In this special issue of FOCUS, six specialists examine the implications of selected presentations at the Fifth International AIDS Conference, which took place in Montreal from June 4 through June 9. They discuss neuropsychiatric issues, prevention, education, basic science, clinical issues, legal and ethical issues, and international issues. In addition, FOCUS inaugurates our special quarterly Supplement on Antibody Test Counseling by including it with this Montreal issue. The supplement is financed through a grant from the California Office of AIDS and distributed only to antibody test counselors in California. It is included here as a one-time bonus to enrich our coverage of the conference.

Neuropsychiatric Issues

Among the most controversial aspects of the Fifth International AIDS Conference was the increased emphasis on psychosocial issues of HIV infection, including behavioral aspects of HIV transmission, the treatment of the neurologic consequences of HIV, and the interrelationships among HIV activation, immunity, and psychological state. One of the most complicated psychosocial issues discussed was the effect of HIV on neuropsychiatric functioning, in particular, the manifestation of AIDS Dementia Complex (ADC), a progressive dementing disorder caused by HIV infection of the brain.

Cognitive Impairment

Oral presentations about neuropsychiatric issues for adults focused on the epidemiology of ADC and the incidence and natural history of cognitive impairment in asymptomatic seropositives. The Centers for Disease Control (CDC) reported that, based on an analysis of 38,666 adults and 666 children, the proportion of each group that demonstrated encephalopathy (degeneration of the brain) as the first manifestation of AIDS were 3.0 percent and 3.3 percent, respectively. Overall, the proportions of these patients who developed encephalopathy were 6.5 percent among adults and 11.5 percent among children. In general, rates of encephalopathy increased with age in adults and decreased with age in children. Thus, encephalopathy is rarely reported as the only early manifestation of AIDS, and appears to be most common at the extremes of age: older adults and younger children.

The existence and extent of cognitive impairment in asymptomatic seropositives remains controversial, although conference presentations demonstrated a growing consensus on this point. While an asymptomatic seropositive person may develop some degree of cognitive impairment, this is not a rare event and appears to be most common at the extremes of age: older adults and younger children.

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Development of cognitive impairment does not necessarily imply that progressive deterioration is a certainty.

Descriptive studies of neurologic development in HIV-infected infants found a variable, but generally consistent, degree of impaired neurologic growth. These data suggest a 30 to 87 percent rate of developmental delay within the first year to 15 months of life, and a trend toward more apparent disability at older ages. There was also agreement that the more severe the neurologic disability, the more likely children were to die within the first two years of life.

Loss and Bereavement

In addition to formal neuropsychological studies, several other interesting psychosocial papers were presented. Among these was a presentation by the HIV Center in New York and entitled, "Is There Adaptive Habituation to Loss?" The study examined the question of whether there was a direct correlation between experiencing loss after the death of an acquaintance and experiencing psychological distress. Using a demoralization scale, a grief scale, and a measure of depression, the researchers studied 208 men who had experienced one or more AIDS-related losses in the past five years. The results of the study suggest that while scores on the grief scale are correlated positively with the number of losses experienced by the individual, there was no correlation between demoralization and number of losses, and no increase in the number of depressive symptoms as a result of loss. The authors concluded that, while the individuals experiencing multiple losses continued to grieve, they did not seem to become demoralized or clinically depressed as the number of losses increased. These results were the same regardless of the HIV antibody status of the individual.

The quality of the neuropsychiatric and psychosocial research presented in Montreal was generally high, although few studies included control groups. However, a greater number of longitudinal studies are needed to fully address these questions.

The conference, which gave equal weight to psychosocial and biomedical research, demonstrated the importance of acknowledging the complementary relationship between these two perspectives. It is only through a clear sense of this relationship that participants can gain a full understanding of the impact of AIDS on society and the individual.

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### Education Issues

The results of research from around the world were consistent with strategies that educators in the field have found to be most useful in promoting behavior change to prevent HIV transmission. There is increasing evidence that effective prevention requires community-based and individual education programs, in addition to the media campaigns often developed by governments and large non-governmental groups such as the Red Cross. This article focuses on these community-based programs.

