

Fashion and Compassion Pave the Way to Innovative Research

By Joan Moyer Schwing

Visualize the glitz and glamour of the fashion runway with celebrity models and stars like **Magic Johnson**, **Elizabeth Taylor**, and **Sharon Stone** providing a Hollywood feel – how does it help AIDS research and the fight against AIDS? The answer is, “in millions of dollars.” Every September, Macy’s presents their annual Passport event in both San Francisco and Los Angeles. The proceeds of the fashion theatre event are granted to HIV/AIDS organizations in California and in other areas where Macy’s West has stores. Over the past five years, the UCSF/Macy’s Center for Creative Therapies has been one of the recipients of this generosity.

The mission of the Center is to forge closer working relationships between the UCSF academic staff and the pharmaceutical and biotechnology industries. Its emphasis is on moving novel therapies into and through the clinic as

quickly and effectively as possible. The Center was originally the brainchild of **Dr. Joseph “Mike” McCune** (see sidebar, page 5), but it would not have been created without the financial support of Macy’s Passport. With the help of \$1 million from the Macy’s Passport Fashion Show, the Center has made significant progress over the past five years.

Since its inception, the Center has promoted interactions and collaborations between AIDS investigators at UCSF. Its example catalyzed a university-wide forum, which led to the creation of the UCSF AIDS Research Institute (ARI). The Center, in partnership with the General Clinical Research Center (GCRC) and Center for AIDS Research at San Francisco General Hospital (SFGH), and the Gladstone Institutes, used its funding as seed capital to form three key Core Labs essential to the current HIV/AIDS research being done by UCSF investigators: The Core Virology Lab headed by **Dr. Robert Grant** and the Core Immunology and Core Genomics and Molecular Biology Labs, both headed by **Barry Brett**. With the Center’s leadership, the creation, resources, and staffing of both the Core Virology and Immunology Labs have been made top priorities by the University and ARI.

“Traditional physicians need labs like the Core Labs nearby to interact with and discuss clinical observations. Basic science labs cannot do this.”

– Dr. Robert Grant, head of the Core Virology Lab

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Creative Therapies

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University of California
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AIDS Research Institute



Thomas J. Coates, PhD
Director
AIDS Research Institute

Connections

San Francisco hosted the recent 7th Annual Conference on Retroviruses and Opportunistic Infections, where the news was decidedly mixed. The wonderful advances in therapeutics seem, for the most part, to be holding. Concerns about their side effects remain, but those effects do not appear to be as prevalent or as toxic as initially feared. Nonetheless, there is a need to simplify regimens and to keep the drug pipeline full so that products can keep ahead of the virus. And there is the constant concern about how to make these drugs available to the 95% of the world where the virus is

prevalent but the drugs are unaffordable. Finally, hope remains for a vaccine that will protect against infection, or at the very least slow the progression of disease. But there were few tangible prospects on which to pin those hopes.

The AIDS Research Institute at UCSF remains committed to stopping this terrible epidemic, and we will be committed to that endeavor until HIV goes the way of smallpox. What is our strategy? The answer is simple: connections. We believe that the solutions to the next phase of the epidemic lie in developing connections that will lead to better, more comprehensive, and hopefully more effective solutions.

- We are connecting our basic and clinical scientists to understand better how combination therapy stays effective, and how better to provide salvage therapy for patients with HIV.
- We are connecting our immunologists with our clinicians to determine how we can boost the immune system's natural abilities to fight HIV.
- The Center for AIDS Research, directed by **Paul Volberding, MD**, and **Warner Greene, MD, PhD**, connects the basic, clinical, and population sciences in translational research to bring insights of the lab to the clinic and the field, and vice versa.
- The California AIDS Research Center, directed by **John Greenspan, BDS, PhD, FRCPath**, with Paul Volberding, MD, and **Margaret Chesney, PhD**, connects the basic, clinical, and population sciences to improve our understanding of biological issues in HIV transmission. Our hope is that insights for vaccines and better therapeutics will come out of this work.
- The Center for AIDS Prevention Studies, directed by myself with **Susan Folkman, PhD**, and Margaret Chesney, PhD, connects the social, behavioral, public health, and policy sciences to better understand how to stop the spread of HIV in vulnerable populations.
- The new ARI International Program, directed by **Nancy Padian, PhD**, connects our widespread international research, training, and clinical efforts under one umbrella.
- The AIDS Policy Research Center, directed by **Stephen Morin, PhD**, connects public health and policy researchers with the policy community to conduct important policy research that will advance our ability to prevent and treat HIV.

We remain committed to connecting the UCSF research community with infected and affected populations here and around the world. These connections will break the back of the epidemic.

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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AIDS Research Institute

Retrovirus Conference Update

By Sue Rochman

The National Conference on Retroviruses and Opportunistic Infections is widely recognized as the premier opportunity for basic and clinical science investigators to present, discuss, and critique the latest developments in human retrovirology and related opportunistic infections.

The 7th annual conference, held January 30 to February 2 in San Francisco, highlighted HIV/AIDS research areas ranging from virology, pathogenesis, and host-virus interactions to the diagnosis, treatment, and prevention of associated opportunistic infections. To help bring this information into the community, the Conant Foundation and the UCSF AIDS Research Institute co-sponsored a Community Forum on the conference on Thursday, February 17.

