CRIA®

CRIA UPDATE

COMMUNITY RESEARCH INITIATIVE ON AIDS

VOL. 9 NO. 3

AIDS On The Margins

When dealing with any disease, particularly a relatively new epidemic like HIV, the information gleaned from previous individuals' experience often proves beneficial to current ones. Treatment has to be tailored to fit the individual, and *CRIA Update* has long been committed to providing people living with AIDS (PLWAs) and their caregivers with information on treatment advances and the real life experiences of those living with HIV.

For our Summer 2000 issue we have chosen to offer a discussion on some of the more marginalized members of the PLWA community. To that end, we have asked several of our colleagues to discuss some of the HIV treatment issues faced by specific populations. Jen Curry looks at the real and perceived obstacles confronting homeless people living with HIV, while Mary Jane Nealon, R.N. tells of her first hand experience working with this community. Michael Haggarty writes on the dilemmas faced by PLWAs in our prison system, and Gopal K. Upadhya, M.D. presents some of the treatment complications faced by PLWAs who are mentally ill and chemically addicted (MICA). Finally, Richard Jefferys offers an overview on demographic representation in HIV clinical trials.

It will be clear to readers that our writers' experiences have made them strong advocates for their constituencies and this issue of *CRIA Update* is something of a departure from our normal recounting of HIV treatment advances. While the challenges presented in this issue are not universal among all PLWAs, they present important ramifications for all men and women living with AIDS and the world at large. Unfortunately, many PLWAs don't have the luxury of dealing only with HIV; frequently they are affected by multiple epidemics. Learning not to overlook the experiences of anyone fighting AIDS has certainly been one of the most important lessons of the past two decades.

J Daniel Stricker, Editor-in-Chief

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Gender, Ethnicity & Clinical Trials

BY RICHARD JEFFERYS

Since the first reported AIDS case in 1981, hundreds of thousands of people have participated in r esearch related to this epidemic. From trials of new drugs to surveys and questionnaires, the thirst for knowledge has driven a massive effort to recruit people with HIV into such studies. In the early years, attention focused on the community that appeared hardest hit – predominantly white gay men. In retrospect, it is clear that gay men of color, particularly African-Americans, were also heavily impacted, and many remember that the disease was affecting injection drug users and their partners as early as the late seventies.

The fact that HIV traverses demographic boundaries has now become clear, but clinical trial participation is still skewed such that white gay men are over-represented compared to other affected populations. This raises important questions about how complete our knowledge of HIV really is, questions to which recent – and not so recent - studies have provided some disturbing answers. Clearly, there are issues of fairness and

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SUMMER 2000

CRIA UPDATE

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CRIA is an independent, non-profit, community-based AIDS research and treatment education organization dedicated to rapidly improving the length and quality of life for people living with HIV/AIDS. CRIA studies new treatments for HIV-related diseases through its clinical research and conducts a comprehensive treatment education program. Bulk copies of *CRIA Update* are available free to agencies that provide services to people living with HIV/AIDS. For more information call Meredith Snow at 212-924-3934 ext. 121.

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CRIA TRIALS IN PROGRESS

Study of 3 Different Drug Combinations in Drug-Naïve, HIV+ Individuals (Currently Enrolling)
CRIA is participating in a 96-week study sponsored by Glaxo Wellcome. This study will look at the effect of three different anti-HIV drug combinations on people infected with HIV. Some individuals with HIV experience changes in body shape as a result of fat redistribution. The primary purpose of this clinical trial is to study this effect. The study is for adults who are HIV-1+, have a CD4+ lymphocyte cell count greater than or equal to 50 cells/mm3, have a viral load greater than 1,000 copies/mL and less than 200,000 copies/mL, *and have NOT received anti-HIV drugs in the past or have very limited use of certain anti-HIV drugs.* Participants will be reimbursed $15 plus a $3 MetroCard per visit after enrollment.

Topical Aspirin for Peripheral Neuropathy (Currently Enrolling)
CRIA is now enrolling a 5-week double-blinded study looking at the efficacy of topical aspirin to treat painful sensory peripheral neuropathies in people with HIV. Over the course of the trial, participants will be given two separate bottles of solution: one with aspirin in diethyl ether, another with an inactive placebo in diethyl ether. The order in which these bottles will be provided is randomized. The solution will be applied on the skin over the painful area 3 times a day. HIV-infected adults with painful sensory neuropathy that has been present for at least a month are eligible. There will be a total of 5 study visits. Study participants will be reimbursed $15 plus a $3 MetroCard per visit after enrollment.

SAM-e for Depression in HIV+ Individuals (Currently Enrolling)
Enrollment has begun at CRIA for an 8-week open-label study of the efficacy and safety of using S-adenosylmethionine (SAM-e) to treat depression in HIV+ individuals. SAM-e is a naturally occurring compound that is sold as a food supplement in this country. HIV-infected adults with diagnosed clinical depression may be eligible for this study. There will be a total of 7 study visits.

Metabolic Effects of Protease Inhibitors
CRIA is conducting a study in cooperation with Dr. Ann Danoff, Chief of Endocrinology at Bronx-Lebanon Hospital, to examine whether there is an association between short-term antiretroviral therapy (ARV) and glucose intolerance, hyperlipidemia, or body habitus changes. The trial will study HIV negative persons who have sustained needle stick injuries, before and at the conclusion of a course of ARV prophylactic therapy. This study will provide the opportunity to examine the impact of protease inhibitor therapy independent of HIV infection.

FOR MORE INFORMATION ON ANY OF THESE STUDIES, PLEASE CALL DR. IRENE CERGNUL OR DR. DOUGLAS MENDEZ AT (212) 924-3934, OR VISIT OUR WEB SITE (WWW.CRIANY.ORG).

Editor's Notes

* All material in *CRIA Update* is presented for educational and informational purposes only, and is not intended as medical advice. All decisions regarding one's personal treatment and therapy choices should be made in consultation with a physician.
* *CRIA Update* refers to all drugs by both their commercial and scientific names upon their *first reference* in an article. Thereafter in the article, they will be identified with the name by which we feel they are most commonly known, either commercial or scientific.

Clinical Trials

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potential racial, sexual and socioeconomic discrimination when it comes to representation in clinical trials. There are also potentially important differences in genetics and physiology (how our bodies work) that may have profound implications for the health of people with HIV.

Viral Load, T-cells & Disease Progression

Perhaps the most glaring example of a study conducted solely in one population (and then applied to everyone else) is John Mellors' study linking viral load levels and T-cell counts to the rate of disease progression. The current US HIV treatment guidelines' recommendations on starting drug therapy are based heavily on this study, which was conducted almost exclusively in white gay men. In fact, the ethnic breakdown of study participants was not even provided in the widely cited publication by Mellors in the Annals of Internal Medicine in 1997. The study population was simply defined as "1,604 men infected with HIV." The reasons for this bias may not have been intentionally racist. The study was conducted in what is called the MACS (Multi-AIDS Center Study) cohort, which began in 1984 when the full demographic spread of HIV infection was not appreciated. The MACS' focus on gay men in major cities was understandable and continues to provide an invaluable source of regularly donated blood samples for testing and analysis. However, similar studies focusing on women (the Women's Interagency HIV Study, or WIHS) did not start enrolling participants until 1994, and only after considerable community advocacy efforts.

