ARI

A visionary institute for AIDS research

AIDS RESEARCH INSTITUTE

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

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New Frontiers in Organ Transplantation

By Jeff Stryker

UCSF is one of only a handful of medical centers around the world poised to transplant organs into HIV-positive patients, a procedure that remains controversial both in terms of its medical success and social acceptance.

The prospect of offering transplants to HIV-positive individuals is one of the spillovers of the success of treatments with "cocktail" combinations of the anti-HIV drugs known as HAART—highly active antiretroviral therapy. Suddenly, HIV-positive individuals are living long enough to make it reasonable to consider transplantation as a treatment for hepatitis and other co-morbidities that imperil liver or kidney function.

> *"You have all the transplant people and their multidisciplinary approach and all the HIV people and our multidisciplinary approach…so the collaborative process has been challenging."*
>
> —Michelle Roland, MD

The decision to transplant organs into HIV-positive recipients remains controversial, in part because the demand for organs continually outstrips the supply. According to the United Network for Organ Sharing, a national group responsible for allocating organs for transplantation, 13,600 people are on the waiting list for livers; last year 1,319 people died while on the list. The list for kidneys is even longer, but kidney patients can often be sustained by dialysis while awaiting an organ.

Some observers have expressed doubts about the wisdom of opening up the transplant waiting list to HIV-positive individuals. "It seems almost crazy to be exploring new possibilities for transplant when the shortage is so severe," said **Arthur Caplan,** director of the University of Pennsylvania's Center for Bioethics, in an interview with the Pittsburgh Post-Gazette. "You don't want to discriminate against anybody, but you want to take into account the chances of success and the likelihood that people will live with the transplant."

Dr. Caplan's skepticism has been shared by insurers, a fact that is not surprising to UCSF's **Michelle Roland,** an internist who treats patients with HIV disease. "There are reasonable reasons for third party payers to say 'Why do we want to

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Transplantation

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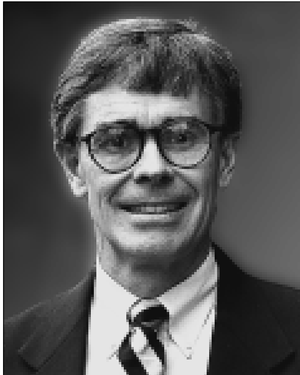
University of California San Francisco

AIDS Research Institute

From the Director: What Are We Doing about HIV in the Developing World?



Thomas J. Coates, PhD
Director
AIDS Research Institute

It is one thing to live through an epidemic as devastating as HIV and quite another to write its history from the perspective of time. Will future generations looking back on this epidemic chronicle our achievements or criticize our failures? Undoubtedly, there will be some of both. The U.S. and other industrialized countries have made HIV a top scientific priority. The U.S. research budget for HIV/AIDS will climb to $1.8 billion in 2000. The activities of the world's scientists have led the way to better diagnostics, therapeutics, and prevention strategies. We continue to inch our way along to improved evidence-based policies as well.

But history should be less kind when it comes to our response to HIV in the developing world. Jesse Jackson Jr., in Congressional testimony, asked us to consider the following facts:

- Deaths from AIDS in sub-Saharan Africa will soon surpass the 20 million deaths in Europe from the plague of 1347.
- AIDS will kill more people in sub-Saharan Africa in the next decade than were killed in all of the 20th century wars.
- 20% to 30% of children in sub-Saharan African will lose their parents to HIV/AIDS this year.
- AIDS has reduced life expectancy in Kenya, Botswana, Zambia, Zimbabwe, and South Africa. Life expectancy had been growing, but began a precipitous decline in 1985, due to HIV/AIDS.
- HIV is having a devastating financial effect; it will reduce the economies of sub-Saharan Africa by 25% over the next 20 years.
- Asia will catch up with Africa in HIV cases by 2005; new infections are expected to double every 14 months in India.

Life-extending multi-drug cocktails begin at $12,000 per year and thus are out of reach for all but a few in the developing world. The answer must lie in better prevention strategies, policies that will permit their implementation, resources devoted to getting effective programs put into place "on the ground," cheaper and more effective therapies, and anti-HIV vaccines. At present, the U.S. spends only $142 million through USAID for HIV in the entire developing world, and the NIH may spend another $60 million for HIV research in the developing world. That's a drop in the bucket relative to the problem.

We at the UCSF AIDS Research Institute are continuing and expanding our commitment to the fight against HIV both at home and in the developing world. I would like to briefly highlight some of our new initiatives, which include:

- To continue our highly successful International Scientists Exchange and Collaboration Program. The Center for AIDS Prevention Studies has worked with over 50 scientists

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Mission Statement

The University of California San Francisco created the AIDS Research Institute in recognition of its obligations to the people of the city of San Francisco, the United States, and the world to prevent, understand, and treat HIV infection. The AIDS Research Institute fosters outstanding, innovative, and integrated programmatic research in HIV/AIDS and excellent training for new scientists to continue working on the HIV epidemic.

The AIDS Research Institute works in close collaboration with affected communities. Scientific results are disseminated as quickly as possible to maximize their usefulness to these communities and to fellow scientists, policymakers, community-based organizations, and the public.