More than 300 people crowded into the Sheraton Palace Hotel's Gold Ballroom for the forum, which gave Bay Area residents the opportunity to hear San Francisco-based HIV/AIDS experts discuss some of the most significant developments from this year's meeting.

Co-moderated by **Marcus A. Conant, MD**, Conant Foundation founder, and **Thomas J. Coates, PhD**, Director of the UCSF AIDS Research Institute, the two-hour forum explored issues such as side effects of HAART, strategic drug holidays, new drug approaches, AIDS vaccine research, and the expansion of genotypic and phenotypic resistance testing.

Warner Greene, MD, PhD, Director of the Gladstone Institute of Virology and Immunology, kicked off the Forum with a pathogenesis research review. Eighteen separate studies on treatment interruption trials were reported at the conference, but Greene emphasized that many of these trials were small and not well controlled.

"Taken as a whole," he continued, "the results were inconclusive — some positive, some negative. On balance, we still don't know whether scheduled treatment interruptions represent an effective means to augment a protective immune response against HIV. Additional studies examining different types of interruptions monitoring a broader range of immune parameters are required. Stay tuned."

Ruth Greenblatt, MD, Professor of Clinical Medicine and Epidemiology at UCSF, summarized the latest research on treatment decision-making. Regarding the optimal number of medications, she said, "the simple answer is three. When and if a fourth drug is added, it's more for its pharmacokinetic value than its antiretroviral value."

Greenblatt also delved into the area of treatment failure. "We need to be careful how we define 'fail'. There may be situations where there is virologic rebound without CD4 decline, and in those cases it could be a mistake to reject the current regimen because it is actually still effective. If, however, CD4 decline occurs along with virologic rebound," Greenblatt continued, "a change in regimen would be indicated." In that case, "a treatment holiday is an option to try and re-establish a wild type virus, but doing so is only a temporary fix and it can be associated with significant problems."

Turning her attention to women, HIV, and pregnancy, Greenblatt noted that the risk of vertical HIV transmission is correlated with maternal HIV RNA level; that the risk of transmission increases with prolonged rupture of membranes; and that although cesarean sections have been found to be protective against HIV transmission, they are not clearly beneficial in women with consistently undetectable RNA, after rupture of membranes, or for women already in labor.

Exploring the subject of resistance testing, **Robert M. Grant, MD, MPH**, Director of the Gladstone/UCSF Laboratory of Clinical Virology, discussed the results of two randomized, controlled studies presented at the conference on the effectiveness of phenotypic resistance testing to direct salvage therapy. Because researchers only presented interim results and a large number of individuals dropped out of the study due to the lengthy wait for phenotypic testing results, Grant emphasized that it was too early to fully and accurately assess potential benefits of testing.

"We've seen that there is a benefit early on, when salvage therapy is started," said Grant, "but we're still not certain how long the benefit will be seen. Also, it must be noted that the change in therapy was delayed while waiting for testing results, and although that's not necessarily bad, it needs to be discussed."

Carl Grunfeld, MD, PhD, a Professor of Medicine at UCSF, noted that the controversy over metabolic change and fat redistribution was prevalent at the conference. To help elucidate reasons for the ongoing debate, Grunfeld discussed conference presentations on pharmacokinetic interaction between protease inhibitors and selected HMG-COA reductase inhibitors, also known as "statins"; clinical factors related to the severity of fat redistribution in the HIV Outpatient Study; and cardiovascular disease and HIV.

"The take-home message was, 'Be careful which statin you use,'" Grunfeld said. "Statin toxicity is thought to be related to plasma levels, so if you are on a protease inhibitor, and treating low density lipoprotein with a statin, atorvastatin or fluvastatin should be

used. It is very important to treat people with HIV who have very high cholesterol or risk factors such as hypertension, smoking, or diabetes, but that doesn't mean you need to rush out and treat everyone. Those who don't have very high cholesterol or risk factors like hypertension should be treated in the same way as someone who is HIV negative."

Moving the forum into the realm of AIDS vaccines, **John Curd, MD**, Senior Vice President at VaxGen, discussed the current state of AIDS preventative vaccine research. "The clinical vaccine effort is really in its early stages," Curd said. "For now, the primary endpoint for an AIDS vaccine is sterilizing immunity, a high bar for the first successful HIV preventative vaccine. The FDA is very supportive of vaccine development and may consider additional endpoints in the future based on the evolving body of information relating to the importance of the 'set point' and measurements of viral burden."

Ben Cheng, MS, Assistant Director of Information and Advocacy at Project Inform, wrapped up the forum with a presentation on Hepatitis C (HCV) and HIV co-infection. Approximately one in every 65 people in the U.S. is infected with HCV. Further, between 50% and 90% of injecting drug users with HIV are co-infected with HCV, as are 4-8% of gay men. "Right now," said Cheng, "there is very little data on treating co-infected individuals, and there was, disturbingly, very little information presented on HCV and co-infection at the conference."