Illustrating that this is more than just an academic problem, a recent analysis by Kathryn Anastos, MD directly compared viral load and T-cell count data from MACS and WIHS. Anastos found that viral load levels in women averaged 32% to 50% lower than those in men. Other differences uncovered by Anastos were that white participants averaged viral loads that were 42% higher than those of their counterparts of color. Study participants with a history of injection drug use had average viral loads 23% lower than those with other risk factors for HIV transmission.

When it came to T-cell counts, MACS and WIHS comparisons turned up even more disturbing surprises. Overall, women experienced more significant declines in T-cell counts each year than men, losing an average of 45 more T-cells from the blood annually. Among women, however, the T-cell decline was more rapid in white women than in women of color, averaging 115 cells per year versus 77. The difference was 70 cells per year in white men versus a 31 cell per year decrease in men of color. The same trend held true for participants of color overall, who on average lost 41 fewer T-cells a year than their white counterparts.

Although Anastos tried to eliminate any factors that might bias the results, it is hard to draw firm conclusions from these preliminary data when it comes to the speed of disease progression among differing groups. It is noteworthy, however, that Anastos' data support a military study from 1994 that noted potentially slower disease progression among African-Americans. A 1992 Johns Hopkins University study that focused solely on gay men also uncovered slower progression rates among participants of color. One finding that's slightly askew from these results was reported in a 1997 study published in the Journal of Infectious Diseases. Among 545 men in the military, researchers uncovered no significant differences in viral load levels between African-Americans, Hispanics and Caucasians.

It is reasonable to wonder if lower viral load in women translates into altered disease progression. Unfortunately, a widely publicized study by Johns Hopkins investigators reported that progression appeared to occur at the same rate in women despite lower viral load

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Ethnicity and Genetics

As immune-based treatments and therapeutic vaccination fall back into favor, another set of issues arises around ethinicity and genetics. The ability of the immune system to respond to infectious threats can be profoundly influenced by genes inherited from our parents. These genes are called HLA (human leukocyte antigens) and basically control how much of an infectious agent the immune system can "see" and respond to. Several HLA genes have been consistently associated with slower HIV disease progression and, in some cases, apparent resistance to HIV infection. These genes can also influence the response to vaccines. The distribution of different HLA genes can vary between ethnic groups and might even be involved in Kathryn Anastos' observation of lower viral load and T-cell decline in people of color. Only forethought and adequate representation in clinical trials of immune-based therapies will allow these questions to be addressed.

FORUM UPDATE

CRIA co-sponsors monthly educational forums on AIDS research and treatment issues. Upcoming forums:

Wednesday, July 19
Diet & Exercise and HIV/AIDS

Wednesday, September 6
Update from the International Conference

Wednesday, October 18
Sexually Transmitted Diseases & HIV

The forums are held at 7PM in the Cronin Auditorium, 10th Floor of St. Vincent's Hospital at 11th Street and 7th Avenue, Manhattan. Forum summaries are available on CRIA's website: www.criany.org

Homelessness & HIV

By Jen Curry

At any given time, one out of four people living with HIV in New York City is homeless or marginally housed. This is a recent finding of the Community Health Advisory Information Network (CHAIN) at Columbia University's School of Public Health. CHAIN studied patterns of housing instability in people living with HIV. Studies focusing on national homeless populations offer further data for these overlapping communities. Few homeless individuals are aware of their HIV status. Only a handful are informed about HIV treatment options, and even fewer are able to access such care. Depending on who's counting and where, HIV infection rates in homeless communities run from 8.5% to as high as 19.5% in the United States.

It is no secret that HIV in the United States is increasingly becoming a disease of poor and traditionally marginalized urban communities, with disproportionate rates of infection in homeless people, injection drug users, and people of color. Though community activists have long demanded that more attention be paid to homeless populations at risk of infection, research efforts have only recently begun to focus on documenting how much and in what ways the disease impacts homeless communities. Also under investigation is the usefulness of traditional treatment education and delivery approaches in communities with so many structural barriers to accessing and receiving care.

Just as it is impossible to generalize about a group as diverse as all persons living with HIV, it is similarly useless to discuss "the homeless" without being more specific. Homelessness is not an identity. Nor is its meaning universal. The word is often used to refer to people who live on the street. While this definition reflects the reality of some individuals who are marginally housed, it does not begin to describe the full range of living situations of those who might not live on the street but who are without homes. Often left out of "homeless" but nonetheless crucial to its definition are individuals staying in shelters, treatment facilities, welfare and boarding houses, single room hotels, and other person's homes. We need to be clear about who and what we mean when discussing "homeless communities" and HIV "treatment issues."

Barriers to treatment

Recent community-based health studies throughout the country suggest that homeless people continue to be the anonymous faces of the HIV epidemic. The marginalization of HIV positive homeless people has created one of the most persistent barriers to treatment education and delivery. A 1993 abstract from a two-year study of 1001 homeless people in San Francisco found that 33% of those testing positive for HIV were unaware of their status and had *never* been tested before. Similarly high rates of unknown HIV status were reported in 1999 for shelter dwellers and soup kitchen frequenters who tested positive in New York, Miami, New Orleans and Denver. This high incidence of unknown status for HIV positive people studied suggests that many homeless men and women with HIV are likely to be overlooked by treatment educators, service providers and medical practitioners.

"Recent data reveal that many homeless people living with HIV continue to be unaware that antiviral treatment for HIV exists."

Lack of information about antiviral therapy, lack of access to routine preventive care, and competing life priorities for homeless people are frequently cited as barriers to HIV treatment in these communities. Recent data reveal that many homeless people living with HIV continue to be unaware that antiviral treatment for HIV exists. In one San Francisco based study of homeless drug injectors, a research group examined access to antiviral therapy for HIV in a group of homeless persons with histories of substance use. Among the participants testing positive for HIV, more than half of those who had never received antiviral therapy had never heard of such therapies. A similar San Francisco study looking at access to protease inhibitors by HIV positive homeless persons found that only 7% of the people studied had previous access to protease inhibitors, compared to 50-70% reported in standard clinical settings.

Such severely restricted access to antiviral therapy in homeless populations might indicate a lack of information about treatment options, or it might also point to larger questions of access to the medical system, or even discrimination within that system itself. Access to care is certainly an issue in homeless communities. In 1998, one of the first surveys of homeless people using mental health self-help agencies provided valuable insight into this group's health care utilization. The study demonstrated that an overwhelming majority of homeless individuals were accessing health care only in the form of emergency services at hospitals and clinics. Less than ten percent had access to primary or preventive care. 22% had not received care of any kind for more than a year.

Health Conditions Common in this Population

Homeless people often face numerous and overlapping health challenges. Despite this reality, we know very little about the relative physical health of homeless people compared to other groups in the nation. The information we do have suggests that homeless men and women have higher rates of a number of health conditions, many of which can affect HIV and vice versa.

Tuberculosis infection is a serious health threat to homeless people living with HIV. As early as 1994, a now famous research project on HIV and TB infection in San Francisco's home-

less adults reported a TB prevalence rate of 32% in a large representative sample of homeless individuals in San Francisco. 17% of those testing positive for TB were co-infected with HIV. Since then, TB infection rates have been on the rise for people living in boarding homes, hotels, residential treatment programs and jails. In New York City, rates of co-infection with active TB and HIV ran as high as 20% for homeless individuals at public hospital clinics in 1999. These numbers support multiple research findings that time spent homeless - specifically in low-income hotels, shelters, prisons and boarding houses - is itself a risk factor for tuberculosis infection.