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HIV among Women in Developing Countries

By Pamela DeCarlo

During her pregnancy, Mercy Maklehema, a South African woman with HIV, followed a zidovudine (ZDV) regimen to prevent transmission of the virus to the child she was carrying. After her daughter was born HIV-negative, Maklehema discontinued taking the ZDV. No one warned her that her newborn daughter could become infected with HIV through breastfeeding. Tragically, the infant did become infected and later died. Lack of information is just one of the many problems with life-threatening consequences that confront women with HIV in resource-scarce countries. Another, the high rate of HIV infection, confronts all women.

Women account for nearly half of all new HIV infections worldwide, and the number of women becoming infected is increasing each year. Last year, more than 2 million women were infected with the virus. Moreover, young women are especially vulnerable. Half of all new HIV infections occur in young people between the ages of 15 and 24, and two-thirds of these infections are among girls and young women.

In several ways, women are more vulnerable than men to HIV infection. Male-to-female HIV transmission is about eight times more likely to occur than female-to-male transmission, often for a strictly biologic reason: During intercourse, the exposed mucosal surface of the female genital tract is much greater than the exposed surface of the male genital tract, and this facilitates infections by the virus. Women are also more vulnerable to coercion and sexual abuse, situations that increase their risk for contracting HIV. In general, gender, social, and economic inequalities usually result in women being less able to negotiate for safer sex or to choose their sexual partners.

Availability of Treatment and Care

In industrialized nations in the past few years, combination therapy–that is, therapy that involves the simultaneous use of several antiviral drugs–has helped increase health and prolong life among many people infected with HIV. However, in resource-scarce countries, most people with HIV find it nearly impossible to receive the latest treatments. These treatments not only involve drugs that are expensive and complicated to administer, but they also require frequent visits to a healthcare provider.

In many developing countries, women have access to ZDV only when they participate in clinical trials investigating perinatal transmission. Once their babies are born and the trials end, women may lose access to ZDV and to specialized care. At the International Conference on AIDS held in Geneva in 1998, perinatal transmission of HIV was the most frequently discussed topic relating to women. According to Robin Gorna, chair of the conference's Community Planning Committee, the emphasis on preventing perinatal transmission is "good news for the babies, but not good for the women." She believes programs should "not just focus on women who are giving birth" but should instead address the multitude of prevention and care needs that confront all women.

Maklehema echoes Gorna's concerns. "These trials set out to save the lives of babies," she says. "How do they support and prolong the lives of women?"

Access to Information Is Critical

Health care for women with HIV also needs to include up-to-date and accurate information on treatment options and on the effects of treatment. For example, in developing countries, it is vitally important that pregnant women with HIV who participate in clinical trials of drugs such as ZDV understand what may occur to them or to the children they are carrying as a result of their participation in a study.

"Doctors think that because we're women and mothers that we're ignorant," says Maklehema. "They don't explain the side effects of the drugs, so we can't recognize them and know when there might be a problem."

Women also need to have access to professionals who can help them make meaningful choices. However, this need often goes unfilled in developing countries because there is usually little funding available for counselor training or similar efforts. "In South Africa," says Maklehema, "the doctors are all elite men and they only speak English. Do you think they can provide adequate counseling?" Makelehema believes that HIV-infected women need to be included in counselor training and support programs.

Women's Sex and Sexuality

In many countries, sex and sexuality are taboo subjects for women and men alike. Yet, with vaginal intercourse the most common source of HIV transmission in developing countries, women must be educated in order to make informed decisions about their sexual health. Communities as a whole also need to break down the barriers to discussing sex and sexuality.

"In India, because AIDS first showed up in female commercial sex workers, it was easy for the government to sweep it under the rug,"

says Radhika Ramasubban, professor at the Centre for Social and Technological Studies in Bombay. Although India currently has the highest number of people infected with HIV of any country in Asia, the topics of sex and sexuality are excluded from public discourse.

"It is assumed in India that all people get married and are monogamous," Ramasubban says. "So topics like condom use, homosexuality, and multiple sexual partners are very difficult to address."

Successful Programs Meet Basic Needs

While the overall situation for women with HIV in developing countries is sobering, some regions have shown success in slowing the spread of the virus. In parts of Tanzania, for example, HIV infection rates among young women have been halved as a result of strong prevention programs.

To be effective, programs aimed at women must address education, equal rights, and access to full and comprehensive information. "AIDS is a social issue," says Maklehema. "We need to help women deal with their own social problems before we can deal with HIV-related problems."

Excerpted with permission from an article that originally appeared in The Harvard AIDS Review, Spring 1999.

Pamela DeCarlo is Communications Specialist at the Center for AIDS Prevention Studies, a part of the AIDS Research Institute at the University of California San Francisco.

Developing world,

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from all over the world to establish and implement science that will improve prevention strategies locally, regionally, and internationally. Many of these scientists now sit in positions of authority and are making important decisions about the future of their countries.

- We began collaborating with USAID under AIDSCAP and will continue that collaboration as we partner with TvT Associates in the Syngery, a program designed to bring the best of prevention science into country-level planning for HIV prevention and care.
- HIV InSite now records 2.8 million hits per month, many of which are coming from the developing world. We will continue to enhance the international offerings on this important dissemination vehicle.
- We will work to continue and enhance support for the HIVNET site in Harare, Zimbabwe led by **Nancy Padian, PhD,** and **Willi McFarland, MD, MPH,** in collaboration with scientists from Stanford and the University of Zimbabwe. This site has tested and evaluated important preventive interventions including counseling and testing, peer outreach, microbicides, STD treatment, and others.
- UCSF is one of the collaborators in the new HIV Prevention Trials Network sponsored by NIAID, NIMH, NIDA, and NICHD. Other collaborators in this network include Family Health International, Johns Hopkins, the University of Alabama, the San Francisco Department of Health, Columbia University, the University of Pittsburgh, the California State Labs, the University of Washington, the New York Academy of Sciences, and the Elizabeth Glaser Pediatric AIDS Foundation.
- We have established new HIV prevention trials in Mumbai (India), Lima (Peru), São Paulo, Santos, and Rio de Janeiro (Brazil), and Ho Chi Minh City (Viet Nam). We have worked with our group of international scholars to implement multi-year major projects with funding from the NIH and other major funding agencies.