Cheng went on to review what is known about co-infection, emphasizing that cirrhosis is more severe and frequent in co-infected individuals and that HCV levels tend to be higher as well. He also noted that in one study, "protease inhibitors appear to be protective against fibrosis." Cheng also drew attention to the often overlooked statistics on African Americans and HCV. Compared with Caucasians, African Americans have higher rates of liver cell cancer and hepatitis C infection; have lower response rates to interferon monotherapy and to interferon plus ribavirin; and are more likely to be infected with genotype 1. "Why this is the case is not yet known," Cheng said. "The NIH held a meeting on this issue, but no one can yet explain why African Americans have such an abysmal response to these drugs."

By the evening's end, it was clear that Coates's opening remarks had proved prescient. "Nowhere," he had noted, "is the field of learning more rapid than in the field of HIV."

The forum, which was broadcast live on the Internet, can be heard at <http://www.webcastreporter.com/aidsupdate/>.

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The Center has been instrumental in establishing and managing these Core Labs. The growth has been significant: staffing in the Virology and the Immunology Labs has grown from three to 20 since 1996. The Core Labs have supported a large number of AIDS clinical trials and many UCSF investigations, such as the Options Project, Women's Interagency HIV Study, AIDS Pediatric GCRC studies, several AIDS Clinical Trials Group studies, and a study involving total lymphoid irradiation in the setting of HIV disease. The Core Labs are themselves supported by a growing number of NIH grants. "The Core Labs are crucial to our ability to conduct patient-oriented HIV and AIDS research at UCSF," said McCune.

The Center has provided the Core Labs with both the equipment and the funding necessary to quantitatively analyze clinical and laboratory data, and to develop novel assays to assess the value of both traditional and alternative medical regimens in AIDS therapies. "Traditional physicians need labs like the Core Labs nearby to interact with and discuss clinical observations. Basic science labs cannot do this," said Grant.

Although upon initial observation the development of novel assays and the quantitative analysis of clinical and laboratory data may appear less exciting than the discoveries of basic research laboratories, the excitement for the Core Lab researchers is the direct clinical relevance of their findings. "These results can and have changed the shape of AIDS treatment worldwide," said Grant.

A good example of how equipment can make a difference is the Center's support of the purchase the Affymetrix equipment needed for the analysis of high density probe assays. Four years ago, the Center granted \$35,000 to the Virology and Genomics Labs to help purchase this important piece of equipment. This enabled the implementation of virology assays for HIV-1 drug resistance that were previously unavailable at UCSF, and created the infrastructure necessary for functional genomics studies. This equipment was used by the Virology Core to identify the first case of sexual transmission of multi-drug resistant HIV-1, which led to studies of primary drug resistance throughout the world. It was also used to assess primary drug resistance in the HIVNET vaccine trials network, to identify trends in drug resistance in San Francisco, and to detect the high prevalence of virologic failure of protease inhibitor-containing regimens in clinical practice.

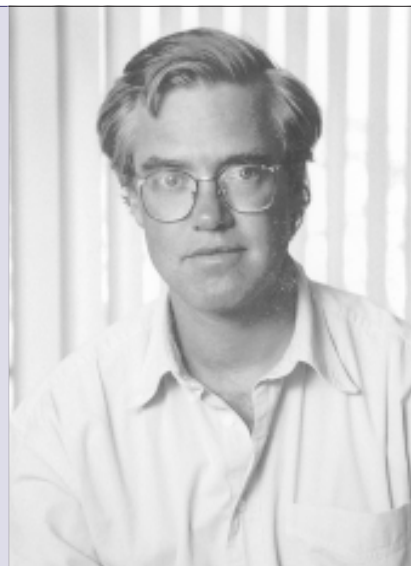
The Immunology Core has also been instrumental in assisting UCSF investigators to pursue a number of important questions about HIV disease and treatment. Ongoing studies have evaluated effective

immune responses against opportunistic agents; the contribution of the thymus towards facilitating immune reconstitution in late-stage patients; the pathogenic role of T-cell regeneration in HIV disease; patients who do not respond to potent antiviral therapy but who nonetheless sustain their CD4 counts; treatment of neurologic disease in patients with HIV disease; and the development of an animal model for the virus that causes Kaposi's sarcoma. In perhaps its most significant contribution to date, the Immunology Core has developed a method to quantify antigen-specific CD4+ responses by cytokine flow cytometry, and has applied this method to the analysis of immune function in HIV positive individuals.

The Center has also been instrumental in facilitating closer interactions with the pharmaceutical and biotechnology industries. Early on, the University granted the Center permission to begin a pilot study to decentralize industry contracts and grants negotiating authority. **Joan Moyer Schwing**, Executive Director of the Center from 1995-1999, initiated the program with the help of several SFGH investigators. This pilot program was successful in decreasing contract turnaround time and increasing industry interactions, and has served as a model to implement the concept university-wide. The Center provides this service free of charge to all investigators at SFGH interested in working with industry to do clinical trials.

So, what does the future hold for the Center? "Current drug regimens are not working," said McCune. "The key to the future success of eradicating HIV is the development of successful vaccines." It is in this direction that the Center is moving. "We can use the Core Labs to help us understand which vaccines are most likely to work," said McCune. The Center is helping ARI work toward the establishment of a Vaccine Center at UCSF. The Bay Area is uniquely suited to drive this challenge given its current infrastructure. It has the ARI, the largest institution outside of the National Institutes of Health dedicated to HIV research; a large activist community and patient population that supports novel research approaches and therapies; a strong biotechnology industry with several companies actively pursuing HIV vaccine programs; a state government that supports such research; and a strong and active City and County Department of Public Health very involved in the HIV pandemic.