Because HIV can hasten the progression to active TB, this frequency of co-infection in homeless communities is particularly alarming. The current standard of care for individuals at risk for developing active TB is isoniazid (INH), or isoniazid in combination with other antituberculotic agents such as rifampin, rifabutin, or clarithromycin. Treatment can last from six months to a year. This regimen presents multiple challenges to HIV positive homeless people. INH comes with its own set of side effects including nausea, diarrhea, peripheral neuritis and liver dysfunction. Peripheral neuritis, the most common adverse effect of INH, occurs most frequently in malnourished patients, thus posing a particular threat to many homeless people. Liver dysfunction is equally hazardous. For people with pre-existing liver disease resulting from alcohol abuse, substance use, or viral hepatitis, further INH-induced stress to the liver can be very dangerous.

To complicate matters, rifampin, the most common antituberculotic agent, cannot be used with several anti-HIV drugs, including indinavir (Crixivan), saquinavir (Invirase or Fortovase), nelfinavir (Viracept), nevirapine (Viramune), and delavirdine (Rescriptor). Rifampin can lower blood levels of other anti-HIV drugs - ritonavir (Norvir) and amprenavir (Agenerase) - thus altering their effectiveness and potentially

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A Medical Provider's Perspective

By Mary Jane Nealon, RN

As a nurse who has worked for twenty-five years, more than half that time in AIDS care, I admit to some prejudices of my own. I always imagined I would be able to recognize someone who was homeless. Somehow I would *know*. After three years of working with the homeless, I now understand that they are completely unidentifiable. People who are homeless must be resourceful to survive. Most know where to get food, where to shower, and how to get clothes. In the medical clinic they most likely present with an address.

So now I ask details. How long have you lived there, how many other people live there, is your name on the lease, have you ever been homeless? I've learned that people who are homeless may have full-time jobs, spouses, children or partners. When discussing treatment options, knowing the answers to these questions is crucial in anticipating the needs individuals may have and the obstacles they may face in treatment adherence.

There are some obvious problems connected to homelessness and medication adherence. If someone has no refrigerator and a medication needs to be kept in one, that medication is obviously a poor choice. While most people know how to get some food, they may not have regular meals. Even programs that serve three meals per day often serve the last meal in the afternoon. Medication that must be taken three times a day with food can be problematic. So is medication that must be taken on an empty stomach. It is dangerous to assume that a patient can anticipate when she will be offered food or that she can access water.

Adherence is complicated by fear of disclosure. Thousands of people utilize homeless shelters, but very few of the homeless men and women I've met sleep in them. Violence is rampant and conditions generally poor, but more importantly, most homeless HIV-infected individuals report an increased risk of victimization if there is a perception that someone has AIDS.

Theft of belongings poses another obstacle to treatment adherence. When homeless men and women fall asleep in shelters or on the street, their chances of being victimized increase. Replacing stolen medication is often complicated by the loss of all identification that generally accompanies such thefts. The huge emotional toll of starting over in the system may lead the client to give up on the treatment regimen.

Medication side effects can also impact adherence. Due to the recent policing of homeless persons in New York City, many people who live on the streets and fear the shelter system walk all night and sleep in day programs. Peripheral neuropathy, nerve damage in the feet and, sometimes, the hands, may impact a person's ability to stay on his feet, exposing him to possible arrest. Neuropathy might also make someone vulnerable to injury in extreme temperatures.

As a nurse, I frequently discussed comfort measures with clients who experienced nausea after starting a regimen. "Some people find it helpful to munch on pretzel sticks or crackers, keep a cool wet cloth on the back of your neck," I'd offer. Of course I never thought to ask, "Do you have any way to get a few crackers? Do you have access to running water, or a cloth?" Usually, side effects like nausea will go away after a few weeks. However, people who go through those weeks with no comfort measures are less likely to continue treatment.

Lack of access to restrooms is a problem for homeless people who experience treatment-related diarrhea. Our impulse as health care providers is often to recommend dietary changes, but that suggestion is meaningless to someone who gets all his meals from food vans or soup kitchens. Even homeless clients with temporary addresses in flophouse hotels rarely have cooking facilities. Treatment-related fatigue in the absence of a safe resting place is another serious obstacle. Other side effects,

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Incarcerated Populations & HIV

By Michael F. Haggerty, MPH, editing assistance by Steven Nesselroth

Since the beginning of the HIV/AIDS epidemic, the disease has struck incarcerated populations extraordinarily hard. The "War on Drugs" has produced a prison population overwhelmingly dependent on illicit drugs. The confluence of drug use and national drug arrest policies has made HIV infection rampant in the nation's prisons and jails.

According to the Department of Justice, almost 1.9 million people were incarcerated in America as of June 1999. That's one out of every 147 residents behind bars. Rates of incarceration disproportionately affect men of color. An estimated 11% of Black males and 4% of Hispanic males in their twenties and early thirties are incarcerated, compared to 1.5% of white males of the same age. Nationally, at the end of 1997, 2.1% of male prisoners and 3.5% of female prisoners were known to be HIV positive. The rate of confirmed AIDS was 5 ½ times higher in the prisons than in the general population. A study of infectious diseases among people passing through correctional facilities in 1996 found that 17% of all prison and jail releasees were HIV positive.

HIV antibody testing policies vary among correctional jurisdictions, with only 18 states testing all inmates either at admission or while in prison. Most correctional systems rely on voluntary testing, testing based on clinical indications, or prisoner involvement in accidents. This makes tracking the actual rate of infection difficult. Stigmatization, the potential threat of violence, poor HIV education, and lack of confidentiality cause many prisoners to avoid voluntary testing even when they know that they are at risk for infection. If a prisoner knows that he's HIV positive before entering prison and does not need HIV specific medical care during the course of the sentence, he can escape identification as HIV positive. Anecdotal evidence leads many people to believe that the actual rate of HIV infection is much higher than that reported by the Department of Justice.

By definition, the common condition of imprisonment is that there is very little choice in every aspect of life. This is also true for medical care, where prison authorities have a financial interest in limiting choice (much as HMO's do in the free world, but with even greater restrictions). The ability to make the most basic decisions about HIV antibody testing, HIV status disclosure, prevention education, or medical treatment are often denied to prisoners. In 1976, the Supreme Court found that prisoners are the only class of citizen guaranteed "the right to adequate medical care" (*Estelle v. Gamble*). The courts define adequate care as meeting community standards. However, the *Estelle* decision did not allow for inspection and enforcement of those standards. Litigation has become the routine means of improving medical care and general prison conditions. Without successful litigation, medical care is defined entirely by the prison and rarely reflects community standards.

> ***"Doctors drawn to prison practice often have little or no first-hand experience treating HIV in their communities"***

The spectrum of prison health care is as widely varied as in the "free world." It is impossible to generalize about conditions across one state, much less across the entire country. A select few prisons provide care equal to or even better than that available on the outside. However, the great majority do not even approach that level and quality of care. Some provide conditions seen only in developing countries. A recent report by the Correctional Association of New York looked at services provided by twenty-two correctional facilities in the New York State system. The report found "uneven clinical management, a vagueness among staff physicians about critical HIV/AIDS issues, wide variations in HIV testing, support services and education, and an absence of prevention measures."

COMMON OBSTACLES TO HIV TREATMENT IN CORRECTIONAL SETTINGS:

Prisons are not health care facilities

In correctional terms, the job of prisons is the "Care, Custody and Control" of prisoners. Most often, control comes first. This mandate directly conflicts with proper medical care. Prisons are most concerned with security, limiting prisoner movement and keeping tight control on when and where prisoners are in specified locations. Security concerns take precedence over any other matters within the prison confines.