The AIDS Policy Research Center at UCSF has completed policy analyses on the issues of vaccines, local planning for maximum efficacy, and adolescent sex education. These monographs can be found on the web at http://www.caps.ucsf.edu/bibindex.html#mono. In addition, the Center is working on policy analyses to increase the inadequate USAID budget.

Finally, the AIDS Research Institute is working with the Gladstone Institute of Virology and Immunology, the Macy's Center for Creative Therapies, the San Francisco General Hospital, and the Institute for Global Health to create a Center for Vaccine Development and Evaluation. An anti-HIV vaccine is a world imperative. Our goal will be to develop and test the best vaccine concepts against HIV, and against other pathogens (such as malaria and TB) which are killing the developing world.

Our commitment is clear.

- The UCSF-ARI will use its four arms of basic, clinical, prevention, and policy science to develop and evaluate the best evidence-based strategies in the fight against HIV.
- The Center for Vaccine Development and Evaluation will make important strides against HIV and the other major contributors to death and disability in the developing world.
- Our Policy Research Center will conduct the policy analyses necessary to insure implementation of effective HIV policies and programs, and to work for more funding.
- We will use our dissemination tools such as HIV InSite and our participation in Synergy to get the word out.

None of us can rest until HIV goes the way of smallpox.

ARI Leadership Advisory Board to Be Launched

The AIDS Research Institute will launch a Leadership Advisory Board for the first time since its founding in 1997. Plans are underway to announce the initial membership on World AIDS Day, December 1. Although membership on the Board is expected to grow significantly in the first year, the core group will be comprised chiefly of individuals who have supported the ARI and UCSF AIDS research programs since their inception by providing private funding, business and organizational expertise, and contacts who have contributed significantly to pursuing the mission of excellence and innovation in AIDS research at UCSF.

Advisory Board members will work together, creatively, to seek out private funding and other key resources to benefit *all* AIDS research programs affiliated with the ARI, research for which we are internationally recognized.

The Board will focus on the original vision of the ARI—to support and encourage research innovation and coordinate multidisciplinary approaches to developing more lasting and effective solutions. Increased private funding distributed by the ARI among UCSF's many AIDS research programs will help bridge the funding gap for initiatives for which government funding is inadequate or unavailable.

As with government grants, most private donations to date have been restricted and directed immediately to specific research programs. While this type of funding is very much appreciated, the higher profile programs tend to benefit most. Only 5%, or about $150,000, of the private funding ARI staff was involved in securing last year was designated by donors as "unrestricted."

The ARI leadership and Executive Council concur that these critical, unrestricted resources must be increased dramatically to fund the ARI's efforts to coordinate UCSF's 50 AIDS research programs. As these resources grow, they will benefit essential programs like the AIDS Policy Research Center that receive little or no government funding, and will fund clinical renovations, community outreach, and the pursuit of innovative research ideas.

The Leadership Advisory Board aims to help the ARI raise enough unrestricted money for program coordination and research innovation to eventually replace the temporary budget allotment generously provided through 2003 by Medical School Dean **Haile Debas.** Support of clinical programs at San Francisco General Hospital and at UCSF's Parnassus Campus, now suffering greatly from drastic cuts in government reimbursement, will also be a chief priority.

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Celebrating the launch of the new UCSF C-ARC and the successes of the ACRC are (L-R) Drs. Thomas Coates, Marcus Conant, John Greenspan, and John Ziegler

Launching of the C-ARC

On September 8, 1999, investigators and friends gathered to mark the closing of the UCSF AIDS Clinical Research Center (ACRC) and the launch of the new **California AIDS Research Center** (C-ARC). The C-ARC, sponsored by the University-wide AIDS Research Program (UARP), was formed to support research into biomedical approaches to HIV/AIDS prevention. The reception, held in the Lange Reading Room of the UCSF Library, was hosted by C-ARC Director **John Greenspan** and emceed by ARI Director **Thomas Coates.**

Warm tribute was paid to the first two directors of the ACRC, **Drs. Marcus Conant** and **John Ziegler,** for the significant role each played in the development of clinical AIDS research at UCSF. Conant and Ziegler shared with the audience some thoughts on the current state of the fight against AIDS, emphasizing the success thus far of AIDS research in developing new treatments as well as the need for further work and vigilance to ensure that these successes do not lead to a false feeling of security.

Special recognition for past and continuing contributions went to Greenspan and Coates, and to ACRC Deputy Director **Paul Volberding** and Associate Director **Margaret Chesney** as well.

