Remembering Alfred Gellhorn, MD

ADARC Director Alfred Gellhorn, a distinguished physician and health care policymaker, died March 24 at age 94. Dr. Gellhorn was a pioneer in oncology at Columbia University, Dean of the University of Pennsylvania School of Medicine, and founding Director of the Sophie Davis School of Biomedical Education of the City University of New York, as well as of the Gateway Institute in New York's public schools.

"Alfred was a giant in American medicine, and we were very fortunate to have him on our Board for most of ADARC's existence. He will be deeply missed," said Dr. David Ho. He was also a board member of the Aaron Diamond Foundation and advisor to the Irene Diamond Fund.

Dr. Gellhorn was known for instilling a sense of social mission into medicine. At the University of Pennsylvania and CUNY, he worked to attract minority and women physicians by recruiting in underserved neighborhoods, and encouraged them to return to serve those communities. He passionately supported the Gateway Institute for Pre-College Education, which in partnership with New York City's public schools prepares disadvantaged youth for careers in science.

Dr. Gellhorn joined ADARC's Board in 1992, recruited by close friend Irene Diamond. He was an active and involved Director, getting to know ADARC's scientists and the projects pursued by their labs. He also proposed Dr. David Ho's successful nomination to membership in the National Academy of Sciences' Institute of Medicine.

New York City continued from page 1
among City residents, and the second most common among those between the ages of 35–44. The epidemic hits hardest among minorities: 81% of new diagnoses and deaths are among African-Americans and Hispanics. Today, one in six black men between 40–49 in Manhattan has been diagnosed with HIV or AIDS.

Alarmingly, recent data show HIV infections are increasing among young gay men in the City: diagnoses have increased by about one-third in those under age 30 and almost doubled in those ages 13–19 over the last six years. Dr. Frieden warns: "We're headed in the wrong direction. Unless young men reduce their number of partners, and protect themselves and their partners by using condoms more consistently, we will face another wave of suffering and death from HIV and AIDS."

The DOHMH runs comprehensive prevention, testing, and treatment programs, but too many of those infected have not been tested, according to Commissioner Frieden. Those people unknowingly infect others, and often learn they are HIV-positive when already sick with AIDS (about 1,000 patients a year). The City encourages all health care practitioners to offer HIV tests as part of routine medical care. In addition, New Yorkers over age 12 can get tested at 10 confidential clinics provided by the Department of Health in all five boroughs. These clinics offer rapid testing, as well as counseling and treatment. HIV tests are also available through the City's public hospitals.

Since 1971, the City has distributed free condoms, initially to STD clinics, and subsequently to HIV/AIDS service organizations and community groups. In 2007, in an unprecedented effort, the City launched the NYC Condom campaign, featuring an eye-catching condom package inspired by the MTA symbols. Soon, the City was distributing over three million condoms a month. In 2008, the NYC Condom was given a new design by industrial designer Yves Béhar. NYC Condoms are available in bars, restaurants, community service agencies and STD clinics.

For information about NYC testing sites visit:
http://www.nyc.gov/html/doh/html/std/std2.shtml

Markowitz continued from page 2
At ADARC, Dr. Markowitz continues to focus on development of therapeutic alternatives. "The average HIV infected patient is in his or her mid-30s. Lifelong treatment means over 35 years of drug taking. That is not an acceptable treatment paradigm. We should be striving for something better than lifelong daily therapy."

An important unanswered question is whether viral replication continues despite apparently highly suppressive therapy. Dr. Markowitz and his colleagues are comparing the results of a five-drug regimen to standard three-drug therapy in acute infection cases. They also study the effects of intensified treatment regimens on levels of T cell activation and virus expression in tissues of well treated patients. These critical studies will provide better understanding of obstacles to achieving durable virologic remission in patients infected with HIV. Another study underway in Dr. Markowitz's lab investigates the effects of aggressive treatment early in the infection to boost the immune system, then removing treatment. The hope is the body may be able to keep HIV in a form of remission—not a cure, but patients would be able to live healthy lives without constant drug taking. Dr. Markowitz believes patients with treated acute infection may be most likely to benefit from immune-based approaches, as their immune systems are less damaged compared to individuals infected for prolonged periods before treatment.

HIV remains one of the most formidable pathogens, both for scientists in the lab and health care providers in the clinic. Dr. Markowitz, a physician and a scientist, has a passionate and continuing commitment to understanding how innovative treatments can enable HIV infected patients to live longer, healthier lives.

Bieniasz continued from page 3
Dr. Bieniasz also researches extinct retroviruses carried in the human genome—which occupy almost 10% of human DNA—shedding light on evolutionary processes that have enabled mankind to overcome epidemics of viruses related to HIV that devastated human populations in the past.

