basic health care, much less high-priced antivirals, the stuff of legend; and hope, particularly in those communities hardest hit by the epidemic. While optimism seems justified, the implementation of a widespread vaccine program remains distant.

Psychosocial and Neuropsychiatric Issues. Conference studies confirmed the importance of social support and suggested factors that might lead to long-term survival. While some studies offered insights into risk reduction, the lack of a foundation for behavior change continues to complicate prevention, even in the face of the global success of HIV education.

Jonathan Mann, Director of the Harvard International AIDS Center, reflected on the hope and apprehension we face: "Our own 'status quo' frightens us. A revitalization, a creative renewal of efforts is needed—building upon success, yet capable of facing the evolving circumstances and even greater challenges of the 1990s."

Next Month

The prevailing mythology is that drug users lack the competence and their communities lack the existing structure to organize effective prevention and social support efforts like those of the gay and lesbian communities. In the October issue of FOCUS, Samuel R. Friedman, PhD, Senior Principal Investigator at Narcotic and Drug Research, Inc. in New York, explains the importance of drug user organization for HIV risk reduction and offers a critique of two drug user organization experiences, one in Amsterdam and one in New York.

The stuff of myth also enters into the debate regarding syringe exchange, perhaps the most potent risk reduction intervention for injecting drug users. Also in the October issue, Holly Hagan, MPH, Principal Investigator of the Tacoma Syringe Exchange Study, reviews the data on syringe exchange to determine whether such programs increase drug use among current injectors and attract new injectors.