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Margaret Chesney, Associate Director, and John Greenspan, Director of the new UCSF C-ARC

Visionary Donors Fuel Groundbreaking Accomplishments

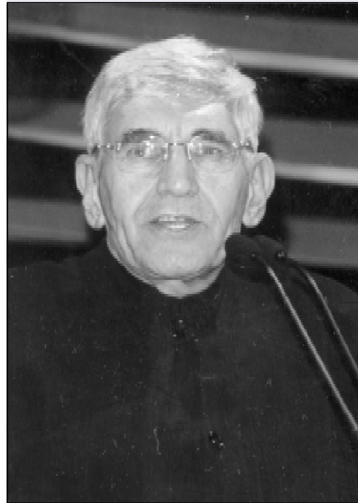
Many people believe that the University of California's annual budget is provided entirely, or at least in large part, by the State of California. In truth, only about 16% of the $1.1 billion UC San Francisco budget is provided by the state. Federal grants account for about 20%; another 5% comes from the City of San Francisco. The balance, a striking 59%, depends on tuition, medical care reimbursements, and the generosity of private donors.

For medical centers everywhere, the percentage of reimbursement received is dropping as insurance plans move toward managed care. To maintain both accessibility and effective student-to-instructor ratios, UCSF's tuition income has remained relatively stable. Federal grants are restrictive and typically require a great amount of preliminary data. Faced with these challenges, UCSF, and the AIDS Research Institute's programs, depend more than ever on private funding.

In the past year, some of the best new ideas at UCSF to help individuals with HIV disease have been funded by generous private donors, donors who understand that the battle against HIV needs to be pushed ahead as rapidly as possible. Strengthened by remarkable progress, these donors believe that UCSF's leadership will continue to be critical to stopping AIDS permanently within our lifetimes. A few of the recent achievements made possible by private support are described below.

Macy's Passport a Success

In addition to being the world's largest annual fashion event, Passport is the highest profile component of Macy's commitment to give back to the communities in which it does business.



"In the past our greatest challenges were ignorance and fear. As we move toward the new millennium, our enemy is complacency. Although great strides have been made in prolonging the lives of some of those infected with HIV/AIDS, the crisis is by no means over. Our young people continue to be infected at an alarming rate and the most disenfranchised in our communities often do not have access to information and treatment. With HIV infection rates growing rapidly in developing countries like South Africa, we must look beyond our own communities and remain extremely focused on finding a vaccine that will finally put an end to this world-wide epidemic."

—Macy's West Chairman and CEO, Michael Steinberg

PEP Feasibility Studies

An antiviral medication regimen that blocks initial HIV infection if administered within 72 hours of exposure has been evaluated in San Francisco as a collaboration between UCSF and the San Francisco Department of Public Health (SFDHP). Known as Post Exposure Prevention (PEP), this therapy was initially developed by **Mitchell Katz, MD,** Director of the SFDPH, and **James O. Kahn, MD,** at the Positive Health Program at San Francisco General Hospital (SFGH). PEP was piloted at SFGH in a program made possible by a private grant from the William McCarty-Cooper Trust and John Hutchinson. Due to this outstanding success, the National Institutes of Health plans to fund this program for four more years as a national model expected to reduce infection dramatically in high-risk populations across the United States.

Extending the PEP program internationally should have an even more profound impact, especially in Africa, where new strains of HIV emerge constantly. UCSF already supervises some HIV prevention programs and medical services in Africa. The ARI now seeks additional private funding to establish PEP programs throughout Africa and in other high-incidence regions internationally.

A New Vaccine Concept

With lead funding by Macy's West, **Dr. Joseph "Mike" McCune** heads a team of clinical researchers that have developed a new model of how HIV causes the immune system to crash. It has been understood for some time that HIV infects CD4 cells, and that their decline marks and hastens the failure of immune functions resulting in AIDS. However, until now a direct functional link between HIV infection and the decline in CD4 cell production by the thymus was not identified.

A breakthrough came when McCune's group observed SIV, the equivalent of HIV in humans, in monkeys. SIV does not cause CD4 cells in monkeys to become depleted as HIV does in humans; instead, cells killed are replaced by the thymus even when copies of the

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Award-Winning HIV InSite Reaches More with Private Support

By Mark Kelleher

Two years ago, UC San Francisco's award-winning HIV InSite (http://hivinsite.ucsf.edu) faced an uncertain future. Even then, as now, it was the most accessed site in the world devoted to HIV. HIV InSite was receiving around 200,000 hits per month in early 1998; now, the site commands nearly 3 million hits a month, far outpacing peer sites.

HIV InSite is a collaboration of the Positive Health Program at San Francisco General Hospital and the Center for AIDS Prevention Studies, both programs of the UCSF AIDS Research Institute. It is directed by **Paul Volberding, MD,** and Co-Directed by **Thomas Coates, PhD.** Reflective of the breadth of AIDS research at UCSF, HIV InSite offers the most comprehensive original coverage of HIV disease health care—from policy to prevention, basic science to treatment—of any source, along with links to related sites.

What were the challenges? As with many start-up projects at UCSF, initial funding for HIV InSite from very generous foundations was phased out after the first couple of years. Typically, foundations grant money to launch innovative ideas like HIV InSite, but then it's up to the projects to figure out how to sustain themselves. Many new projects at UCSF secure government grants after data is gathered and initial hypotheses appear credible; but few "community outreach" efforts qualify for sustaining federal or state funding, no matter how successful.

Two companies, **Bristol-Myers Squibb** and **Merck,** recognized the potential of HIV InSite even before a concerted effort was kicked off to increase private funding. Nonetheless, by the second year of operation it was clear that burgeoning demand and the fast-paced progress of HIV research would require more financing. Recognizing what appeared to be quite a predicament on the horizon, HIV InSite staff worked with the ARI to set a new course by dramatically expanding the site's donor base.