Lack of HIV-specific medical expertise

Prisons are often in rural locales with few or no HIV patients in the area. Doctors drawn to prison practice often have little or no first-hand experience treating HIV in their communities. This limited knowledge of HIV/AIDS is dangerous considering that studies have shown a direct correlation between practitioners' HIV experience and positive patient outcome. Some prisons, hard-pressed to hire medical staff, utilize any available medical personnel. Infectious disease specialists are rare in prisons, where state budgets demand that resources be stretched.

The report by the Correctional Association of New York testified to the lack of board-certified or board-eligible physicians. Prisons have been known to hire practitioners with suspended licenses or with licenses from foreign countries. Unsubstantiated stories abound of veterinarians practicing medicine within the walls. Whether true or not, the persistence of such tales reflects the low regard in which prison medical staff is held by those they are treating. Similarly, non-medical staff in prison have little experience

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MICA Populations & HIV

By Gopal K. Upadhya, MD

MICA is a medical and public health acronym used to describe people who are Mentally Ill Chemically Addicted (or Mentally Ill Chemical Abusers). The number of individuals with mental illness and chemical dependence who are living with HIV has increased exponentially in recent years.

- A 1998 article in the American Journal of Addiction reported 19% HIV sero-positive status in a group of patients with mental illness and substance use. Women were 3.8 times more likely than men to be HIV positive. Cocaine users were 4.5 times more likely than non-users to be positive.

- Environmental conditions such as inadequate housing, self-neglect and poor nutrition often accompany substance use, making it difficult for many MICA patients to access quality, long-term medical and psychiatric care in any one location.

- These same conditions can lead to an increased exposure to diseases and a reduced ability to fight off infections. Injection drug use carries higher risk of blood clots, severe skin infections, and blood-borne infections including viral hepatitis and life-threatening endocarditis (inflammation of the lining of the heart and valves), further complicating HIV infection.

- Although some societal misconceptions and myths about chemical dependency and mental illnesses are slowly changing, insurance coverage for MICA patients has dropped significantly. An unpublished study by the American Society of Addiction Medicine looked at insurance coverage for employees of medium- to large-sized companies over a ten-year period. The value of coverage for substance abuse treatment declined by 75% between 1988 and 1998 compared with a 52% decline for mental health coverage and a 12% decline for general health care during the same period.

- Psychological and social factors strongly influence MICA patients' dependence on inpatient services. Disjointed ambulatory care and problems in timely coordination and accessibility ultimately lead to deficiencies in preventive care. Delays in the diagnosis of complications of HIV infection often follow. Social isolation further complicates the situation with an increased reliance on hospital emergency rooms and inpatient beds for conditions that might otherwise be managed with adequate family and social support.

- The degree of perceptual distortions caused by street drugs on a mentally ill person makes it especially difficult to adhere to complicated drug regimens - particularly in the absence of support. Too often the result is poor prognosis and premature death.

- Specific components of effective, integrated treatment delivery for MICA patients include harm reduction, stage-wise treatment, motivational interviewing, cognitive behavioral interventions, and modified 12-step self-help groups.

- A physician's ability to provide proper pain management to an HIV patient with underlying drug addiction can be a challenge. In order to relieve pain, the physician needs to *believe* in the patient's pain and understand that tolerance to narcotics may be high.

- MICA patients and their providers face complicated interactions between psychotropics, HIV medications and street drugs. As the liver breaks down the various drugs, levels of one may increase in the body while levels of another may decrease. Protease inhibitors, for example, can raise amphetamine blood levels by as much as three times. At high doses, many sedatives can interact with protease inhibitors and some NNRTIs so as to cause respiratory failure. Protease inhibitors can also increase blood levels of barbiturates like phenobarbitol (Luminal), making overdose more likely. Interactions between cocaine or heroin and antivirals are unknown, but street drugs are rarely pure, and the substances with which they're cut could cause potentially serious interactions with medications.

- Some medication side effects can be problematic for people with multiple diagnoses. Videx (ddI) increases the risk of pancreatitis, as does alcohol use. A Videx-containing regimen could be dangerous for a patient who drinks heavily. The central nervous system effects of Sustiva (efavirenz) can include dizziness, mental confusion, feeling lightheaded, forgetfulness and nightmares. Elavil (amitriptyline), often used to treat the painful symptoms of HIV-related or antiviral-induced peripheral neuropathy, can cause feelings of being lightheaded, dulled and groggy. Some MICA patients can have particularly disturbing experiences with either of these medications.

Gopal K. Upadhya, M.D. is Chief Psychiatric Consultant for the Department of Medicine/ AIDS Program at The Bronx-Lebanon Hospital Center and an Assistant Professor at Albert Einstein College of Medicine.

New Drugs in Development

By James Learned

PEGYLATED INTERFERONS FOR THE TREATMENT OF HEPATITIS C

Between one-third and one-half of everyone living with HIV in the United States is co-infected with hepatitis C (HCV), including up to 90% of those who acquired HIV through injection drug use. The effect of co-infection on an individual's health is unclear. HCV seems to have little impact on the progression of HIV, except in people with hemophilia. But HIV usually speeds up HCV progression, and co-infected people with less than 200 T-cells are at much higher risk of developing serious liver scarring (cirrhosis). Since the liver breaks down HIV medications, HCV-related liver damage may make it difficult for the body to process HIV medications. This could lead to a higher HIV viral load and limited HIV treatment options.

The current standard of care for the treatment of chronic HCV is alfa interferon, injected subcutaneously (under the skin) three times a week, combined with oral ribavirin capsules taken twice a day. Course of treatment is six months to a year. Alfa interferon is a naturally occurring protein produced by the body to interfere with a virus' ability to infect cells. Bio-engineered alfa interferon is used to treat many cancers and was investigated in the 1980s as a possible HIV treatment, although without success. In HCV, the success rate of alfa interferon monotherapy is only 5 to 25%. Success is defined as achieving an undetectable HCV viral load (<100 copies per ml) six months after finishing treatment (sustained response). In June of 1998, the FDA approved Schering-Plough's Rebetron, a kit containing two products packaged together - Intron A, the company's brand of alfa interferon, and ribavirin capsules. Interferon/ribavirin combination therapy achieves an overall sustained response rate of 41%, clearly superior to interferon monotherapy.

Many people can't tolerate interferon's side effects. These can include everything from what are generously called "flu-like" symptoms to weight loss, low white blood cells and platelets, irritability, depression, and, sometimes, suicidal thoughts. The side effects are usually worse during the first weeks of treatment, and each person experiences them differently. Ribavirin can cause severe anemia (low red blood cells), and both drugs can cause severe birth defects.

While everyone looks forward to the day when interferon treatment is obsolete, the next step toward more successful and tolerable HCV treatment is pegylated interferon. Pegylation is a process that allows interferon to stay in your body at consistent levels for up to a week. Currently available interferons only stay in your body for about a day, resulting in insufficient pressure on the virus in between the usual three weekly doses. By providing steady levels of drug, pegylated interferon allows for more convenient, once weekly dosing, as well as higher success rates. Preliminary results of Phase III trials of two pegylated interferons in development are promising. The data were presented at the 35th Annual Meeting of the European Association for the Study of Liver Disease (EASL) in May. Neither trial included co-infected participants, but early data from ongoing co-infection trials as well as the experience of physicians who treat co-infected patients suggest that the response rates of co-infected individuals are similar to those of people with only HCV.

