Studying HIV-related sexual behavior has always been a challenge. From one view, the tasks of behavioral researchers supporting intervention design are to help select and define the behaviors to be changed; to identify underlying behavioral determinants, that is, the factors that explain, cause, or are associated with the behavior; and, based on this understanding, to make recommendations about which determinants should be modified in order to impact behavior.

For a number of reasons, these tasks are especially difficult for researchers supporting the design of HIV prevention programs. First, sexual behaviors are complex. Their determinants are diverse and differ from community to community. Second, proven research methods are difficult to apply when people will not or cannot talk about the behavior under study and when many populations are difficult to reach. Third, sexual behavior is a sequence of behaviors and involves interactions between people. Thus, behavioral theories, which work best studying one behavior of one person, can easily break down. Fourth, in the context of HIV prevention, sexual behavior must be studied and interventions must be developed in a complex political environment.

This article will report on the VIII International Conference on AIDS, and information on the sexual behaviors that place people at risk of HIV infection, the determinants of these behaviors, and the efficacy of interventions designed to influence them. It will show that research on sexual behavior is alive and well; that although it is difficult to summarize conference findings, some modest developments show promise; and that behavioral researchers face an important challenge and opportunity in the light of the social nature of the epidemic.

The Status of Behavioral Research

Although it does not yet have its own track at the international conference, behavioral research continues to be well represented. An examination of the populations studied, theories applied, and methods used demonstrates an improvement in the quality of this research.

Populations. Behavioral researchers are studying an increasing number of diverse countries, cultures, and communities, including developing as well as industrialized nations; rural as well as urban populations; and various ethnic and social groups. There continues to be much research on men who have sex with men and on people involved in commercial sex work. This research demonstrates the need for distinctions by ethnicity, social and economic status, age, and drug use and sex work history.

Researchers are also paying greater attention to general populations. Some of this research focuses on samples representative of national populations. Some is based on samples drawn by selecting people at convenient study sites, such as recruits entering the military, people attending sexually transmitted disease (STD) and other health clinics, adolescents in schools, inmates and staff of prisons, and people who live on the streets.

After years of neglect, research with women is also increasing. While some involves female partners of bisexual men or injection drug users, and women attending family planning clinics, much of this research is limited to pregnant
Editorial: The Feast of Information
Robert Marks, Editor

Once a year, if at no other time, we all become researchers. In late spring, the international conference is convened and, like fish alert to feeding time, we gather in a frenzy all the latest information on the epidemic.

The pickings are usually good—plenty of data on everything from vaccines to antiviral drugs to transmission prevention to counseling. But it's raw, and for those of us who are not specialists, ingesting this information is bound to cause some digestive discomfort.

How best to partake in this feast? The savvy researcher takes the easiest road to synthesizing knowledge. In the areas where he or she is particularly well-informed, consulting the raw data—the latest studies memorialized in the 1,000 pages and three volumes of abstract books—may prove useful. This is especially true, if the reader has identified a specific topic. The abstract book index can help, but to summarize even a narrow subject may require looking at 20 different citations.

To approach areas with which a reader has only limited knowledge, using secondary sources may be the most efficient process. Start with media stories that are published at the time of the conference, but don't end there. The media, seeking sound bites in the complicated world of AIDS, is likely to cover only the most easily summarized stories, especially if they can be expressed in terms of "human interest." The best sources for good summaries of conference presentations, particularly related to clinical medicine and basic science, are the several newsletters that are listed in this month's AIDS Treatment News, BETA, and Treatment Issues.

These reports are usually written by knowledgeable lay people or clinicians like HIV and infectious disease specialist Stephen Follansbee, who offers his view of the conference in this month's FOCUS. For the best overview, practitioners should consult more than one newsletter: when 12,000 people come together to present 5,000 papers, as they did in Amsterdam, no single article can do justice to the richness of the enterprise.

This month's FOCUS offers another approach to understanding the conference. Susan Middlestadt discusses trends in the ways behavioral scientists are handling the difficulties of studying this topic. How can they investigate a highly politicized behavior about which people are unwilling to talk? How do they approach it when it confounds normal research techniques designed to study only one behavior, rather than a sequence, and only one person, rather than the interactions between two or more people?