Mark the date on your calendar – September 14 – for this year's Macy's Passport event. Be part of the excitement of fashion theatre and know that it is helping pave the way for breakthrough research.



Dr. Joseph "Mike" McCune

An Entrepreneurial Spirit

In the early 1990's, Mike McCune envisioned the Center for Creative Therapies while still at SyStemix, a biotechnology company he helped found. Frustrated with the way clinical trials were then being done in academia, he envisioned a better way that they could be done if the proper infrastructure was in place. With McCune's enthusiasm and the support of **Dr. Merle Sande**, then Chief of Medicine at San Francisco General Hospital (SFGH), they enlisted the help of three other investigators at SFGH, **Drs. Warner Greene, Morrie Schambelan, and Paul Volberding**. This group was instrumental in the Center's establishment, becoming the first example of one of the Center's major goals: to bring together researchers at UCSF and to maximize limited resources by sharing core functions without stifling investigator entrepreneurial spirit. The group proposed the concept of the Center to the Macy's Passport team, as well as to the biotechnology industry. Both greeted the concept with great enthusiasm. Macy's Passport provided a crucial missing piece: the financial support to seed the project. **Dean Haile Debas** said, "Without Macy's partnership, UCSF could not have launched this additional avenue of attack on the AIDS virus." Macy's West Chairman and CEO **Michael Steinberg** and the Passport Team were recognized on World AIDS Day with ARI's Visionary Leadership Award (see Development News, page 7).

The Center is currently managed by the Clinical Advisory Board, Drs. Courtney Broaddus, Warner Greene, Jim Kahn, Talmadge King, Mike McCune, Morrie Schambelan, and Paul Volberding. All seven are investigators at San Francisco General Hospital.

Family Affair

by Mark Kelleher

It's not unusual for UCSF faculty members to contribute to programs that are important to them while they are actively involved with the University. A decade after leaving UCSF and the Bay Area, **Dr. Robert Stempel** and his family continue to support the HIV health, prevention, and outreach programs that are part of the UCSF AIDS Research Institute. Bob's commitment to UCSF remains even though he left the area to take a faculty position in the Department of Public Health at Florida International University, where he continues to pursue interests including HIV health research and prevention. He also helps to manage the **Ernest E. Stempel Foundation**, named for his father.

Stempel never lost track of his friends at UCSF, chief among them **Drs. Paul Volberding, Tom Coates, and Dennis Osmond**. That bond and Bob's appreciation for both his formative experience at UCSF and the innovative progress pursued by UCSF in the fight against HIV disease inspire him to recommend that considerable funding from the Stempel Foundation and other sources be directed to critical HIV health information and prevention programs.

Bob Stempel and the Ernest Stempel Foundation have contributed, nearly from its inception, to the success and reach of UCSF's *HIV InSite* (<http://hivinsite.ucsf.edu>), which has grown to become the world's most accessed and broad-based HIV/AIDS web site, now logging about 3 million "hits" per month from users in 150 different countries. *HIV InSite* now attracts increasing corporate and foundation sponsorship, but Bob was on board during the critical start-up phase when funding was difficult to secure.

"I heard about HIV InSite while on a sabbatical at UCSF's Center for AIDS Prevention Studies several years ago," explains Stempel. "I was impressed with the comprehensive 'one-stop' concept, the very attractive user-friendly layout, and the energy of the staff working on the project. I have found myself using the site regularly, as well as recommending it to my students and colleagues. Even now there's nothing like it on the web, and it links to everything else. With all the challenges people face with HIV, securing useful information shouldn't be one of them. All the awards and support are well deserved by the clearly exceptional staff."

Recently, **Ernest Stempel** secured \$200,000 for international prevention outreach programs from the renowned **C.V. Starr Foundation**, of which he is a trustee. Under the leadership of UCSF's **Dr. George Rutherford**, the program is aimed at training scientists, public health officials, and workers from non-governmental

organizations in the developing world. This training will provide the skills to understand the nature of a community's behavioral trends and how to respond most pragmatically with tailored interventions designed to turn back the increasing rate of HIV infections.

The leadership of the AIDS Research Institute and its affiliated programs could not be more grateful to the Stempel family – and to their partners such as the Starr Foundation – for their continued vision and belief in the progress of HIV research, prevention, and treatment at UCSF.

Providian Gift Fulfills Children's Wishes

The **Providian Financial Corporation** presented a check for \$20,000 in December to the Pediatric HIV Quality of Life Gift Fund, a nonprofit program administered by the UCSF Pediatric AIDS Treatment Center, part of the AIDS Research Institute.

Established five years ago, the fund is dedicated to meeting the basic quality-of-life needs of the Center's patients and their families, many of whom live in poverty. Providian's gift, the largest single donation in the Center's history, ensures that patients will continue to receive gifts on their birthdays, school supplies, clothes, and other basic necessities that promote a sense of normalcy in their lives. The fund is also used to cover the cost of families' transportation to and from appointments, meals and hotel expenses for overnight stays, rent, utility bills, other expenses necessary to meet basic quality of life standards, as well as funeral expenses.