PEG-Intron (pegylated interferon alfa-2b)

One study compared three doses of Schering-Plough's PEG-Intron (0.5, 1.0 or 1.5 micrograms per kilogram [ug/kg], once a week) and standard dosing of Intron A (three million international units, three times a week). The trial lasted 72 weeks – 48 weeks on treatment, with 24 weeks of follow-up. The 1,219 participants had never undergone interferon treatment for HCV. The majority were Caucasian (91%) and male (63%), with HCV viral loads above two million copies per ml (73%) and genotype 1 (70%), the most predominant genetic strain of HCV and the hardest to treat. 9% of the participants had fibrosis scores of 3 or 4 (cirrhosis).

All three doses of PEG-Intron had significantly higher sustained response rates (undetectable viral load six months after completing treatment) than Intron A (only 12%). The most successful overall rate (25%) was seen in participants who received PEG-Intron at the 1.0 ug/kg dose. People with HCV viral loads under two million to begin with and genotypes 2 or 3 usually respond best to interferon treatment. As expected, this proved to be the case in this trial. The highest sustained response rate (62%) was seen in participants with beginning HCV viral loads under two million and genotypes 2 or 3 on the 1.5 ug/kg dose. This compares to only an 8% sustained response rate in participants with beginning HCV viral loads over two million and genotype 1 on the 1.0 ug/kg dose.

New Drugs in Development

Pegasys (pegylated interferon alfa-2a)

The other pegylated interferon in development is Hoffmann-La Roche's Pegasys. Roche's study included 531 interferon-naïve participants. Half of the participants received Pegasys (180 micrograms once a week). The other half received Roferon, Roche's brand of alfa interferon. Participants in the Roferon arm received six million international units (MIU) three times a week for the first twelve weeks, followed by standard three MIU three times a week for the remaining 36 weeks of treatment. Although some HCV physicians begin interferon treatment at these higher doses, hoping to achieve better results, the decision to use this approach in a head-to-head comparison trial is surprising.

The study group was similar to that of the PEG-Intron trial - predominantly Caucasian (85%), male (67%), and genotype 1 (61%). The percentage of participants with HCV viral loads above two million copies wasn't reported, but the average viral load was over 7.5 million. 13% of the participants had or were developing cirrhosis.

The overall sustained response rate in the Pegasys arm at 72 weeks was 39%, compared to 19% in the Roferon arm. Looking at the results by genotype, the sustained response rates for participants in the Pegasys arm were 28% for genotype 1, 64% for genotype 2, and 54% for genotype 3. These compare to 7%, 50% and 32% respectively in the Roferon arm. Baseline HCV viral load was also an important factor in the success of treatment. Participants who began Pegasys with viral loads under two million achieved a sustained response rate of 52% compared to 27% who began with viral loads over two million. The respective rates in the Roferon arm were 25% and 13%.

Analysis

Although many people had hoped otherwise, the side effects of pegylated interferon are no less severe than those of standard interferon. In the first study, dropout rates due to side effects in the PEG-Intron arms were 9-11%. This compares to 6% in the Intron A arm. Similar percentages of participants required dose reductions due to side effects: 9-15% in the PEG-Intron arms and 6% in the Intron A arm. In the second study, the dropout rates due to side effects were 7% in the Pegasys arm and 10% in the Roferon arm. Dose reductions due to side effects were necessary for 9% in the Pegasys arm and 14% in the Roferon arm.

It's tempting to compare the two pegylated interferons based on the results of these Phase III trials. Pegasys' overall sustained response rate of 39% would seem to make it superior to PEG-Intron's best overall rate of 25% at the 1.0 ug/kg dose. And looking only at sustained response rates for people with genotype 1, Pegasys achieved 28%, while PEG-Intron achieved only 14% (at the 1.0 and 1.5 ug/kg doses). However, the data in these studies were broken down and presented differently, and the PEG-Intron trial included more than twice as many participants. Direct comparisons need to be made carefully. Men don't usually respond as well as women to interferon treatment, and people of African descent don't usually respond as well as other ethnic groups. If the data from these trials were available based on sex and race, the variations in response rates might be even more extreme.

Undetectable HCV viral load six months after completing treatment is the measure of success in these trials, but a primary goal of treatment for HCV is histologic improvement – in other words, a healthier liver. This is measured by normalized liver enzymes, lower or undetectable viral load, and a follow-up liver biopsy. Even without sustained response or significantly lower viral load, treatment can give your liver a much-needed break. Histologic improvement at week 72 was seen in 63% of the participants on Pegasys and 55% of those on Roferon. Similar information on PEG-Intron and Intron A wasn't presented.

Pegylated interferon + ribavirin

The additional benefits of combining pegylated interferon with ribavirin have been highly anticipated. Results from two small Phase II trials of combination therapy were presented in May. One looked at PEG-Intron +/- ribavirin in 72 people; the other looked at Pegasys + ribavirin in 20 people. As hoped, combination therapy achieved higher overall sustained response rates than either pegylated interferon monotherapy or alfa interferon + ribavirin, the current standard of care. The highly preliminary results must be viewed cautiously because of the small number of participants. No co-infected individuals were included in either trial.

Both PEG-Intron and Pegasys are likely to receive FDA approval late this year or early in 2001. Meanwhile, a large program is planned that will allow people with chronic HCV free access to Pegasys. Three-quarters of the program participants will also receive ribavirin. Because there is so little data on pegylated interferon in combination with ribavirin, the FDA is calling this a safety trial rather than a conventional expanded access program. It is expected to begin this summer. Unfortunately, co-infected individuals are excluded from the program.

Incarcerated

CONTINUED FROM PAGE 6

dealing with HIV. Administrators, counselors, security personnel, and chaplains are prone to treat HIV and AIDS as a problem of "others" – those from the city, people of color, drug users, homosexuals – and not something that requires an investment in educational, medical or staff resources.

Language barriers

The Latino Commission on AIDS in New York City estimates that 10% of prisoners in New York State are Spanish-language dominant. Other states with large immigrant populations such as California, Texas and Florida also see high numbers of Spanish speakers. With most prisons located in rural areas far from the large cities, it is very difficult to find bilingual medical or non-medical staff who can communicate complex medical concepts. In the absence of bilingual staff, inmates who do not speak English often must rely on bilingual inmates as translators. In doing so, they jeopardize their confidentiality.

Stigmatization and lack of confidentiality

Inmates have been attacked and killed for being perceived as gay and/or HIV positive in prison. HIV is still largely considered a 'gay disease' inside. If an inmate becomes too interested in treatment or education he or she may be labeled as gay, adversely impacting health, housing, and life.

Many jurisdictions segregate HIV positive inmates. Inmates often refuse to test or begin treatment if they know they will be separated from existing inmate friends and support systems. Some prisons transfer HIV positive inmates to special units far from family and visitors. Despite the possibility of better medical care, a segregated inmate may lose the ability to hold a job, be considered for educational or work release, or to have contact visits with family and relatives. In this instance, disclosure can lead to a longer sentence.

Adherence issues

Two ways of dispensing medication are used in prison settings: keep-on-person (KOP) and directly-observed-therapy (DOT). With KOP, inmates are issued a day's or week's worth of medications to keep in their cells and take at the appropriate times. The prison schedule may not allow for appropriate meals or fluids being available, or medications may be stolen for re-sale to other inmates. DOT means that the inmates must be released from their housing to stand in a pill line. Someone watches them take the medications and insures that they've been swallowed. Lockdowns or other circumstances sometimes make it impossible for inmates to go to the pill line. DOT often means the inmate surrenders all chances of confidentiality. Other inmates see him routinely appear at a window and take "those big pink horse pills." To make matters worse, medication delivery often breaks down when inmates are transferred from one facility to another or taken to court. Medical records are routinely lost in the process, requiring the inmate to be re-tested and all medications suspended until the new results are received.