This sort of analysis sacrifices the specificity of most conference summaries, but it provides the synthesis of ideas so often absent from conference reviews. It is this synthesis that helps practitioners apply the lessons of the conference to their professional pursuits.

women. More work is needed on behavioral determinants of women not in the commercial sex industry. Key to making this research useful for intervention design remains the identification of behaviors that are under a woman's control.

Theories. Theories of behavior and behavior change are playing an increasingly important role in guiding research and intervention design. Some research explicitly uses and even compares general theories—such as the health belief model, social cognitive learning theory, and stages of change models—as well as theories specific to HIV disease, such as the AIDS Risk Reduction Model and the AIDS Applied Behavior Change Framework. While not explicitly mentioning them, many researchers use determinants from these theories in their studies.

It is becoming clear that HIV-related research needs to consider a limited and consistent set of underlying determinants, factors that extend beyond general knowledge about HIV disease and perceived risk of infection. For example, researchers now examine a variety of aspects of HIV-related knowledge—knowledge about the disease, about modes of transmission, and about methods of prevention. In addition, they investigate "beliefs about the consequences" of a variety of more or less risky behaviors; they have amassed considerable quantitative evidence substantiating the importance of "perceived and actual social norms"; and they refer increasingly to actual "skills" and "self-efficacy" when designing interventions.

Methods. Behavioral research is applying more sophisticated qualitative and quantitative tools. In addition to traditional focus group discussions and Knowledge, Attitude, Belief, and Practices (KABP) surveys, researchers are using tools like sexual and social network analysis, ethnographies and other forms of in-depth interview, linguistic analysis, policy analysis, and observation studies.
In addition, methodological researchers are examining and comparing the validity of sexual behavior research methods. For example, face-to-face interviews, which allow the study of populations with lower literacy, compared favorably with self-completion instruments, which allow privacy and confidentiality.

**Descriptive Research**

These trends are leading to improved behavioral research—both descriptive and evaluative—and more effective interventions. The goal of descriptive research is to identify which of the potential underlying determinants is most associated with a behavior and, thus, would make an effective intervention point. The results of this research are difficult to summarize and depend on two parameters.

First, they depend on the population being studied. A review of conference presentations clearly shows that different patterns of sexual behavior and different underlying determinants correspond to different populations and often with different segments within populations. For example, studies reported that women in the sex industry who work the street have less knowledge about HIV disease, have more customers, and are less likely to use condoms than those who work in brothels or clubs. Not surprisingly, many studies compared men and women: some found differences in the determinants of sexual behaviors, while others did not. This suggests the importance of factors other than gender, such as ethnicity, relationship status, sexual experience, and stage in sexual development.

Second, results depend on the context of the behavior. For example, studies from the conference showed once again that sexual behavior with a primary partner differs from behavior with a new or casual partner. People are more likely to use condoms with new or casual partners. Furthermore, perceived norms—that is, what we think other people think—are stronger determinants of condom use in the context of primary partners than in the context of casual partners.

Finally, it is also clear from the conference that determinants differ depending on the point in the sexual history at which an individual is studied. For example, there is evidence that people with no sexual experience hold more positive attitudes towards condoms than those with some “first” experiences; and those with long histories of successful condom use seem to regain positive attitudes.

With these limitations in mind, three determinants show promise across a variety of behaviors and populations. First, research points to the importance of identifying “beliefs” about the consequences of safer sex other than HIV prevention. Being told that condoms protect against HIV disease rarely motivates condom use. Instead, research is identifying other reasons like protecting the family, being modern and responsible, preventing other STDs, preventing pregnancy, and being erotic. Second, many studies identify perceived “social norms” as predictive of behavior. Not only do these interventions appear to influence social norms, but research suggests that changes in actual and perceived norms do mediate changes in behavior. And, third, research regarding “perceived and actual skills” for the purchase and correct use of condoms and for communicating and negotiating safer sex has demonstrated the promise of skill-building interventions. Of particular interest are interventions that allow behavioral rehearsal, social modeling, performance feedback, and video modeling.