Compelling facts underscored the case for support, especially among pharmaceutical firms, the principal prospective donors. An analysis of the site's hits showed that approximately 25% were physicians and other healthcare professionals, 35% were HIV/AIDS researchers and students, and 15% were people living with HIV. Bolstering this, HIV InSite had won numerous high-profile accolades including Smithsonian Permanent Collection membership, Omnivision Winner, Yahoo! Pick, *USA Today* Hot Pick, Dow Jones Select Site, Go.com Editor's Choice, and *Los Angeles Times* Pick.

One challenge which arose was to formulate a policy regarding donor listings. Feeling it was critical that no endorsement of any product be presumed or implied, it was agreed that higher-level sponsors, with logos and hyperlinks to their sites, would be listed on a margin of the homepage. However, no sponsor's name or logo is shown on a page associated with the presentation of specific medical treatments or research. Also, banners and "cookies" generated by sponsors would not be allowed. All involved agreed to these policies, and they continue as guidelines for sponsorship.

The following generous sponsors now make it possible for the HIV InSite staff to continue this outstanding project:

Project Partners
($100,000+)
Bristol-Myers Squibb
Dupont Pharma
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Pharmacia & Upjohn
Roxane Laboratories
Robert Stempel and the Stempel Foundation
Sun Microsystems

Contributing Sponsors
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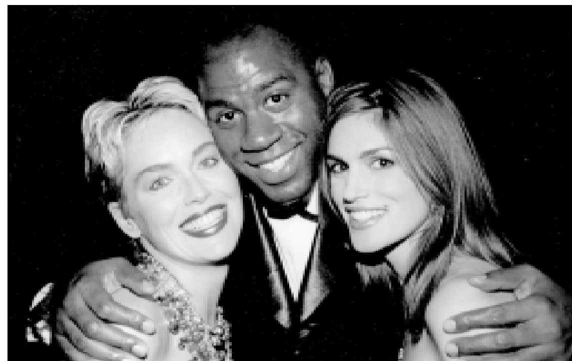
ALZA Corporation
BTG Pharmaceuticals
Celgene Corporation
Gilead Sciences
Hewlett Packard Company
Informix Software
Larry Novida

Founding Sponsor: The Henry J. Kaiser Family Foundation

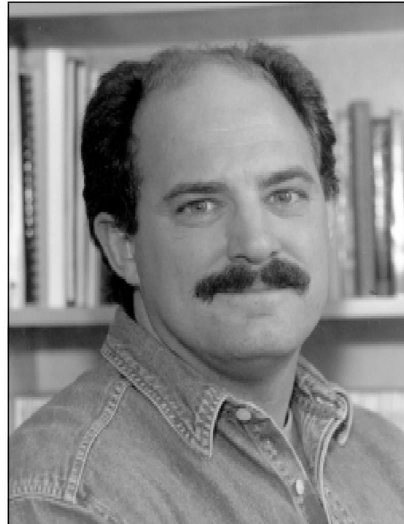
Mark Kelleher is Director of Development for the AIDS Research Institute. He may be contacted at (415) 476-9878 or mkelleher@dismail.ucsf.edu.



Event Chair Earvin "Magic" Johnson, Co-Chair Cindy Crawford, and special guest Sharon Stone joined together for Macy's Passport '99 Extreme, which raised over two million dollars for HIV/AIDS agencies and research with shows in San Francisco and Los Angeles.

STOP AIDS Project Honors CAPS Researcher Ron Stall

Ron Stall, PhD, MPH, Associate Professor of Medicine at the UCSF AIDS Research Institute's Center for AIDS Prevention Studies (CAPS), was honored on September 13, 1999 by the Stop AIDS Project with their Chuck Frutchey Board of Directors' Award. Ron's work has focused extensively on public health approaches to the substance use and HIV/AIDS epidemic. Stall was a founding member of the Technology and Information Exchange Core of CAPS. Over the years, he has worked with many community-based organizations, including Stop AIDS. We thought we would share his acceptance speech, as it puts a very personal touch on the work that so many of the researchers do at the ARI.



"Although I'd like to believe that this award was earned only by me, in fact, awards of this kind reflect the contributions of an entire group of scientists. It acknowledges the commitment of **Maria Ekstrand,** the rigor of **Jay Paul,** the talent of **Michael Crosby** and **Andy Williams,** the originality of **Greg Greenwood** and **Katherine Fritz;** and anticipates the future contributions to our group of **Andres Maiorana** and **Eric Murphy.** And it also reflects the daily support of my husband, **Tom Mills,** who makes it possible for me to hold down this job.

Usually, when I get up to talk in front of rooms of people like this, it is to describe data. On this occasion I hope that you'll excuse me if I talk a bit about myself.

I was raised in a middle class neighborhood, a sea of endless square yards and rectangular houses, all of them the same. I learned early on that about the only way for me to escape all of those endless square yards and rectangular houses was to go to the local library and read every book I could find on history. I read about the raising of the Temple of the Sun at Teotíhuacan. I read about the life of Joan of Arc. I read in amazement about how my European ancestors pushed dying people out the gates of their cities in the hope that they might be spared the Black Death. And I read about how the military might of the slave-holding South was crushed at the battle of Gettysburg, thereby making the end of slavery in our country inevitable.