"Access to the most basic prevention measures - condoms, clean needles and syringes - remains nonexistent in most correctional systems."

Lack of education & prevention

Until very recently, there was little prevention or treatment education available. Many within the correctional system (inmate and officer alike) were woefully ignorant of the most basic information. Since 1996, a number of national conferences and professional organizations such as the National Commission on Correctional Health Care and the Correctional HIV Consortium have promoted educational opportunities which have begun to improve the quality of all medical services in correctional settings. Ninety-four percent of state/federal prison systems reported to the Department of Justice that they had instructor-led HIV education programs, and 41% reported peer-led education. These figures are misleading. Advocates report that prison systems often advertise brief, one-time orientation sessions as HIV education programs.

In prison, HIV is primarily transmitted through unprotected sex or injection drug use with shared needles. Access to the most basic prevention measures - condoms, clean needles and syringes – remains nonexistent in most correctional systems.

Where good prevention education programs exist, infection rates inside are reduced. Testing and treatment inceptions rise. Treatment outcomes and quality of life improve significantly. The Pastoral Care Service and AIDS Education Programs at the California Medical Facility, The COCOA Project in Washington State, the ACE (AIDS Counseling & Education) Program at Bedford Hills Correctional Facility in New York and pilot programs in Texas, Florida, and within the Federal Bureau of Prisons are good examples of such programs.

The numerous obstacles discussed above lead to increased stress levels, more rapid disease progression, shorter life expectancy and a depressed quality of life. In this population, where HIV/AIDS and other infectious diseases such as hepatitis C are growing at alarming rates, only a radical shift in public opinion and public policy will result in the changes necessary to bring about meaningful improvements in education, testing, and access to treatment.

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Homelessness CONTINUED FROM PAGE 5

allowing for drug resistant HIV to develop. These treatment challenges are so overwhelming that co-infected homeless persons must frequently choose between treating their TB or HIV, or have that decision made for them and enforced by public "health" officials. In the case of the latter, TB always wins out.

Arthritis, asthma, diabetes and elevated blood pressure also seem to be more common in homeless populations. Two of the few physical health surveys ever done of homeless people suggest that all of these conditions were reported twice as often by homeless 18-44 year olds than by the population at large. One set of surveys found significantly higher morbidity rates for asthma in homeless individuals of *all* age groups. The group surveying only homeless persons using mental health self-help agencies reported that 70% of those surveyed had dual diagnoses of drug and alcohol dependence. Anemia, frequent cough, headaches, bowel/urination trouble, heart trouble, joint and muscle ache, and teeth/gum problems were the most frequently reported conditions.

With so little information, it is impossible to draw conclusions about why these conditions are so prevalent in homeless communities. We would expect that environmental factors, such as inadequate ventilation, poor nutrition and crowded living conditions might contribute to an increased incidence of certain types of diabetes, asthma, and even joint/muscle pain. Without specifics, we simply can not make this jump. The surveys do tell us that homeless people are at least more likely to report poor health due to asthma, arthritis, heart trouble and diabetes. HIV infection can present treatment obstacles for any of these conditions. We do not know exactly how these confounding health factors are affected by a compromised immune system. This is an area in desperate need of further clinical research. So is hepatitis C infection in homeless communities. Due to the relative frequency of injection drug use in certain homeless populations, it's likely that HCV rates would also be high among HIV positive homeless persons who were infected through injection drug use. Hepatitis C and HIV co-infection can be enormously complicated to treat, especially for homeless people with multiple social service needs.

Real and perceived adherence barriers

Homeless people are frequently denied combination therapy by healthcare providers who presume them to be bad adherents. The assumption - homeless people are too unstable to follow the complex and demanding regimens for HIV antiretroviral therapy. In a gross example of this reasoning, a nurse, rehearsing this argument in the Journal of the American Medical Association in 1998, conflated homelessness with chemical addiction and mental illness and, on these grounds, rejected the suggestion that antiviral therapy be made accessible to homeless people. This misguided reasoning positions homeless individuals opposite the "public health," disregards real treatment needs and falsely suggests that adherence to antiviral therapy is only a problem in homeless communities.

The more attention we give to these communities, the clearer it becomes that not all homeless people are unstable, without health care, and unable to stick to complex regimens. Though access to primary care is a serious problem, most homeless people do maintain some contact with the health care system and are committed to improving their health. Lack of access, not lack of desire, continues to be the number one problem in HIV care for homeless people. Current studies of adherence to combination therapy in homeless populations support this idea. At least five research groups in the last four years concluded that *once treatment needs are addressed, homeless people have high levels of adherence, reduced HIV viral load, and low levels of viral mutations.* Where clear information about medications, flexible physicians, and accessible clinics, pharmacies and services exist, homeless people consistently show dramatic health benefits from anti-HIV therapy.

Jen Curry is a treatment educator at CRIA.

Provider CONTINUED FROM PAGE 5

such as headache, anemia and sleep disturbances, are also complicated by homelessness.

Homeless clients often have multiple social service needs. There are many reasons clients are homeless, and unless the health care provider understands what those reasons are, and how to assist the client, treatment of their HIV infection may be impossible. Once you understand some of the reasons why an individual is homeless, you can institute a treatment plan. Complicating factors include substance use, mental health issues, domestic violence, illiteracy, unemployment, immigration, histories of arrest and incarceration, and co-infection with other sexually transmitted diseases, tuberculosis, and hepatitis. Methadone maintenance can affect medication levels and vice versa. All of these concerns must be addressed prior to instituting treatment.

I've had someone who is homeless say to me: *you're the first person to talk to me, the first person to actually look me in the eye in three weeks.* The social isolation implicit in this comment means that clinic staff and physicians are the sole support systems for many HIV-infected homeless clients.

In order to treat clients successfully, health care workers must suspend judgement and treat within an individual's existing framework. Many health care providers assume that homeless individuals will not adhere to treatment regimens. I've found the opposite. Once the obstacles to treatment are addressed and individuals receive education and support, they are committed to therapy. Unlike many other people with HIV we serve, the homeless client has already had to confront a number of obstacles to get to the clinic in the first place. We need to recognize these challenges and understand that homeless clients need education, advocacy, referral to services, and on-going support in their struggle to live with their disease.

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 CONTINUED FROM PAGE 3

levels. This once again raises the question of whether basing treatment guidelines on the MACS study may have been premature. Even more worrying, a 1994 study of male and female intravenous drug users with HIV concluded: "These data suggest a greater risk for death for women compared to men among IDUs, despite lesser degrees of immunosuppression." One firm conclusion can be drawn from these data: we need to know more.

Drug Metabolism and Side Effects

Several studies have shown that there can be gender and ethnicity-related differences in the way drugs are processed, or metabolized, in the body. Yet this remains an understudied area, with extraordinarily little data available on blood levels of HIV drugs in women compared to men or among various ethnic groups. The same problem applies to variations in the risk of drug side effects (see table on opposite page).

In 1995, researchers from Holland reported that women metabolized AZT (Retrovir) 42% slower than men. In a large US trial that included ddI (Videx), women were more likely to require dose reductions of the drug but still seemed to get the same health benefits. This suggests slower metabolism of ddI. More dramatically, a study of the NNRTI delavirdine (Rescriptor) found that drug blood levels were 1.8 times higher in women than in men. Another recent report noted that women are eight times more likely than men to develop a severe rash from the NNRTI nevirapine (Viramune) This suggests that there may be gender differences in the metabolism of this NNRTI as well, although the labeling claims otherwise.