**Evaluation Research**

The goal of evaluation research is to determine if and how an intervention has an impact. As with descriptive research, evaluation research is difficult to summarize because the effectiveness of an intervention is likely to depend on the target population. In addition, such summaries would be facilitated by three improvements in evaluation research. First, studies must assess quantitative as well qualitative impact. Second, they should be designed so that any changes found can be accurately attributed to the intervention implemented, for example, by adding control and comparison groups or by assessing the degree of exposure to the intervention. Third, they need to be based on fully articulated conceptual models that describe what the intervention is and how it affects behavior. Useful summaries of intervention research will need to be able to say more than, “This intervention worked with this population.”

Keeping these limitations in mind, research evaluating the impact of prevention interventions is showing promising evidence of changes in sexual behavior.
and underlying determinants of these behaviors. A wide variety of educational, communication, and counseling interventions were studied including safer sex workshops, group discussion sessions, individual counseling, pre- and post-test counseling, peer education, school-based education and counseling programs, community-wide programs, street outreach, work site education projects, public service campaigns using radio, mass media, and media events, and films and other dramatic forms. In addition, studies have evaluated structural interventions such as increasing accessibility of condoms and establishing safer sex policies.

Most if not all evaluation studies demonstrate changes in knowledge. Sometimes changes in beliefs, attitudes, norms, and intentions are also demonstrated. Only a few studies from the conference demonstrated changes in behavior that were attributable to an intervention. This was true for three reasons. Sometimes, the study designs did not allow for the assessment of behavior. To measure changes in behavior, one must give participants an opportunity to behave, thus, studies of behavior change must occur over months if not years. Often studies demonstrated that behavior change occurred, but they could not isolate the cause of that change. Finally, it is more difficult to change behavior than its underlying determinants.

The Social Dimension of Behavior Change

One of the major contributions of this year's conference was its focus on the larger social context of HIV disease. What is the appropriate role for the behavioral scientist if the poverty, powerlessness, and marginality of large numbers of people underlie the epidemic? Is there any role for behavioral interventions that focus on changing individual sexual behaviors in the face of such cultural, political, and social factors?

As an illustration, consider the case of a married woman who is socially, emotionally, and economically dependent on her husband. Behavioral research may show that her “beliefs” that he will be angry, hurt, or leave her, and her “skills” around negotiating condom use may be associated with the behavior of “asking my husband to use a condom.” Further, research may show that women who are more highly educated are less likely to hold these beliefs and more likely to have these skills. Should AIDS educators respond with short-term interventions focusing on changing beliefs and improving skills, or on longer-term interventions that increase educational levels of women in the country? The challenge is to recognize rather than ignore the larger social context, and to design interventions that are not only sensitive to the larger context, but also helpful in reaching longer-term goals.

Conference presentations did not directly answer these questions, but there was one positive development that may reconcile social context with individual prevention goals: behavioral research is increasingly collaborative and interdisciplinary. Research teams are composed of professionals from many specialties, many health domains, and often several countries, including developing nations. There is also more evidence of interaction among researchers, program designers, implementors, and constituents. These collaborations serve as hope for the future not only in terms of behavior change interventions, but also in terms of developing the cooperation necessary to respond to the pandemic on all fronts.
Researchers, clinicians, social scientists, and patient advocates gathered at the International Conference on AIDS to summarize the advances of the past year and challenge each other about future areas of research. Progress hinges on developing knowledge in areas of virus structure and function, immunology, and new drug development.

The Virus and the Immune System

Progress in understanding the basic structure and genetic composition of HIV is leading to ways to “catalog” virus isolates and to a better understanding of disease progression. Researchers compare the in vitro (laboratory) characteristics of the virus from a single individual over time (PoA 2057). Such studies have found that as infection progresses HIV changes so that it can infect a greater variety of human cell types, cause more cell damage, and lead to more cell-to-cell fusion or “syncytia,” which renders cells less functional (PoA 2374). Researchers are genetically mapping these changes in hopes of developing new antiviral drugs.