"Previously you got infected by a retrovirus and you keeled over and died, or you survived —nobody could make much sense of it," he observes. "But we, the descendants of the survivors of countless prehistoric epidemics, evolved remarkably sophisticated defenses against these ancient retroviruses. That would have happened only if their impact had been quite severe. Epidemics came and went, and in their fossil record—recorded in man's own DNA—may lie insights that will help us defeat AIDS."

Microbicides continued from page 3
texture, and whether products can be used discreetly, without the male partner's knowledge. A large share of the market for microbicides is in developing countries, so products must also be affordable, and accessible to rural populations.

Dr. Cheng-Mayer says that the challenges involved in developing and testing microbicides are unique. "As a bench scientist, you worry about the science. You don't usually have to worry about how people will feel about a certain product." She has collaborated not only with pharmacologists, but also with sociologists and psychologists. "Microbicide research puts you back in the real world," she says.

Once an effective product is identified and tested, many other professionals will get involved in packaging, marketing and distribution. But ultimately, women will be responsible for using these products. "That is key," says Dr. Cheng-Mayer. "Studies have shown that once women are educated, they will do what is necessary to better and protect themselves."

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You Can Help ADARC's Scientists Fight HIV/AIDS

Private giving is vital to the Center's research mission, allowing rapid exploration of new ideas that have not yet attracted government funding. As costs rise and the pace of science increases, ADARC counts on your support to sustain the research environment critical to new discovery. Your contribution is an investment in the people and promise of ADARC.

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ADARC

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David D. Ho, MD
Director and CEO

Dear Friend,

Welcome to the first issue of ADARC, news from The Aaron Diamond AIDS Research Center. I am thrilled we now have a forum to share scientific progress from ADARC's labs, as well as developments and ideas about the HIV/AIDS epidemic.

ADARC was established by Irene Diamond in 1991 in response to the AIDS crisis that had taken a devastating toll in New York City. Since then, AIDS has become a global pandemic and over 30 million people are infected with the virus worldwide. In the United States and other developed nations, people with HIV can now live long and productive lives due to treatment breakthroughs that took place right here at ADARC. But the epidemic is far from over, and in fact continues to grow.

Today our scientists—75 professionals comprising the largest private center dedicated to HIV research—continue the battle with a two-pronged approach. First, we research the virus' basic biology, to gain understanding of how it operates at the molecular level and develop strategies to combat transmission. In this issue, you will learn about an exciting recent discovery by Dr. Paul Bieniasz of a mechanism that inhibits HIV from spreading, which could open a family of new therapies.

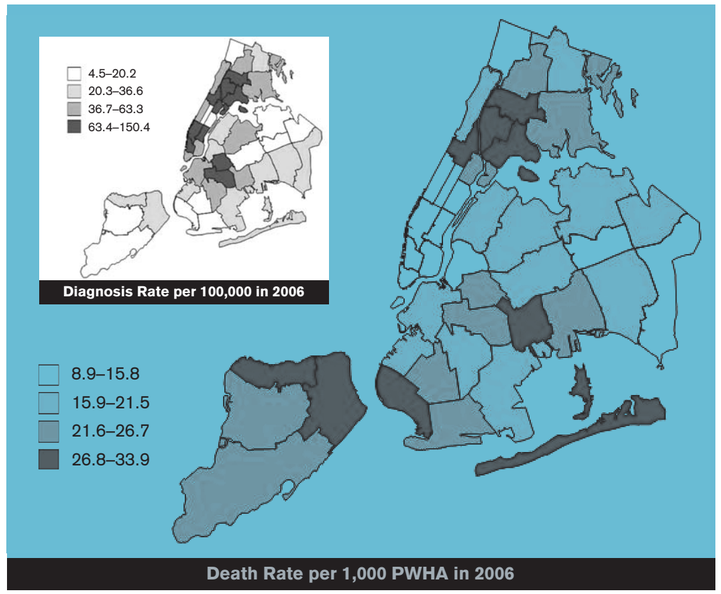
Our second focus is translational research: the application of laboratory discoveries to patient treatment. Dr. Martin Markowitz, featured inside, is ADARC's Clinical Director and Professor of Clinical Research and Investigation. His lab conducts paradigm changing research with potential to directly benefit millions of people undergoing treatment for HIV.

In future issues of ADARC we will introduce other scientists behind the breakthroughs—our team of exceptionally talented and dedicated faculty who make ADARC stand out in the field. I believe you will be inspired by their passion and commitment.