In terms of side effects, a study of the protease inhibitor ritonavir (Norvir) reported more nausea, vomiting, depression and fatigue among women than men. And recent studies of lipodystrophy have found that women are more likely to have central fat accumulation (initially dubbed "protease belly"), whereas men seem more likely to have higher levels of fat and lower levels of HDL, a blood fat that can lead to cardiovascular disease.

Although the underlying reasons are almost certainly different, there may be similar issues related to ethnicity. One example is a recent finding that people of Asian descent appear to be at greater risk for the side effect of rash from the NNRTIs (Viramune, Sustiva, and Rescriptor). Hispanics have also been reported to have a slightly elevated risk of NNRTI-related rash compared to African-Americans and Caucasians.

African-Americans have long experienced a relatively unique toxicity of AZT - discoloration of the fingernails. Often dismissed by doctors as a "cosmetic" problem, there is as yet no convincing explanation of the ethnic specificity of this side effect. The problem reportedly occurs in around 67 - 81% of African-Americans compared to 20 - 30% of Whites or Hispanics. Whatever the cause, it is clear that the unequal incidence of side effects among ethnic groups is not just hypothetical. Conversely, African-Americans appear to have slightly lower risk of allergy to sulfa drugs such as Bactrim for *pneumocystis carinii* pneumonia (PCP). Since sulfa allergy has been linked to an eightfold increased risk of NNRTI rash, African-Americans may also be at lower risk for this latter problem, although this has not yet been reported. This may be due to too few African-American participants in NNRTI trials. This brings us to the next issue – how do you actually spot examples of gender and ethnicity-specific outcomes?

Powering Up

It's often said that there are lies, damn lies and statistics. Grappling with the statistical shenanigans employed in clinical trials often reinforces this impression. However, there are statistical issues that bear direct relation to our level of knowledge about gender and ethnic differences in HIV. The most important is what statisticians call "power."

If a study of an HIV treatment only includes a small number of women or is not ethnically diverse, then it may be impossible to work out whether different outcomes among groups are meaningful or just due to chance alone. The more people from each different group that are included, the more confident we can be that divergent results actually mean something.

Researchers represent the degree of certainty in a result as what's called a "p value." A p value of less than 0.05 indicates that the results of the study are statistically accurate and did not occur by chance. Achieving a significant p value is heavily dependent on the number of people in the groups that are being compared. If a hypothetical NNRTI study includes 100 Caucasian participants and twenty get a rash, while only ten African-Americans participate and only one gets a rash, it might look like African-Americans are at less risk for this side effect (and it might even be true). However, the small number of African-American participants would make the p value greater than 0.05, indicating that the result could have been due to chance alone. When we read research studies that say the results were "significant," that almost always means that the p value was less than 0.05 and the researchers were confident that the outcome was not due to chance. Although this all sounds terribly nerdy, it's one of the fundamental reasons why diverse representation in clinical trials is important.

Obstacles to Trial Participation

While it's clear that broad representation in clinical trials is essential, there are many reasons why this has not occurred. For example, the infamous Tuskegee experiment exposed a medical establishment steeped in racism. Bill

(Cont. on page 14)

INFORMATION ABOUT GENDER AND RACE ACCORDING TO THE FDA-APPROVED LABELING OF ANTI-HIV DRUGS

Drug	Gender	Race
AZT (Retrovir) zidovudine	No information provided	No information provided
ddI (Videx) didanosine	"The effects of gender on didanosine pharmacokinetics have not been studied."	No information provided
ddC(Hivid) zalcitabine	No information provided	No information provided
d4T (Zerit) stavudine	"The effects of gender on stavudine pharmacokinetics are not known."	"The effects of race on stavudine pharmacokinetics are not known."
3TC (Epivir) lamivudine	"There are no significant gender differences in lamivudine pharmacokinetics."	"There are no significant racial differences in lamivudine pharmacokinetics."
abacavir (Ziagen)	"The pharmacokinetics of Ziagen with respect to gender have not been determined."	"The pharmacokinetics of Ziagen with respect to race have not been determined."
nevirapine (Viramune)	"In one Phase I study in healthy volunteers (15 females, 15 males), the weight-adjusted apparent volume of distribution (Vdss/F) of nevirapine was higher in the female subjects (1.54L/kg) compared to the males (1.38 L/kg), suggesting that nevirapine was distributed more extensively in the female subjects. However, this difference was offset by a slightly shorter terminal-phase half-life in the females resulting in no significant gender difference in nevirapine oral clearance or plasma concentrations following either single- or multiple-dose administration(s)."*	An evaluation of nevirapine plasma concentrations (pooled data from several clinical trials) from HIV-1-infected patients (27 Black, 24 Hispanic, 189 Caucasian) revealed no marked difference in nevirapine steady-state trough concentrations (median Cminss = 4.7 mg/mL Black, 3.8 mg/mL Hispanic, 4.3 mg/mL Caucasian) with long-term nevirapine treatment at 400 mg/day. However, the pharmacokinetics of nevirapine have not been evaluated specifically for the effects of ethnicity."**
delavirdine (Rescriptor)	"Following administration of delavirdine (400mg every 8 hours), median AUC was 31% higher in female (n=12) than in male patients (n=55)."	"No significant differences in the mean trough delavirdine concentrations were observed between different racial or ethnic groups."
efavirenz (Sustiva)	"The pharmacokinetics of efavirenz in patients appear to be similar between men and women and amoung the racial groups studied."	"The pharmacokinetics of efavirenz in patients appear to be similar between men and women and amoung the racial groups studied."
amprenavir (Agenerase)	"The pharmacokinetics of amprenavir do not differ between males and females."	"The pharmacokinetics of amprenavir do not differ between Blacks and non-Blacks."
indinavir (Crixivan)	"Pharmacokinetics of indinavir appear to be comparable in men and women based on phamacokinetic studies including 32 women (15 HIV-positive)."	"Pharmacokinetics of indinavir appear to be comparable in Caucasians and Blacks based on pharmacokinetic studies including 42 Caucasians (26 HIV-positive) and 16 Blacks (4 HIV-positive)."
nelfinavir (Viracept)	"No significant pharmacokinetic differences have been detected between males and females."	"Pharmacokinetic differences due to race have not been evaluated."
ritonavir (Norvir)	"A study of ritonavir pharmacokinetics in healthy males and females showed no statistically significant differences in the pharmacokinetics of ritonavir."	"Pharmacokinetic differences due to race have not been identified."
saquinavir (Fortovase)	"The effect of gender was investigated in healthy volunteers receiving single 1200-mg doses of Fortovase (n=12 females, 18 males). No effect of gender was apparent on the pharmacokinetics of saquinavir in this study."	"The effect of race on the pharmacokinetics of saquinavir when administered as Fortovase is unknown."

* Rough translation: more Viramune seemed to get into the system in women, but didn't stay there quite as long as in men. Hopefully this means that the differences will all come out in the wash. Note that a recent study suggests that this more extensive distribution in women may be associated with a higher incidence of rash (see main article).

** Rough translation: when the company looked back at study samples, Viramune levels didn't seem to vary too much between ethnic groups. However, they didn't design a study specifically to look at this issue, so they don't know for sure.