Presentations on the immune response to HIV focused on the role of T-suppressor cells (CD-8 lymphocytes). Early in the course of HIV infection, one T-suppressor cell is able to suppress infection in up to 20 T-helper cells (CD-4 lymphocytes) (PoA 2184). As infection progresses, the potency of this suppression diminishes and the T-suppressor cell population decreases. Researchers are working to isolate, describe, and harness the “activity substance” in T-suppressor cells.

While exploring immune system responses that are “protective” against viral infection and damage, researchers are also defining responses that may actually “enhance” viral activity and lead to further disease (Sessions 21, 54). Several studies investigating maternal factors that influence the risk of infection in newborn infants have begun to identify neutralizing antibodies, viral characteristics, and other maternal factors that may affect vertical transmission (Sessions 120, 147: PoA 2463). Understanding which maternal factors prevent infection may result in therapy to enhance these immune factors in all HIV-infected people.

Researchers are working to isolate, describe, and harness the “activity substance” in T-suppressor cells.

Presentations at the conference confirmed the imprecision of markers of disease progression, including T-helper cell counts, p24 antigen levels, and HIV cultures (Sessions 35, 202).

Antiviral Drug Development

Given the narrow range of activity and limited effectiveness of current nucleoside analogues—zidovudine (ZDV; AZT), didanosine (ddI), and zalcitabine (ddC)—many investigators are focusing on other antiviral strategies. Presentations on antiviral research ranged from new com-
A new reverse transcriptase inhibitor, d4T (staduvine) appears to have good antiviral activity, based on increase in T-helper cell count and declines in p24 antigen levels, although it resulted in a few cases of neuropathy (Web 1010, Web 1011). Discussions of combination therapy with different nucleoside analog RT inhibitors (ZDV and ddI; ZDV and ddC) resulted in no consensus on when to use combinations or which combination was best (Sessions 23 and 209). There was agreement that combinations may offer a longer duration of "response" than one drug alone.

The TAT gene of the virus produces a protein that amplifies the production of other proteins necessary to HIV replication. Researchers presented preliminary results of a TAT gene antagonist that can be absorbed orally to achieve drug levels in excess of those determined in the laboratory to decrease viral activity by 90 percent (MoB 0021).

Several studies characterized the nature of antiviral drug resistance and the genetic changes that lead to the virus's production of altered RT enzyme that can escape inhibition by antiviral drugs (Sessions 53, 170, 258). It appears that relatively few changes in the RNA account for resistance. This fact may lead to the development of rapid tests for drug resistance, making it easier to decide when to switch from ZDV to ddI or ddC.

Immune Therapies

Immune therapy research is progressing (Sessions 104, 257) with the clearest progress in the use of alpha-interferon. Studies with currently available alpha-interferons, the only immune therapy that is far into clinical trials, have had good results, particularly in combination with ZDV early in the course of HIV infection (PoB 3581, 3582, 3584, 3586). While these studies have had high drop-out rates because of chronic flu-like side effects, results are promising.

Other immune therapies seek to strengthen or change immune system components so they are more effective against HIV. For example, one study found that T-suppressor cells can be harvested, grown outside the body, and reinfused into donors to boost suppression of HIV-infected T-helper cells (PoB 3444, 3446, 3452).

Finally, last year's excitement about vaccine therapy for those already infected, which would boost immunity and inhibit HIV production, continues to advance through the research process. Vaccine studies were encouraging: all therapeutic vaccine candidates appear to be safe. Of particular note, subjects vaccinated with the gp160 viral surface protein, seemed to maintain "stable" immune function over 18 months of observation (MoA 0011, TuB 0562, 0563).

Opportunistic Conditions

There were few presentations about opportunistic conditions that reported new findings. BW566-C80, a new oral medication for Pneumocystis carinii pneumonia, appears to have a good cure rate and low incidence of side effects (Web 1019). Several papers suggested that in combination with other standard Mycobacterium avium complex agents, patients using clarithromycin and azithromycin may avoid the resistance to these new antibiotics reported in another paper (Web 1052).