And then it hit me: Not only had I been cheated by being raised in a nondescript neighborhood of endless square yards and rectangular houses, but I had also been cheated because all of the history had already happened. I've grow up since then, and if there has been a theme in my life, it is that all of the history has most certainly *not* happened.

While I never saw the raising of the Temple of the Sun at Teotíhuacan, I did watch a group of community-based gay men design a pioneering prevention strategy to stop the AIDS epidemic. One of these men was **Chuck Frutchey,** for whom this award is named. This was an architecture certainly as interesting as that of any pyramid.

While I never met Joan of Arc, I did get to live during the lifetime of Harvey Milk, who taught us that with mobilization, moxie, and hard work, we can create a safe refuge for the gay community to grow and prosper—a gift very similar to the one that Joan of Arc gave France.

While I never experienced the Black Death, I did get to witness something even more amazing. I saw how the citizens of San Francisco opened our hearts, our wallets, and even our homes to people with AIDS, so that our fellow citizens could live out their lives in dignity and hope.

And while I never saw the battle of Gettysburg, I was part of the research group that charted amazing reductions in gay men's sexual risk practices. These remarkable reductions, *if maintained,* will end the AIDS epidemic in our city as surely as Gettysburg ended slavery.

I want all of you to look around this room and see all of the people who have made so many important contributions in the fight against AIDS. And I want you to smile as you think about some bored kid born two centuries from now, doomed to a childhood in a neighborhood of square yards and rectangular houses, who reads about *our* lives and feels cheated because all of the history has already happened."

Primary HIV Prevention for HIV Positive Individuals: ARI Playing Leadership Role Locally and Nationally

By Steve Morin, PhD, and Mike Shriver

In 1996, at the behest of **Rep. Nancy Pelosi** (D-CA), Congress directed the Centers for Disease Control and Prevention (CDC) to begin to address the primary HIV prevention needs of persons living with HIV disease. Up to that point, no direct mention or clear indication of this need had been made.

For individuals living with HIV disease, the past three years have been nothing short of overwhelming. With the data showing a decline in AIDS deaths, it became clear that access to anti-HIV treatment regimens could improve both the quality and quantity of life for people with HIV disease. In real terms, thousands of Americans with HIV disease saw their physical health improve dramatically.

Logically, since there was now a longer time lapse between when someone seroconverted and when they developed AIDS defining conditions, and since the new therapies helped people with AIDS begin an almost new life, more healthy people with HIV disease were and are continuing to live or returning to a relatively normal, active social and sexual life.

> *"Risky behavior by positive people is not the norm. Most of us take extraordinary steps to make sure that we are not infecting our partners, and we're doing so without a whole lot of support. There aren't big campaigns supporting us staying safe in our relationships. We're doing it of our own accord."*
>
> —Terje Anderson, Deputy Executive Director, National Association of People with AIDS

But with the awesome news there also came a challenge that to date has only partially been answered. As far back as mid-1996, it was clear that HIV prevention interventions to assist people with HIV disease in adopting and maintaining healthy risk reductive behaviors were urgently needed and almost nonexistent. This was to some degree understandable, given the appropriately targeted tenor and focus of much of the HIV treatment, research, and prevention advocacy; but in the big picture, it left a whole community critical to breaking the chain of new infections without the skills, programs, and support known to be essential for people to sustain consistently safe sex and safe drug using behaviors. In many areas of the country, people with HIV disease were thought solely to need better anti-HIV medications, health and housing services, and effective psychosocial programs (i.e., programs to help with coping, adherence, and disease management).

Researchers at UCSF's Center for AIDS Prevention Studies(CAPS) and at our key partner research institutions, however, were able to see the problem approaching. We successfully bid for a National Institute of Mental Health (NIMH) multi-site prevention research trial across four cities in the United States (New York, Los Angeles, Milwaukee, and San Francisco) to develop interventions that assist people with HIV disease in adopting and maintaining risk reductive behaviors. **Dr. Margaret Chesney,** the Principal Investigator, has been working with a team of CAPS researchers to help bring relevance, urgency, and the unique perspective of San Francisco to this interactive multi-site trial.

Two years ago, the CDC took a first step toward honoring the Congressional directive of 1996 by funding **Dr. Cynthia Gomez** of CAPS to embark on an exhaustive qualitative research initiative looking at issues surrounding HIV positive gay men's ability to adopt and maintain safe sex and drug use. The Seropositive Urban Men's Study (SUMS) was done in collaboration with researchers in New York City and at the New Jersey Medical College. A great deal of this data was presented at the International Conference on AIDS in Geneva, 1998.

In late 1998, the CDC awarded 5 jurisdictions funding to create demonstration projects to "develop comprehensive continuums of primary HIV prevention for HIV positive individuals." The expressed desire to collect as much data as possible and to get programs up and running quickly remains the clearest signal to date from the CDC on the importance of this work.

San Francisco successfully competed and was awarded approximately $750,000 to be one of the demonstration project sites. A four-tiered proposal for community-based organizations in San Francisco was created and has gone out to bid. ARI staff assisted the Department of Public Health with secondary data analyses and facilitation so that the demonstration project would be evidence-based and also responsive to the needs of real people.

Finally, in ARI's efforts to break new ground on this critical component of our HIV prevention efforts, CAPS was funded by the Office of AIDS Research, in coordination with the CDC and NIMH, to host a workshop June 17-18 of this year to look at the real needs of researchers, community-based providers, and individuals living with

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Accomplishments,

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virus reach into the millions in an infected monkey. Something in a monkey's thymus—something that becomes dysfunctional in humans—remains "turned on," producing CD4 cells even under the onslaught of heavy viral load.