GLOSSARY:

AUC (Area Under the Curve): a way of calculating the amount of drug that gets into the system and how long it stays there.

Healthy: not HIV-positive.

Median and Mean: two slightly different ways of calculating averages.

Pharmacokinetics: a term used to describe the action of a drug in the body over a period of time, including the processes of absorption, distribution and elimination.

Trough Level: the level of drug in the system just before you take the next dose.

Clinical Trials CONTINUED FROM PAGE 12

Clinton's apology notwithstanding, deep-rooted distrust of the medical and research system persists particularly in communities of color.

Other factors also come into play. Socio-economic disparities may make travel to a clinical trial site harder for some than others. Many academic research centers are located far from African-American and Hispanic neighborhoods, emphasizing the need for community-based research sites.

The ability of women to participate in research can be affected by many factors. Women often bear the burden of maintaining a household and have time constraints that make regular visits to a trial site difficult. For women with children, the only option for participation may be going to one of the few trial sites that offer childcare. Each clinical trial has specific criteria (called inclusion and exclusion criteria) for participation, and burdensome requirements for multiple forms of birth control are commonly required of all female participants.

Inclusion and exclusion criteria can also discriminate against other groups. For instance, most studies exclude persons with ALT (a liver enzyme) levels greater than four or five times the Upper Limit of Normal (ULN). Since many current and former injection drug users have chronic hepatitis C which can cause elevated ALT levels, they are effectively excluded from these trials. Although safety concerns are certainly one reason for this exclusion, it is disturbing since we know that protease inhibitors in particular are metabolized through what's called the CYP450 pathway in the liver. Clinical trials also sometimes use current drug and alcohol use as an exclusion criteria, based on pre-conceived notions that substance users are unreliable in showing up for scheduled visits. The result is little safety data on the use of anti-HIV drugs in a large portion of the HIV positive population.

Without community input, trial designs can also be off-putting to potential participants even if they meet the inclusion criteria. Ensuring that no one in the trial is receiving substandard care is crucial. Continued access to drugs after a trial is completed can also be important. Lack of health insurance is widespread, and African-Americans and Hispanics are over-represented among those lacking coverage. In this regard, there has recently been a disturbing trend in some pharmaceutical-company sponsored studies to charge people (or their insurance carrier, should they be lucky enough to have one) for some or all of the drugs they are taking. In a recent study of the experimental protease inhibitor ABT-378, participants were required to pay for the other study drugs (such as d4T and 3TC). It is hard to believe that the manufacturer of ABT-378, Abbott Pharmaceuticals, could not afford to provide these treatments for the participants.

Language barriers to trial participation can also be a problem. Joining a study requires signing an informed consent form, acknowedging the potential risks and benefits of participation. It's the right of potential trial enrollees to have the consent form provided in their first language, but in reality this right is not always guaranteed.

The Power of the Community

The community's ability to make observations and raise red flags should not be underestimated. Soon after the first protease inhibitors were approved in late 1995 and early 1996, women at community forums were complaining of disturbances in their menstrual cycle that occurred after starting the drugs. Not until 1999 was a letter finally published in a medical journal describing just this problem in women taking the protease inhibitor Norvir (ritonavir). Likewise, many community-based organizations learned of the problems of fat redistribution and breast enlargement long before any reports appeared in the medical literature. If protease inhibitor studies had been better designed, and more attentive to the risk of such gender-specific toxicities, an information gap of several years might have been bridged.

The Bottom Line

While this represents just some of the issues to consider when it comes to gender, ethnicity and clinical trials, it illustrates that more than just inclusiveness and fair play is at stake. There are scientific issues of genetics and physiology that need to be kept in mind, and broad representation in well-designed trials is key to obtaining information that can be used by everyone with HIV as they make critical decisions about their healthcare.

Richard Jefferys oversees the Access Project, a national database of AIDS drug assistance programs at the AIDS Treatment Data Network.

CRIA Announces Major Staff Changes Within its HIV Treatment Education Department

CRIA's HIV Treatment Education Department has recently experienced several significant staffing changes which, despite the departure of a valued colleague, we believe will result in beneficial long term stability and growth of services.

David Pieribone, who was the founding director of CRIA's Treatment Education Department, has left us to become Deputy Director of Education at AIDS Project Los Angeles. David's performance at CRIA was truly exceptional. He expanded the department from one to five persons, establishing a wide spectrum of valuable services in the process and substantially helped to create our agency's reputation as being among the most effective in the United States at reaching medically neglected populations. CRIA was very fortunate to have someone of David's unique abilities to not only speak about extremely complex healthcare issues in ways which were understandable and engaging for all PLWAs, but also to train his staff to do the same. We will miss David and extend our congratulations to the HIV positive community in Southern California for recruiting someone with such great abilities to lead their education efforts.

However, at the same time, we too feel very fortunate to have hired an individual of national prominence as our new Treatment Education Director. James Learned, who joined our program on a temporary basis last December to operate our special HIV/hepatitis C treatment education initiative, has agreed to take over where David left off. He will ensure that our work to provide life saving medical information continues to meet the needs of every segment of the PLWA population both locally and nationwide. James has an unparalleled breadth of knowledge about HIV treatment and research issues which are of interest to our constituents, as well as significant program management and hands on patient advocacy experience needed for his leadership role at CRIA. We are confident that James' energy and drive will allow our treatment education services to effectively speak about the ever changing healthcare environment for HIV and AIDS in the years to come.

CRIA would also like to welcome Jen Curry as our newest Treatment Educator. Jen comes to us from the Legal Aid Society where she connected disadvantaged individuals to a full continuum of care, including comprehensive health services. Jen has an extensive background in HIV education, service provision and community organizing. In the past, she coordinated Columbia University's anonymous HIV antibody testing service and designed programming for the Gay Health Advocacy Project. She has also been active in several Harm Reduction programs, peer Street Outreach Teams and citywide lesbian gay bisexual transgender youth activism. We are very excited to have someone of Jen's commitment and unique experience on staff.

Meredith Snow has been promoted to a newly created position of Publications Manager. Meredith joined CRIA last year as Treatment Education Assistant and has since taken on increasing responsibilities within the department. She became coordinator of *CRIA Update* in March, and she will now assume much of the responsibility to produce our major new Clinical Trials Directory project for the State of New York.

Last but not least, Eduardo Guzman, who was the second person hired to the department in late 1997, continues to provide a valuable element of stability for the many AIDS service organizations which partner in our treatment education initiative.

CRIA Receives HIV/HCV Contract Renewal

CRIA is very pleased to announce that the New York City Medical and Health Research Association HIV CARE Services has awarded us a major renewal contract to continue our vital work on educating people living with AIDS (PLWAs) about treatments for HIV/hepatitis C (HCV) co-infection. CRIA's $200,000 award will ensure our ability to speak about the relevant medical issues to over 2,800 such individuals who are most at risk of carrying both viruses during the next 12 months. Most importantly, this contract will allow CRIA to substantially broaden awareness within underserved communities throughout New York City that co-infection is an issue which must be immediately addressed both through new prevention and treatment efforts. We look forward to working with approximately 145 community based non-profits to conduct this critical initiative. Please call CRIA's Treatment Education Department to learn more about accessing services under our new city sponsored program.

Visit CRIA on the Internet

Our web address is:
www.criany.org

CRIA Update, summaries of CRIA's monthly Community Forums held at St. Vincent's Hospital, detailed information about CRIA's treatment education services and a list of currently enrolling clinical trials are all available on our web page.

ACKNOWLEDGING OUR FRIENDS...

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