Kaposi's sarcoma (KS) is now believed to be the result of HIV and a currently unknown co-factor, which may be sexually transmitted (ThB 1543). At the conference, liposomal therapy—the use of lipid droplets containing the anti-cancer drug daunorubicin to target drug delivery to KS lesions—seems to offer some therapeutic benefit (PoB 3119, 3123).

Conclusion

Despite a failure to produce significant insights into day-to-day treatment, the conference presented significant advances in knowledge about the basic science of HIV infection. It is clear that this knowledge will be essential in the further development of antiviral and immune therapies.

IX International Conference

The IX International Conference on AIDS will convene in Berlin June 7 through June 11, 1993. The conference is accepting abstracts for presentations in four tracks: Basic Science, Clinical Science and Care, Epidemiology and Prevention, and The Social Response. The deadline for abstract submissions is January 15, 1993.

For further information, write: Congress Secretariat, Inst. for Clin. & Exper. Virology, Free University of Berlin, Hindenburgdamm 27, D-1000 Berlin 45, or call 49-30-798 36 87 or 49-30-834 27 76 (fax: 49-30-834 30 61).
Recent Reports

Changing Treatment from ZDV to ddI

In a multicenter study of 913 participants, substituting didanosine (ddI) for zidovudine (ZDV; AZT)—after at least 16 weeks of ZDV therapy—resulted in a markedly lower rate of progression to new AIDS-defining diseases, but did not affect rates of progression to death. ddI, a nucleoside analog of ZDV, also showed acceptable toxic side effects and improved CD4 counts and lowered p24 antigen levels.

Researchers gave subjects 600 milligrams ZDV or 750 or 500 milligrams of ddI and followed them for an average of 55 weeks. Participants were either people with AIDS, symptomatic HIV-infected people, or people who were antibody positive, asymptomatic, and with T-helper cell counts under 200. They were primarily White gay or bisexual men who had tolerated at least 16 weeks of ZDV treatment. (The median was 13.9 months of ZDV therapy.)

Progression to new, nonrecurring, AIDS-defining disease or to death occurred in 115 (37 percent) of the study subjects receiving 750 milligrams of ddI, 94 (32 percent) of those receiving 500 milligrams of ddI, and 125 (41 percent) of those receiving ZDV. Among HIV-infected subjects without AIDS at the time they entered the study, treatment with either dosage of ddI was significantly better than ZDV at delaying onset of the first AIDS-defining illness or progression to death. Subjects who received 500 milligrams—but not 750 milligrams—of ddI had significantly lower rates of new or recurrent AIDS-defining conditions and death than subjects who received ZDV.

ddI toxicity was not significantly different from ZDV toxicity. However, severe anemia and leukopenia was more prevalent with ZDV use, and significantly higher rates of pancreatitis and elevated serum amylase were associated with taking 750 milligrams of ddI.

566C80 to Treat PCP


566C80, a new anti-Pneumocystis carinii pneumonia (PCP) drug, can reasonably be used to treat patients who are intolerant of or fail to respond to the other widely used treatments, according to a review of the literature on the drug. It was given investigational new drug (IND) status in November 1991.

Animal studies have revealed that 566C80 has few adverse side effects, a long half-life, and is toxic, not just inhibitory, against the organism that causes PCP. A phase I trial using escalating dosages in six cohorts of four seropositive men found only a mild adverse effect, a rash, in only one patient. The drug was absorbed in sufficient therapeutic amounts. Two additional studies also demonstrated the drug’s efficacy.

A study presented at the VIII International Conference on AIDS compared 566C80 with TMP-SMX and found that it had a similar overall rate of therapeutic efficacy. While patients receiving TMP-SMX had a better therapeutic response, those receiving 566C80 had fewer treatment-limiting adverse effects. The study followed 322 subjects with mild and moderately severe PCP for a treatment course of 21 days.