The promise of new treatment and even a vaccine is based on identifying the factor that enables the immune system of these monkeys to continuously produce protective CD4 cells. Our hope is that once this is identified and understood, this knowledge might be applied to protect HIV-infected humans from disease progression to AIDS. UCSF collaborators on this project include **Drs. Steven Deeks, Mark Jacobson,** and **Robert Halvorsen.**

CD8 Cell and Genetic Research

An exceptionally generous anonymous grant has advanced another lead at UCSF that may result in more effective treatments and even a vaccine. UCSF's **Jay Levy, MD,** and colleagues have now shown that a body's ability to produce unusually high levels of CD8 supressor cells, which prevent HIV from multiplying, is one of the most prominent known attributes common to the immune systems of both individuals infected with HIV but who, after even 15-20 years with little or no treatment, show low viral load and no disease progression; and those documented as having been exposed to the virus continuously over long periods of time (as with some serodiscordant couples, for example) without seroconverting. Something in their systems, apparently a highly active CD8 response, appears to block infection.

Recent advances, made possible by this generous grant, have now positioned Levy's team to begin the process of seeking out partners in academe and industry to formulate effective medical approaches, based on CD8 research and underlying genetic factors, that might be viable enough for early trials.

Expansion for "Return to Work" Coverage and HIV-Positive Organ Transplant OK Approved

Launched less than two years ago by **Dr. Steve Morin,** the AIDS Policy Research Center (APRC) has already secured several key private grants to underwrite profoundly important initiatives that will impact the lives of many individuals with HIV disease. Although the APRC does not lobby directly, it supports select causes through persuasive research, strategic advice, and key contact referrals. As government funding is generally unavailable for projects connected to advocacy and community outreach, Dr. Morin and his colleagues are compelled to seek out private funding.

Thanks to generous support from the **San Francisco Foundation, Until There's A Cure Foundation,** the **John M. Lloyd Foundation,** and other sources, the APRC is off to a great start. Among the Center's chief accomplishments this year is helping to gain Medi-Cal coverage of organ transplants for HIV positive patients who have not progressed to AIDS. Such insurance is generally unavailable in the U.S. no matter how healthy a person with HIV might be. Persons with other chronic but relatively manageable diseases have long been covered for organ transplant.

Looking toward the very near future, APRC researchers designed cost-benefit economic projection models used to push Medicaid expansion proposed by Representatives Richard Gephardt and Nancy Pelosi. Their groundbreaking initiative will allow individuals now on disability to return to work yet maintain coverage for lifesaving medical care and medications for an extended period. Protection against unforeseen relapse is predicted to be very motivating for individuals still challenged by HIV but who desire a meaningful livelihood. Enabling more people to exercise their talents is not only good for the economy, it should be good for them. The pursuit of goals, including professional achievement, is known to help maintain long-term health. Advocates for this important legislation are very hopeful it will pass soon.

Prevention,

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HIV around primary HIV prevention. This workshop, the third in a series sponsored by ARI and the AIDS Policy Research Center, brought together a mix of over 50 providers and researchers of all races and genders from across the country. Over 50% of the participants were individuals living with HIV, and over 50% of the attendees were individuals from communities of color.

The monograph to emerge from the June meeting will play a key role in informing the national research agenda, especially for NIMH; it will also provide an analysis of which programs currently exist across the nation, and which programs work.

With the NIMH-funded project underway, the CDC-funded research project (known as the SUMIT Project) now testing its intervention, the San Francisco demonstration project out to bid, and the monograph from the workshop in progress, this fall promises to be an active and visible time for ARI as it moves the agenda forward to help stave off new HIV infections with sound, effective, and rational policies and interventions.

Dr. Steve Morin is the Director of the UCSF AIDS Research Institute's AIDS Policy Research Center (APRC) and Mike Shriver is APRC's Co-director.

Transplantation, continued from page 1

fork out hundreds of thousands of dollars to do this intervention when you have no data?'"

So far, conjecture about how HIV-positive patients will fare as transplant recipients is based on very circumscribed experience. There are limited historical data from patients whose HIV status was unbeknown to the transplant team; only a handful of transplants have taken place when recipients were known to be HIV-positive. Dr. Roland speculates that insurers will change their tune, "if we can do a reasonable pilot study that shows…patients' grafts are functioning and surviving for a reasonable period of time."

UCSF is about to undertake such a pilot study of liver and kidney transplantation in HIV-positive patients. The study is the result of intensive lobbying by AIDS activists, research by a host of UCSF physicians and surgeons, and support from the state government. Late this summer, the California legislature appropriated $1 million to UCSF to conduct up to ten transplants. The funding earmark came at the behest of Assemblywoman **Carole Migden** (D-San Francisco), with a nudge from the irrepressible Jeff Getty, an Oakland AIDS activist who came to national attention in 1996 when he received a baboon's bone marrow in a transplant procedure directed by UCSF's **Dr. Steven Deeks.**

Although a million dollars is a relatively modest sum when it comes to transplantation (liver transplant costs typically exceed $300,000), the prospect of some public funding helped galvanize researchers and focus their energies. A team led by **Dr. Peter Stock** of the Department of Surgery, Dr. Michelle Roland of the Department of Medicine, and **Dr. Leslie Floren** of the Department of Biopharmaceutical Sciences met with other UCSF researchers and community advisors to hammer out two protocols, one for kidney transplantation and the other for liver transplantation. The protocol development required an almost unprecedented level of interdisciplinary cooperation. "You have all the transplant people and their multidisciplinary approach and all the HIV people and our multidisciplinary approach...so the collaborative process has been challenging," Dr. Roland said in a recent interview, with a politic tone of understatement in her voice.