It is widely recognized that knowledge-enhancing strategies, such as those reflected in mass media campaigns, while necessary, are not sufficient alone to change risky behaviors. Several papers at the conference reported that while these strategies can quickly raise a person’s knowledge level, this rise is not accompanied by a clear change in behavior. Knowledge, attitude and behavior (KAB) surveys from many areas confirmed this report.

The KAB surveys also showed that behavior change was correlated to a sense of personal efficacy and a sense of personal responsibility. This finding was reflected in studies of programs that used interactive techniques, ranging from counseling and professionally-facilitated group work to community-based and peer-led interventions, such as workshops or street outreach. Successful behavior change interventions shared common the inclusion of the opportunity for people to talk about their feelings and attitudes about the epidemic and about behavior change. Participation in these activities was more powerful than learning the facts about AIDS, although that knowledge was almost certainly a necessary foundation for success.

The behavior change findings reflect the direction in which community-based organizations have been heading in efforts to design prevention programs. It was gratifying, therefore, to see these efforts validated by the community of researchers, most of whom work outside of these organizations. The conference generated a new respect among these researchers for the work of community educators, and made educators less suspicious of research efforts. It is becoming obvious to people in both fields that much can be gained by a closer working relationship. In addition, the results of behavior change studies may make it easier to defend education programs and methods to funders.

Many educators were frustrated by the size and biomedical orientation of the conference, which inhibited a valuable exchange of ideas about prevention. While participants at scientific conferences must actively seek ways to exchange ideas, for instance through informal discussions, organizers of future conferences should consider including workshops that encourage more participation and information exchange.

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### Basic Science

The Fifth International AIDS Conference demonstrated continued advances in knowledge about the structure of HIV and how to detect infection, but despite media attention, the news regarding vaccine development was not encouraging.

The Jonas Salk study, which received the greatest media attention, used killed virus to stimulate antibody in 19 people already infected with HIV, and showed an increase in CD4 cell levels and a response to skin test antigens in some of the subjects. The study was conducted in subjects in a plateau stage of disease, during which time these markers are known to vary. Therefore, it cannot be determined for certain that the increase in CD4 or skin test reaction was in response to the vaccine. Results of a second study of the Salk vaccine, using chimpanzees, were limited because the study included only four subjects.

Dani Bolognesi, MD of Duke University reported that a target sequence for a vaccine must be chosen carefully to avoid inducing autoimmunity, the attack of an individual’s own cells by his or her immune system, which could occur if the sequence mimics the normal cell surface. He also stated that studies of chimpanzees have shown no evidence of protection against infection by transfer of HIV antibody from one chimpanzee to another, because HIV strains vary too much among chimpanzees. Bolognesi found that vaccine made from the V3 loop of gp120, a viral protein, induced neutralizing antibody against many strains of HIV and shows promise.

Jay Levy, MD of the University of California San Francisco warned that the biologic variability of HIV makes it unlikely that a vaccine will be able to prevent HIV infection. In addition, Levy detected some HIV antibodies in people with AIDS that actually enhance both viral reproduction and virulence.

Research on testing focused on the sensitivity of assays for detecting infection as soon as possible, and on the meaning of indeterminate test results. The polymerase chain reaction (PCR) received a tremendous amount of attention as a technique that may be able to detect evidence of the virus long after antibody is formed, and also may prove extremely useful in studying genetic changes in the virus. Using PCR, specific portions of the HIV gene that have been incorporated into human cells are multiplied until they can be detected. Since the technique is new, there are questions regarding its accuracy.

In response to several reports of antibody negative and PCR positive individuals, Alan Lifson, MD of the San Francisco Department of Public Health compared HIV antibody testing with PCR and found initially that 107 out of 109 antibody negative results were also PCR negative. After repeated testing, he determined that the two original positive PCR results were false. Lifson concluded that PCR-positive, antibody-negative results for HIV are extremely rare, and that PCR testing must be done carefully.