Epidemiology of HIV Infection

A retrospective survey of medical records—performed in light of the proposed CDC AIDS definition change—found that people with HIV disease suffer from a wide variety of conditions other than those included in the 1987 AIDS definition. These diseases occur more frequently as T-helper cell levels decrease.

Between January 1990 and March 1991, researchers collected data retrospectively on 7,635 HIV-infected persons from nine U.S. cities: Atlanta, Dallas, Denver, Detroit,
Los Angeles, San Antonio, Seattle, Houston and New Orleans. Eight percent of participants were women, 24 percent were Black, 10 percent were Hispanic, and 9 percent were injection drug users. Where possible, disease incidence was correlated with T-helper cell counts as a measure of immunosuppression.

Of infected subjects, 27 percent developed one or more AIDS-indicator diseases, with *Pneumocystis carinii* pneumonia (PCP), esophageal candidiasis, and Kaposi’s sarcoma being the most frequent. For those with T-helper cell information available, 85 percent had counts below 200. At comparable T-helper cell levels, the proportion of subjects who first developed an AIDS indicator disease was virtually the same for men who had sex with men compared with injection drug users, and for all women compared with all men.

One or more of several major infectious diseases—most notably pneumonias other than PCP, pulmonary mycobacterial disease, and bacterial sepsis—occurred in 12 percent of subjects; at fewer than 200 T-helper cells, this frequency rose to 16 percent. These diseases occurred more frequently among injection drug users than gay men and were more common among people with AIDS than among other HIV-infected people.

The association between lower T-helper cell levels and higher incidence of disease was observed for other HIV-related conditions including thrush, herpes zoster, and peripheral neuropathy. Only malignant neoplasms, which occurred in less than 10 percent of the sample, showed no relationship to immunosuppression status.

**HIV Antibody Testing**


Of the more than two million HIV antibody tests administered by public health departments in 1991, 2.8 percent were positive, according to a survey of the 65 HIV prevention project areas that make up the U.S. and its territories.

Among those who reported risk behaviors, gay and bisexual men who also injected drugs had the highest rate of antibody positive test results: 17.4 percent. Among gay and bisexual men who were not injection drug users, seroprevalence was 11.8 percent, and among heterosexual injection drug users, seroprevalence was 8.3 percent. These three groups accounted for 15.9 percent of tests and 58.4 percent of positive results.

Heterosexuals with reported risk behaviors—including those whose sex partners are HIV-infected or at risk for HIV infection and those with multiple sex partners—accounted for 24.5 percent of tests and 16.2 percent positive results. The largest number of test takers—heterosexuals with no history of risk behavior who comprised 58.1 percent of the survey—had a seropositive rate of 1.2 percent.

Of all positive tests, Whites accounted for 34.4 percent, Blacks for 43.3 percent, and Hispanics for 19.5 percent. Seropositivity was greatest among Hispanics (4.6 percent). Men had seropositivity rates of 4.2 percent, versus 1.3 percent for women. Of people 20 to 29 years old, 34.4 percent tested positive; of those 30 to 39 years old, 41.8 percent tested positive; and of adolescents, 0.5 percent tested positive.

The majority of those tested (63.1 percent) received post-test counseling. This was more likely to occur at freestanding clinics, where 81.2 percent received counseling, than at STD clinics, where only 40.6 percent received this service.

**Next Month**

Blame it on the election, or on the recession; blame it on the millennium, or on the hurricanes, the fires, the California drought. Due to forces beyond our control, the content of the November issue of *FOCUS* remains undetermined. We do plan for such natural disasters, however, and have several issues in production.

Among the articles that will appear during the next four months are pieces on: the training and experiences of informal caregivers, that is, friends, family, and lovers of HIV-infected people; vaccine trials and the ethical, scientific, and psychological issues they raise; the application of behavior change theories to safer sex relapse, and a survey of safer sex relapse programs; and the challenges of dealing with HIV prevention in the African-American community, in particular, among adolescents.

Next Month—November 3—is also the most important AIDS event of the next four years. Avoid yet another natural disaster: remember to vote.
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