The \$20,000 gift was presented December 4 at the seventh annual party for the Pediatric AIDS Toy Drive. The party was held at Club Universe in San Francisco. This is the second year that Providian has donated to the fund.

"Providian's generous support has provided us with the freedom and ability we need to establish the fund as an ongoing program," said **Lynn Goldman**, Pediatric HIV Coordinator with the Center.

Diane Wara, MD, Director of the HIV Program at UCSF's Pediatric Immunology Division, added, "We have many wonderful donors who help us out especially during the holidays, and that is enormously important to our little patients. The advantage of a gift at this level is that we can guarantee our help and support of these families throughout the year. It allows us to plan ahead for special purchases, field trips, and family needs."



Special Assistant to the Mayor's HIV Committee Bill Barnes congratulates Leadership Award recipient Michael Steinberg and presents a proclamation from the Mayor

This proclamation from Mayor Willie L. Brown was presented to Michael Steinberg, recipient of ARI's Visionary Leadership Award

Whereas Macy's West, under the leadership of Chairman and Chief Executive Officer **Michael Steinberg**, has fulfilled a multi-year pledge of one million dollars to the UCSF AIDS Research Institute, and

Whereas the Macy's Center for Creative Therapies was created five years ago with these initial resources made possible through the generosity of Macy's West, and

Whereas Macy's West took a stand before it was popular to do so and actively encouraged their vendors to join them in an innovative partnership in the fight against HIV/AIDS, and

Whereas the Macy's Center has helped make the resources and staffing for both the Core Virology and Immunology Laboratories top priorities for the AIDS Research Institute and the University, and

Whereas the Macy's Center for Creative Therapies has promoted interactions and collaborations between AIDS investigators at UCSF, and

Whereas this focus has enabled the core labs to develop new clinical trials aimed at understanding HIV disease and treatment, and

Whereas Michael Steinberg and Macy's West have sustained their support and continue to demonstrate their unwavering commitment to finding a cure and a vaccine for HIV disease for San Franciscans and for the world,

Therefore, in recognition of the leadership and vision of Michael Steinberg and Macy's West and in recognition of the significant resources they have committed to the care of those infected and affected by HIV, and to research to find a cure, **I, Willie L. Brown, Jr., Mayor of San Francisco, do hereby declare Thursday, December 2, 1999 Michael Steinberg and Macy's West Day in San Francisco.**

Dr. Jeff Harris Named Steinberg Fellow

Dr. Mike McCune introduced the Michael Steinberg Fellowship at the ARI World AIDS Day Dinner with these remarks:

"As you all know, the epidemic is still with us. Across the world, more people – not fewer – are infected each day. Looking ahead to the future, we need to stop this spread. The only way to do that is with an effective vaccine. Given the resources that have been provided by Macy's West, we are now in a position to test candidate vaccines and to understand which ones work and which ones don't. This, in my mind, is the mission today.

To signify the importance of this goal – and to honor the vision of Mr. Steinberg – UCSF has created the Michael Steinberg Fellowship. The intent of this significant award is to create opportunities for talented and visionary young scientists. The first recipient of this fellowship is here tonight: **Jeff Harris**. Dr. Harris is an MD with a PhD who is also a specialist in the pediatric immune system. Working with the support of Macy's West, he will now be squarely focusing on HIV vaccine work. Nothing could be more important – and this work could not go forward without Macy's. We hope now to expand it further and to search also for effective vaccines against other major diseases affecting millions around the world, including tuberculosis, malaria, and cancer.

For this and for all of their years of tireless work in fighting the epidemic and helping those affected by it, please join me in honoring and thanking **Michael Steinberg** and Macy's West with the Visionary Leadership Award."



Dr. Mike McCune, Passport Producer Larry Hashbarger, Michael Steinberg, Betty Krogh, Vice President of Macy's West Public Relations, and Steinberg Fellowship recipient Dr. Jeff Harris (L-R) at the ARI's World AIDS Day Dinner

World AIDS Day Symposium

By Sue Rochman

The last World AIDS Day of the 20th century was filled with ceremonies, rallies, and programs that both celebrated the strides that have been made in AIDS research and mourned the ongoing devastation and loss AIDS has wrought.

The AIDS Research Institute (ARI) marked the day with its Third Annual World AIDS Day Symposium. Hundreds of researchers, students, and community members turned out to honor the contributions the ARI has made to the fight against AIDS and to discuss the question posed by the symposium's theme, "How Do We Prevent the Second HIV Epidemic?"

Throughout the day, speakers underscored the ARI's commitment to fund the research needed to end the AIDS epidemic. "We will be here every year until HIV goes the way of smallpox," ARI Director **Thomas J. Coates, PhD**, told a packed Cole Hall audience. "We will be here until scientists are deciding in Geneva what to do with that very last vial of HIV."

Many speakers, including Congresswoman **Nancy Pelosi**, who has a 12-year history of pushing AIDS funding to the forefront of the national budget debate, emphasized the role advocates and researchers have played in changing the nation's response to HIV. "Where we have ignored the science, as we have with needle exchange, it has cost us lives," said Pelosi. "But never forget that it is the outside demanding and persisting that makes the difference in the funding decisions Congress makes."