There were many conference reports of evaluations of new rapid HIV antibody tests. The accuracy of these tests is perhaps even more important than the current ELISA tests because, despite efforts to limit the performance of HIV tests to qualified personnel in licensed laboratories, the rapid tests are being marketed for emergency rooms and doctors’ offices.

Many studies showed that indeterminate Western blot test results are extremely common in people who have had no exposure to HIV. In an intriguing report, Jorg Schupbach of Switzerland attributed some of these reactions to psoriasis: 98 percent of people with psoriasis and 44 percent of blood donor controls had reactions with at least one HIV protein, and 6 percent reacted faintly with HTLV-I. These findings support studies attributing the skin disease to a retrovirus-like particle.

Future research regarding basic science will focus on determining the length of time after infection to seroconversion, vaccine research, developing an understanding of how the virus causes disease, and identifying molecular and viral cofactors.

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### Request for Submissions and Comments

We invite readers to send letters responding to articles published in **FOCUS** or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals, including a summary of the idea and a detailed outline of the article. Send correspondence to:

Editor, **FOCUS: A Guide to AIDS Research and Counseling**
UCSF AIDS Health Project, Box 0884
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**Clinical Aspects**

Data from the international conference, showing the promise of drugs such as AZT, the only FDA-approved antiviral treatment, and soluble CD4, confirmed that HIV disease is approaching the status of a treatable chronic illness. Researchers at the conference suggested that successful treatment of HIV infection will require a combination of antiviral drugs, and emphasized the importance of HIV antibody testing, and the use of prophylactic drugs to slow viral progression and the occurrence of opportunistic conditions.

AZT seems to prolong life expectancy for about one year among patients who can tolerate the drug. Margaret Fischl, MD of the University of Miami reported no significant difference between high doses of AZT (1500 mg. per day) and low doses (600 mg. per day). European data showed that less frequent dose intervals may be adequate and cause less severe bone marrow suppression. The National Institute for Allergy and Infectious Diseases reported data, after the conference, that shows that AZT delays the development of symptoms among some asymptomatic seropositives, and among some people with “ARC” symptoms. Researchers expect the FDA to issue guidelines suggesting treatment with AZT in patients with T-cell count of less than 500.

There was much attention focused on reports suggesting dideoxycytidine (ddC) and dideoxyinosine (ddI) as potential replacements for AZT, or as treatment components in combination with AZT to lower its toxicity. Researchers chose not to report in Montreal on Compound Q (GLQ221), which is also believed to have a significant antiviral effect.

Phase I studies of recombinant soluble CD4 are being carried out by several researchers. CD4 is the human cell binding site for HIV and plays a key role in infection. In theory, soluble CD4 should prevent HIV from binding to the cell membrane by causing the virus to bind to CD4 that is unattached to cells. In the laboratory, soluble CD4 has been shown to protect against HIV infection. Phase I studies presented in Montreal showed soluble CD4 to cause little toxicity; Phase II studies to investigate the efficacy of CD4 are now underway.

**Legal and Ethical Aspects**

The Fifth International AIDS Conference explored more thoroughly than past conferences legal and ethical issues, including current legislative initiatives, the ethics of placebo-controlled research studies, and, perhaps most dramatically, the inadequacy of present standards of doctor/patient confidentiality.

Conference presentations addressed the protection of confidentiality from many perspectives. Clint Hockenberry, JD of the AIDS Legal Referral Panel in San Francisco discussed the erosion of doctor/patient confidentiality. Hockenberry said that California has weakened its AIDS-related confidentiality provisions, so that people with HIV infection can rely upon only general medical privacy to protect them. He added that medical privacy is no longer confidential and, under it, exceptions are the rule. Hockenberry concluded, citing examples from a survey of panel cases, that in California, the state with the strictest confidentiality protection, people with HIV infection should no longer consider communications with health care providers to be confidential. Under these conditions, patients should carefully interview potential providers to ascertain their beliefs about privacy.