The fundamental obstacle the protocol team faced was clear: People with HIV have been excluded from transplantation largely because of concerns that immunosuppressive drugs administered to ward off the body's efforts to reject any foreign organ might worsen a patient's HIV infection or interfere with the workings of antiretroviral drugs.

This led to protracted discussions of just how sick eligible patients should be, echoing a debate already well known to transplant surgeons, bioethicists, and desperate patients and families. Patients would need to be both healthy enough to benefit from an organ transplant and in a position to take care of their new organs. (This latter consideration would bar active alcoholics or injection drug users from receiving organs.)

Jeff Getty, a member of the Community Advisory Board (CAB) advising UCSF on the transplant protocols, described the decision in an ACT UP/Golden Gate Writers Pool article. "CAB members agreed that since there were plenty of [HIV-positive] patients waiting for organs that met this criteria [a nadir of 200 CD4 cells and no previous AIDS-defining opportunistic infections], it would be best to start with healthier patients first.…CAB members agreed that the higher the HIV-positive survival rate, the more likely it will be for medical insurance payment and HIV inclusion in future transplants. Unfortunately, patients with low CD4 numbers or progressed AIDS will be turned away for now. This decision was not taken lightly by the group." Last month, UCSF researchers reprised these discussion in a meeting convened by the National Institutes of Health (NIH). NIH brought together representatives from Mt. Sinai, Georgetown, Loyola, and the University of Pittsburgh to develop, if not a common multi-site research protocol, at least the beginnings of a national registry of HIV-positive transplant recipients.

Jeff Stryker is Senior Editor of the UCSF AIDS information website, HIV InSite, at http://hivinsite.ucsf.edu.

Speaker Sharon L. Hillier, PhD, of the University of Pittsburgh/ Magee-Womens Hospital, talks with Drs. Susan Buchbinder of the SFDPH and Fulvia Veronese of the NIH Office of AIDS Research at the 1999 NIH Centers for AIDS Research symposium hosted by the UCSF-GIVI CFAR at Cole Hall Tuesday, October 12, 1999. The symposium was presented by the UCSF-GIVI CFAR on behalf of the 18 national CFARs and in conjunction with the annual CFAR Directors and Administrators Meeting held on October 13.

Upcoming Meetings

3rd Annual World AIDS Day Symposium: How Do We Prevent the Second HIV Epidemic?
December 1, 1999
2:00-5:00 pm
Reception following
Cole Hall, 513 Parnassus Avenue
San Francisco, CA
Presented by the UCSF AIDS Research Institute

Speakers include:
Dr. Robert Grant:
The Spread of Drug-Resistant HIV
Dr. Michelle Roland:
Post-Exposure Prevention and Primary HIV Infection
Dr. Willi McFarland and Dr. Kim Page-Shafer:
Detection of Recent HIV Infection: New Public Health Opportunitites in Prevention
Dr. Cynthia Gomez:
How Do We Help HIV-Infected Persons Not Spread HIV?
Michael Shriver:
Making Prevention Work for HIV+ Individuals: The Intersection of Policy and Prevention

Free of charge, but registration is requested
To register, call (415) 597-UCSF
or E-mail: ari@psg.ucsf.edu

Call To Oneness: A Conference on Compassion and HIV Disease
December 2-4, 1999
Most Holy Redeemer Parish
100 Diamond St., San Francisco, CA
Sponsored by Multicultural AIDS Resource Center of California
Contact: Chris Sandoval, Director, MARCC
E-mail: marcc@polarisinc.com
Phone: (415) 777-3229 ext. 324/325
Web: www.polarisinc.com/marcc/Index.html
UCSF/AIDS Research Institute is a Co-Sponsor of this conference

Making A Difference: HRSA's HIV/AIDS Programs
Ryan White CARE Act All Titles Meeting
January 18-21, 2000
Washington, DC
Sponsored by HRSA

National AIDS Update Conference HIV/AIDS at the Crossroads: Confronting Critical Issues
March 14-17, 2000
Bill Graham Civic Auditorium
San Francisco, CA
Contact: Felicissimo & Associates
E-mail: felicissimo@total.net
Phone: (514) 874-1998

3rd Annual Retreat of UARP-supported C-ARCs
May 7-9, 2000
San Diego, CA
Contact: Suzi Hedberg, UCSF C-ARC
E-mail: hedbergs@dentistry.ucsf.edu
Phone: (415) 476-8482

COUNTDOWN TO DURBAN

In upcoming issues, the ARI newsletter will feature information about the XII International AIDS Conference to be held in Durban, South Africa from July 9-14, 2000.

For now, here are some key February 1st deadlines:

- Abstract submission
- Scholarship applications
- Early registration fee
- Cancellation of registration with full refund
- Non-governmental, non-profit booth requests
- Satellite meetings requests

Be sure to read the next ARI newsletter for more information on ARI's participation in the conference as we count down to Durban 2000. Visit the conference web site at www.aids2000.com

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Register Today! (415) 597-UCSF