Congresswoman Nancy Pelosi

Robert Grant, MD, MPH, Director of the Gladstone/UCSF Laboratory of Clinical Virology, kicked off the symposium's topical presentations. In his presentation entitled "The Spread of Drug-Resistant HIV-1," Grant emphasized that "even though drug resistance is common, it doesn't mean that patients who have some drug resistance will become ill." He noted that studies have found that people with HIV still have a partial response even after resistance occurs, and emphasized the need for further studies on the potential decrease in infectiousness – and therefore decreased trans-

mission – in individuals who have only a partial response to anti-viral drugs.

To increase awareness of the city's Post-Exposure Prevention (PEP) program, **Michelle Roland, MD**, Assistant Professor of Medicine in the UCSF Positive Health Program at San Francisco General Hospital, discussed the PEP feasibility study begun in October 1997 by the UCSF Center for AIDS Prevention Studies, the San Francisco Department of Public Health (SFPDH), and the UCSF Positive Health Program.

Preliminary findings show that 80% of the 401 patients completed the PEP regimen, although nearly 20% missed at least one dose of their medication. Most who have sought PEP have been young men who had a sexual exposure to HIV. "We found that the majority of those who sought PEP were usually having protected sex," said Roland. "This is important because PEP's risk-reduction counseling would require a different approach if the individuals were engaging in ongoing risky behavior."

San Francisco is the first city in the world to integrate a new HIV antibody test – the "detuned" ELISA – into its HIV surveillance program. In their presentation, "Detection of Recent HIV Infection," **Willi McFarland, MD, PhD**, Director of the HIV Seroepidemiology Unit at SFPDH, and **Kimberly Page-Shafer, PhD, MPH**, a researcher at the ARI's Center for AIDS Prevention Studies (CAPS), described how this new test will improve the City's prevention efforts.

The "detuned" ELISA detects not only whether an individual is HIV positive, but if that person seroconverted within the past four months. This gives researchers the ability to track information including current rates of transmission and new strains of HIV. But it's not only researchers who benefit.

"This information can help clients make treatment choices," explained McFarland. "Also, if someone knows when they were likely to have been exposed, it can help with partner notification efforts in terms of determining who should, and who need not be, contacted."

This test also provides researchers with information on where to direct current prevention efforts. "We've found that one-third of the individuals who test positive at our test sites are men who have sex with men (MSM) or MSM/injecting drug users who have been newly infected with HIV," said Page-Shafer. "This maximizes our prevention opportunities because we know that these aren't infections that happened ten years ago."

Cynthia Gómez, MEd, PhD, Assistant Professor at CAPS, re-emphasized the importance of knowing which communities are now being affected in her presentation, entitled “Retargeting HIV Prevention.”

“We don’t know the half of it in terms of what’s happening with our youth,” said Gómez. “We need frank discussions about sex, and we’re still not ready to have them.” Gómez also underscored the need for prevention efforts to include those already infected. “People with HIV have the social power to make a difference, and they are critical in the prevention equation,” she said. “They need to be engaged and they need to be the leaders—because they are the only ones who know what this about.”

Mike Shriver reinforced Gómez’s key points with his presentation, “Making Prevention Work for HIV Positive Individuals,” and acknowledged HIV positive individuals who made groundbreaking contributions to the fight against AIDS.

“It’s time to give power back to those who are HIV positive,” said Shriver, Co-director for Community Initiatives at ARI’s AIDS Policy Research Center. “We need programs that will give HIV positive individuals the ability to have a healthy, long, sexually safe life.”



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Former Congressman **Ronald Dellums** brought the symposium to a close with his talk, “A Marshall Plan to Save Africa from HIV.” Dellums’s provocative speech emphasized this country’s moral responsibility to look beyond its own borders and to fund the programs needed to address the ravages of AIDS worldwide.

His final call to action brought the crowd to its feet. “It is activists who change the world,” said Dellums, “and our activism must go beyond our borders. How can you whisper about 11 million deaths? That’s why I’m talking loud.”

*“I am a political activist,
and I see myself as a
citizen of the world —
and I am willing to
accept the responsibility
that that brings.”*

— Former Congressman
Ronald Dellums

CAPS’s Peru C-POL Project

Daniel T. Halperin, PhD

As part of the National Institute of Mental Health Collaborative HIV/STD Prevention Trial, a five-country randomized community intervention study, the ARI’s Center for AIDS Prevention Studies (CAPS) is partnered with Cayetano Heredia University in Lima, Peru, recognized as having one of the leading Schools of Public Health in Latin America. The project PIs are **Dr. Thomas Coates**, Director of CAPS, and **Dr. Carlos Cáceres**, previously a scholar in the UCSF/CAPS/UC Berkeley Fogarty Program, who has recently joined the UCSF School of Medicine faculty. The other countries involved in the trial are Uganda, paired with **Dr. Maria Wawer’s** Rakai Group at Columbia University; India, with **Dr. David Celentano** and company from Johns Hopkins; Russia, with **Dr. Jeff Kelly’s** group at the Medical College of Wisconsin; and China, with **Dr. Mary Jane Rotheram** and others from UCLA.