The scientific world has been trying to understand and stop HIV/AIDS for over 25 years, and the virus continues to be a formidable adversary. Here at ADARC, we are committed to this fight for the long run. Through this newsletter I hope we can start a dialogue, by sharing our progress in the lab and inviting your comments and questions. Please join us in this conversation.

Sincerely,

David D. Ho



Neighborhoods with highest diagnosis rates also have the highest death rates, with the exception of parts of Manhattan.

HIV/AIDS in New York City

When HIV/AIDS was identified in the early 1980s, New York was harder hit than almost any other city. By 1995, over 50,000 had died of AIDS-related illnesses in the City. The Aaron Diamond AIDS Research Center was created in 1991 as a partnership between Irene Diamond and the City in response to the epidemic's dramatic toll. At ADARC's opening ceremony, Mayor David Dinkins declared the Center was "an act of faith in our ability to end this epidemic through creative, hard work." Since then, ADARC has maintained a close relationship with New York City's Department of Health and Mental Hygiene. The current Commissioner, Dr. Thomas Frieden, is a member of ADARC's board.

HIV/AIDS is still very much a problem in New York, which remains the epidemic's epicenter in the United States. Over 100,000 New Yorkers are living with HIV, the highest number of cases in the country. AIDS is the seventh most common cause of death

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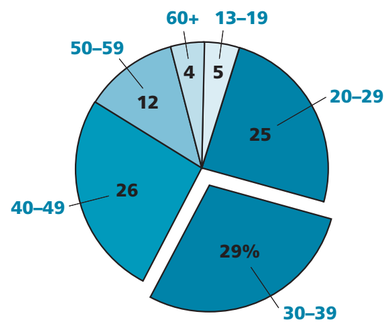
Age at HIV Diagnosis



"In the United States, the average age of a person diagnosed with HIV is 35. It is a young person's disease. Though antiretrovirals have significantly extended life expectancy, treatment is forever. So in most cases we face 30–40 years of drugs, with all the issues of cost and side effects they bring. We have to keep searching for something better. Better drugs, easier regimens, fewer side effects. Maybe even a novel treatment that would put HIV into a form of remission, allowing patients to live healthy lives without medication."

Martin Markowitz, MD

See article on page 2

A *Identified a molecule that serves as a central gateway for HIV's entry into CD4 cells.*

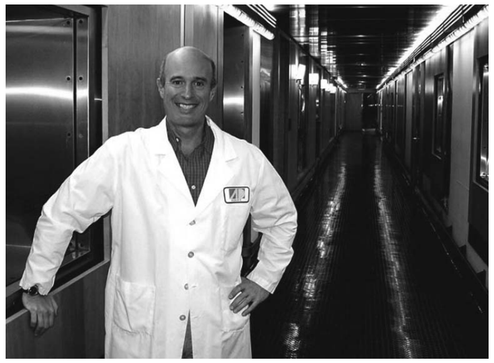
D *Introduced antiretroviral combination drug therapy that has saved millions of lives worldwide.*

A *Proved that HIV begins replicating at an unrelenting rate from the moment of infection, attacking the immune system if left untreated.*

R *Detected HIV in a 1959 blood sample, putting a time frame on the epidemic and providing new insights into the evolution of the virus.*

C

ADVANCING AIDS RESEARCH



Martin Markowitz on the Promise of HIV/AIDS Treatment

From the first reports of a mysterious new illness in 1981 until the introduction of effective antiretroviral therapy in 1996, a diagnosis of HIV/AIDS meant near certain death. Those years were characterized by loss and sorrow, compounded by stigma, fear and ignorance about what caused the illness and how it could be transmitted.

The scientific community mobilized to understand this new disease, and to treat thousands of suffering and dying patients for whom very little could be done. After HIV was identified as the virus that causes AIDS, many believed an effective vaccine, perhaps even a cure, would follow within a few years. Scientists soon learned HIV was like no virus previously encountered. Obstacles to rapid development of effective treatments and a vaccine became clear.

The landscape changed dramatically in the mid-90s with discovery of a treatment that became known as the "AIDS cocktail." Those drugs, used in combination, were able to contain viral replication, allowing the immune system to restore itself. HIV levels in patients' blood dropped dramatically, while CD4 T cells increased and the risk of life threatening opportunistic infections plummeted.

Suddenly, AIDS was not necessarily fatal. Patients felt better, resumed normal lives, and were able to contemplate a future that was previously unthinkable. Seemingly overnight HIV/AIDS became a chronic but treatable disease for those with access to medications.

Dr. Martin Markowitz, ADARC's Clinical Director, conducted one of the earliest breakthrough studies that demonstrated a combination of three drugs could control the virus. Principles of viral dynamics discovered by Drs. Ho and Markowitz at ADARC were the foundation for a 12 patient, three-drug study to test the limits of these potent new weapons in newly infected individuals.