Caitlin Ryan, MSW of the George Washington University Intergovernmental Health Policy Project discussed her survey of U.S. state legislation, and concluded that, in general, legislation showed a balanced non-partisan response to the epidemic. She said that only one-sixth of 2,000 proposed bills were passed, that those that passed were comprehensive—dealing with issues such as testing, confidentiality and notification in a single bill—and that those that were rejected were narrower and more extreme. Ryan noted that there are few antidiscrimination laws, and that some have used laws for people with handicaps to protect themselves.

There was a remarkable increase in the number of cases of Pneumocystis carinii infection of organs of the body, such as the spleen and the liver, in absence of pulmonary infection, particularly in patients who received aerosolized Pentamidine. While there was little new data on treatments for opportunistic conditions, researchers presented preliminary information on several studies dealing with prophylaxis of MAI, salmonella, chronic bronchitis and toxoplasmosis.

There is much interest among clinicians in the development of reliable diagnostic and prognostic tests related to HIV infection. Andrew Moss, PhD and other UCSF researchers documented the significance and value of of CD4 helper cell (T-cell), p24 antigen, beta, microglobulin and neopterin levels in predicting outcome of HIV disease over time.

Clinicians are also interested in changes in the populations most affected by HIV. While incidence of new infection among gay men has decreased significantly, incidence among intravenous drug users in urban areas has increased, heralding a shift of AIDS cases to this population. Reports on the results of free needle exchange programs received a great deal of attention at the conference. In Amsterdam, during 1988, almost 750,000 needles were handed out to I.V. drug users. Researchers found no increases in the frequency of injecting or in the numbers of people who started injecting, and a significant drop in needle sharing that resulted in a drop in new cases of HIV and hepatitis B infections.

Many conference participants—including physicians, epidemiologists, and basic scientists—felt that there were not enough new or interesting findings to sustain a five-day scientific meeting. Organizers of future meetings may want to consider revising the format of these meetings to make them more meaningful, so as to justify the time and expense most researchers spend attending.

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There were several presentations exploring whether to initiate, as well as join, other controlled trials of new therapies. These papers were disappointing: they reduced the human issue of the effects of such trials on a person's psychological well-being to mathematical probabilities of scientific benefit to society versus detriment to individual. They did not discuss the psychological effect on subjects of participating in a placebo-controlled trial. In addition, the presentations did not explore alternatives to placebo-controlled studies, for instance, using other drugs, such as AZT, instead of sugar pills as the control, running smaller controlled studies, or avoiding controlled studies altogether.

The sessions on law and ethics ended with a symposium on discrimination and human rights. Alice Herb, JD of Montefiore Medical Center in the South Bronx described an in-house legal aid program largely oriented to serve a poor, African American, heterosexual population of people with AIDS. This program, which offers services dealing primarily with wills, living wills and the guardianship of children after the death of a parent, could serve as a model for medical centers in other inner city areas.

Other legal and ethical issues discussed in Montreal included partner notification, religious and public conflicts in dealing with HIV infection, antibody testing in prisons, mandatory premarital testing, and AIDS discrimination in the workplace.

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This article does not reflect the views of the Department of Labor.

Robert Gorter, MD

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International Issues

More than 15 million people may become infected with HIV unless international prevention efforts are improved or a vaccine is found and distributed worldwide, according to World Health Organization (WHO) reports released at the Fifth International AIDS Conference. This number represents three times the reported spread of HIV during the 1980s. An update on the spread of HIV worldwide revealed even more sobering statistics: a 10 percent increase of HIV infection among I.V. drug users in Brazil in just one year; a jump from 1 percent to 40 percent of Thai I.V. drug users infected over the last 18 months; and 25 percent of childbearing women in Central African cities found to be infected.

Severe Resource Gaps

At the conference, presentations describing devastation to selected populations and national economies contrasted with scientific reports of promising treatments that may make HIV disease a chronic but manageable illness. Yet the development of effective treatments, even a vaccine, would be only the very first step to coping with HIV disease worldwide. American and European officials noted that their countries would be hard-pressed to deliver the drugs and clinical care needed right now if HIV-infected individuals were to seek such treatment. Physicians from the developing countries spoke of much more basic problems; they are seldom able to provide antibacterial or antifungal medicines or supplies of needles or gloves for their colleagues, not to mention expensive drugs and intensive clinical care.