Instead of utilizing an intervention model primarily based on promoting individual behavior change, the study will employ a “Community Popular Opinion Leader” (C-POL) approach, as developed by Jeff Kelly among men who have sex with men (MSM) in small towns in the U.S. (*Lancet* 1997;350:1500-5)

Although the five-year multi-site study will develop a cohesively unified protocol, each country’s intervention will be tailored to the local cultural, HIV/STD prevalence, socio-economic, and other demographic characteristics. In Peru, the focus will be on young people (ages approximately 18-30), both heterosexual and MSM, who live in the poorer *barrios*, or neighborhoods, of three cities: Lima, Trujillo, and Chiclayo. The project’s ethnographic team, directed by **Dr. Philippe Bourgois**, Chair of the UCSF Program in Medical Anthropology; **Dr. Daniel Halperin**, Assistant Professor at UCSF’s CAPS and Medical Anthropology Program; and their Peruvian anthropologist counterparts, **Maria Rosa Garate** and **Ximena Salazar**, are currently in the process of identifying 30 *barrios*, from which ten intervention and ten comparison venues will then be selected and randomized. Eight of these sites (containing roughly 1000 inhabitants each, about a fifth of them in the 18-30 age range) will be in Lima and six each in the other two cities.

During the current year, the project’s focus is on conducting the ethnographic research and a pre-baseline assessment of STD/HIV prevalence along with a risk-behavior questionnaire, the latter surveys co-directed by **Dr. Jeff Klausner**, Director of the San Francisco City STD Clinic/Department of Public Health. The ethnographic work involves extensive social mapping of potential *barrios*, structured observational analysis, key informant interviews,

and focus groups with young people, in order to identify potential public opinion leaders, appropriate risk behaviors to address, and adequate norm change messages; and to ground the intervention in local socio-cultural contexts.

In succeeding years, a pilot intervention study will precede the larger intervention, under the leadership of the PIs and the rest of the local Peruvian research team, as well as CAPS's **Dr. Susan Kegeles**, who has extensive experience developing community empowerment programs among young MSM in the U.S. Outcome measures will include both behavioral/contextual variables and biological data (various STDs, HIV, and probably unintended pregnancies). The C-POL intervention will include the following elements: motivation and involvement of community stakeholders, selection of a Youth Advisory Board, recruitment and training of the C-POLs (numbering about 15% of the target population, or approximately 30 C-POLs in each intervention *barrio*), development and testing of program messages, as well as a rigorous, multidisciplinary assessment of the evolving intervention. The study's findings will inform prevention efforts in similar settings in Latin America and other developing regions.

Daniel Halperin, PhD, is Assistant Professor with UCSF's Center for AIDS Prevention Studies, Community Health Systems, and Medical Anthropology Program.

Fem-to-Fem: First U.S. Study of Its Kind

The ARI's Center for AIDS Prevention Studies is joining forces with the Centers for Disease Control and Prevention (CDC), Yale University, Montifiore Medical Center, and Whitman Walker Clinic in Washington, DC, to conduct a study with HIV infected women who have sex with women (WSW). The purpose of the Fem-to-Fem Study is to identify possible cases of female-to-female transmission of HIV and to gather information about the sexual behavior and HIV prevention practices of WSW.

Although there have been several documented cases of female-to-female transmission of HIV, there have been no systematic studies to document transmission between women or to describe the sexual and drug-using behaviors of HIV infected WSW. There are few guidelines for WSW about how to protect themselves or their partners from HIV infection. It

is hoped that this study – the first to address these issues – will lead to increased awareness and more information for women.

Cynthia A. Gómez, PhD, is the Principal Investigator in San Francisco, and is assisted by **Sheri Storey**, Project Coordinator, and the project staff: **Kate Giessler, Karen Vernon, Stacey Hopper, Erin Rowley, and Anita Mathew**. The goal in San Francisco is to interview 75 HIV positive WSW and their eligible partners. For more information, please call the study hotline at 1-888-609-5367.

Bay Men to Forge New Prevention Path

In March, the ARI's Center for AIDS Prevention Studies began forging a new path in HIV prevention with the launch of Bay Men, a program designed for HIV positive gay and bisexual men in the Bay Area. The goal of the CDC-funded program is to help reduce sexual risk-taking among HIV positive men. Additionally, Bay Men provides the opportunity for HIV positive men to meet other men living with HIV and discuss sex, dating, health, and other issues that may impact their lives.

The Principal Investigator of this study is **Dr. Cynthia A. Gómez**. The study is also taking place in New York City, with **Dr. Jeff Parsons** from New Jersey State University overseeing that site.

Bay Men is one of the first interventions to target prevention strategies directly toward individuals who have already tested positive for HIV. Dr. Gómez has assembled an energetic, focused, and dedicated team to ensure the program's success. In addition, a 15-member Community Advisory Board consisting of HIV positive gay and bisexual men has been closely assisting the research team in all phases of the program's development.

Bay Men is designed so that two-thirds of the participants will be gay and bisexual men of color, which will help fill a great gap in both the scientific and community program fields. Bay Men is the intervention that emerged from a two-year formative research study, commonly known as the Seropositive Urban Men's Study, also conducted by Dr. Gómez.

Thank you for your generosity

The UCSF AIDS Research Institute depends upon the support of non-governmental organizations and individuals to develop breakthrough projects, foster innovative collaborations, support young scientists, and offer community forums and symposia. The listing below represents corporate and foundation gifts received from July 1 through December 31, 1999. We will list our individual donors in the Summer 2000 issue. We are grateful for support at all levels and encourage you to contact us for more information on making a contribution to our programs.

Please contact Debra Kent, Director of Community Relations, at (415) 597-9370 or dkent@psg.ucsf.edu for more information on how you can become involved with ARI.

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Retraction and Clarification

Please note that in the last *ARI Newsletter*, it was implied that scientists connected with the UCSF Macy's Center for Creative Therapies directly observed distinctive CD4 immune responses in monkeys that would likely lead to therapeutic solutions for humans infected with HIV.

This implication by the writer, made without proper verification, was faulty and premature. Please note that there are *no* direct non-human primate studies which have directly evaluated the relationship between thymic production and SIV pathogenesis conducted by any known scientist associated with the Macy's Center or UCSF in general, including the faculty named in the article: Drs. Mike McCune, Steve Deeks, Mark Jacobson, and Robert Halvorsen.

Further, the studies conducted at the Macy's Center observing human thymic reconstitution in some HIV positive individuals are of an incremental nature. Contrary to the assertion in the previous article, there has been no "breakthrough," and there are not as yet any clinical applications.

Where there has been observational and theoretical progress is with the human studies not involving simian observations. From this research it is speculated – but not yet proven – that the apparent and known resistance of the sooty mangabey monkey to CD4 depletion after SIV infection may be related to the inability of SIV to infect the thymus of this particular species, in contrast to the severe CD4 depletion experienced by infected humans.

Functioning thymic tissue appears to be destroyed in humans by the last stages of HIV disease. In recent work carried out by **Drs. Marc Hellerstein and Mike McCune**, it was noted that treatment with HAART (aka, combination therapy) leads to decreased viral replication and to increased levels of new T-cell production.

In recent work by **Drs. Cheryl Stoddart, Mike McCune, Steven Deeks, and Robert Grant**, it appears that some variants of the HIV virus are able to infect mature CD4 cells but not those in the thymus. These virus types are also associated with continued high levels of T-cells in the patients who carry them, suggesting that CD4 levels will remain intact as long as the thymus is functional.

With continued generous funding from essential private donors like Macy's West, these ongoing studies may one day lead to future insights about how the immune system works. These developments *may* eventually be instructive in the design and development of new vaccines for the prevention or therapy of HIV disease.

Upcoming meetings

3rd Annual Retreat of UARP-supported C-ARCs

May 7-9, 2000

Lowes Coronado Beach Resort Hotel,
San Diego

Contact: Suzi Hedberg at 415-476-8482 or
hedbergs@dentistry.ucsf.edu

International AIDS Candlelight Memorial: "Break the Silence: Honor Every Death, Value Every Life"

May 21, 2000

Sponsor: Global Health Council

Contact: Meggan Cote at
mcote@globalhealth.org or 202-833-5900

XIII International AIDS Conference: "Break the Silence"

July 9-14, 2000

Durban, South Africa

Information: Congrex Sweden AB
AIDS 2000

P.O. Box 5619

Linnégatan 89A

SE-114 86 Stockholm, Sweden

Tel: +46 8 459 6600

Fax: +46 8 661 8155

Email: aids2000@congrex.se

<http://www.aids2000.com>

The Conant Foundation and the UCSF AIDS Research Institute, in collaboration with Project Inform, will be sponsoring a free **Community Forum and Report Back** after the International AIDS Conference Tuesday, July 25, 2000. Consult the ARI website after June 1 for details: <http://hivinsite.ucsf.edu/ari> or call the Conant Foundation at 415-643-1822.

Gay Men's Health Summit 2000

July 19-23, 2000

Boulder, Colorado

Registration and housing information:
www.bcap.org or 303-444-6121

2nd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

September 13-15, 2000

Westin Prince, Toronto

Information: [http://www.intmedpress.com/
lipodystrophy](http://www.intmedpress.com/lipodystrophy).

40th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)

September 17-20, 2000

Metro Toronto Convention Centre

Sponsor: American Society for Microbiology

Information: 202-737-3600 or

Meetingsinfo@asmusa.org

www.asmusa.org/mtgsrc/40icaac.htm

Third National Harm Reduction Conference: "Communities Respond to Drug Related AIDS, Hepatitis, Prison, Overdose, and Beyond"

October 21-25, 2000

Wyndham Hotel Miami-Biscayne Bay, Florida

Sponsor: Harm Reduction Coalition

Information: 212-213-6376; fax 212-213-6582

COUNTDOWN TO DURBAN

Please plan to join us as Tom Coates and the ARI host a *braai* (South African barbecue) on **July 8th** from 4:00 pm to 7:00 pm to welcome everyone to the International AIDS Conference. This will be at the La Montagne Apartments, 30 minutes from the conference site.

See this issue's *Inside Track* for further information relevant to ARI researchers planning to present and/or attend the International AIDS Conference. (Call Dave Robb at 415-597-9203 if you need a copy of *Inside Track*.)

UCSF AIDS Research Institute

74 New Montgomery Street, Suite 600
San Francisco, CA 94105

Save the Date!

The Conant Foundation and the
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to be held Tuesday

July 25

You will be mailed further information as
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