The lack of medical treatment in developing countries forces a focus on the prospect of prevention campaigns worldwide. In these countries, the problem is not solved simply by sending tons of materials—from educational pamphlets to drugs—to recipient countries. Representatives from African and Latin American countries said that the greatest problem in AIDS prevention is a lack of infrastructure in their communities. The most innovative condom promotion campaigns or special outreach efforts will have little impact unless reliable condom distribution systems can be established, and health educators can be trained to sustain HIV prevention message. Representatives from developing countries said they needed international donor agencies to help provide technical assistance as well as funds that could help sustain prevention campaigns and health care in general.

Community Mobilization and Prevention Strategies

Even with all of these institutional restraints, the presentations at Montreal revealed the creativity of extensive prevention efforts that are underway in the North as well as in the South. Perhaps most important at this year’s conference was the emphasis on the work of non-governmental organizations (NGOs) and community-based organizations (CBOs). Several presentations indicated that behavior change appears to occur most extensively when communication campaigns are complemented by strong community-based efforts. When funds are not available to conduct both types of programs, it is the community efforts—with a heavy reliance on volunteer labor—that are most likely to be effective in preventing transmission.

Jonathan Mann, MD, MPH of WHO added the moral and strategic persuasion of his organization to the argument that national campaigns should emphasize full community involvement. In addition, he concluded that programs will work best when there is a supportive social environment.

Michael Helquist

AIDS prevention strategies can fall into certain programmatic patterns, some of which undermine the impact of the overall AIDS control effort. In North America and Europe, a majority of reports in Montreal emphasized work among heterosexuals and I.V. drug users. Yet data and anecdotal reports from these industrialized nations reveal that ongoing efforts to reach gay and bisexual men must be maintained, and in some areas, programs must shift their emphasis to strategies that encourage sustaining behavior change.

In Latin America and the Caribbean, health officials reported that HIV infection has shifted its target from homosexual to heterosexual populations. Health educators from those countries counseled, however, that too little attention is focused on the role of bisexuality and hidden homosexuality in their cultures.

Since last year’s conference in Stockholm, Asian countries have commanded much more attention for the risk of HIV to their populations. The rapid spread of HIV among Thailand’s huge I.V. drug using population and its sex worker industry has shattered earlier hopes that Asia might be relatively unscathed by HIV.

It was apparent in Montreal that these meetings had become conventions and trade shows, as well as scientific gatherings. More than 100 exhibitors displayed the latest in laboratory technology, condoms, and educational materials. The budgets for some of the displays alone could finance major prevention efforts in many of the countries whose representatives filed by in awe.

The Montreal international conference came the closest to being truly global in scope and representation, yet in so doing the gaps in the resources between the industrialized and the developing countries became all the more apparent.

Michael Helquist, Founding Editor of FOCUS, is a Program Officer for the Washington, D.C.-based AIDSCOM, which provides technical assistance on AIDS prevention to developing countries.

Next Month

Political, economic and social realities may influence the medical aspects of perinatal AIDS—the transmission of HIV from mother to fetus—more than any other manifestation of HIV disease. In a society that acknowledges, on some level, a woman’s right to make choices about planning parenthood and terminating pregnancy, it is the responsibility of health professionals to provide information about HIV infection and perinatal transmission. In the October issue of FOCUS, Laurie Hauer, RN, Coordinator of the Bay Area Perinatal AIDS Center at San Francisco General Hospital, offers information to help counsel pregnant women and those considering pregnancy. She covers: risk assessment and reduction, the effects of HIV infection on pregnancy, and options for initiating, continuing or ending pregnancy. Ellen Cooper, MD, Medical Director of the Pediatric AIDS Program at Boston City Hospital, continues the story of perinatal transmission to its unfortunate conclusion, pediatric AIDS. She discusses medical care for infants and children, immunization, the use of prophylactic therapies to prevent secondary infections, experimental treatments and care in foster homes.

FOCUS A GUIDE TO AIDS RESEARCH AND COUNSELING

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