"The 'cocktail' worked, but it was by no means easy to take," Dr. Markowitz recalls. The regimen included an intricate schedule of up to a dozen pills each day, some to be taken with food, some without. Side effects made the medications intolerable to some patients. Complete adherence was also essential for treatment to be safe and effective. "Patients had to be near-perfect pill takers."

Widespread hope that ARVs could permanently eliminate the virus was soon dashed when it became clear that HIV, though undetectable in the blood, remained hidden in the body, and roared back quickly if treatment stopped. "One of the downsides of treatment is that, for now, it is forever," says Dr. Markowitz. Still, at least where medicines are available, people with HIV can now live long and productive lives.

ARV treatment has improved tremendously, becoming more compact and easier to take. Many more drugs are available for combination, targeting HIV at different stages of its replication cycle. Doctors in the United States can currently choose from 25 drugs, with more in the pipeline. "Treatment-naïve patients can now take as few as one pill per day," notes Dr. Markowitz.

But in some patients the virus mutates, becoming resistant to the medication regimen. Treatment must then be modified. "When you get past first-line treatments, it gets more complicated," Dr. Markowitz says. Though newer drugs are tolerated better, pill burden, treatment complexity and side effects are continuing concerns.

ADARC's clinical program is strongly focused on acutely infected patients, preferably those infected within 120 days. Study participants are referred by their health care providers or sometimes self-refer.

"Acutely infected patients are very difficult to identify, but they represent the best case scenario for treatment. If we can change the treatment paradigm here, then perhaps we can work backwards, identify patients that may be treatable with finite courses of antiviral agents and adjunctive therapies."

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Photo: Allan Zepeda/AP, ©HHMI

Paul Bieniasz Named Howard Hughes Investigator

The Howard Hughes Medical Institute has named Paul Bieniasz, Associate Professor at ADARC and head of Rockefeller University's Laboratory of Retrovirology, an HHMI Investigator. The honor is awarded to approximately 50 of the nation's most creative and promising biomedical scientists every few years.

Dr. Bieniasz researches the basic building blocks of HIV, examining how the virus infiltrates host cells and replicates at the molecular level. It's intoxicating to think science might deliver a vaccine or cure that will banish AIDS to history, but Dr. Bieniasz knows such breakthroughs won't be possible without detailed understanding of HIV's life cycle.

"Understanding the biology of HIV is a very large and complicated problem. But our lab has made several key discoveries over the past few years. For example, we've defined a range of host molecules that are important for HIV assembly. We've also learned how some species are able to resist HIV infection."

"Essentially all medicine is built on a foundation of basic science. Our role is to understand as much as we can about how viruses replicate, which knowledge will provide the basis for new treatments and future interventions against HIV."

This year, using tools of molecular genetics, Dr. Bieniasz and his team made a startling new discovery, revealing the inhibitory effect of a protein they named "tetherin" for its ability to keep HIV particles tied to a host cell. Recently announced in *Nature*, this breakthrough could lead to a new suite of therapies.

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Microbicides: Empowering Women in HIV/AIDS Prevention

Microbicides are topical products that help prevent sexually transmitted diseases, including HIV. Deployed as vaginal creams, foams, gels, or rings, they can protect women from infection by imposing a physical barrier and/or killing the virus when applied before intercourse. Microbicide development has been identified as a public health priority, and there are currently several products in different stages of testing. However, a safe and effective microbicide is still a hope for the future.

Microbicides have the potential to revolutionize HIV prevention by giving women the power to protect themselves. In sub-Saharan Africa and other areas where the epidemic has taken a strong hold, women are the victims of a large share of new infections. Poverty in underdeveloped countries, partly caused by the HIV/AIDS epidemic, drives many women to work in the commercial sex industry in order to support themselves and their families. The feminization of HIV/AIDS has already had a brutal social impact.

Several biological factors make women more vulnerable to infection by HIV, and none of the currently recommended prevention methods—abstinence, monogamy, condoms—can be fully controlled by women. The advantages of an effective microbicide are clear. HIV is a formidable opponent, and the strategy against it should be as broad as possible. With a vaccine still many years in the future, microbicides would add a powerful prevention tool, saving millions of lives.

At ADARC, Dr. Cecilia Cheng-Mayer's lab is pioneering safety and efficacy testing of several microbicide candidates using experimental models, screening out products that are low performers and identifying those that show enhancement or protection against HIV infection. Some studies underway in collaboration with other researchers investigate therapeutic substances such as nucleocapsid and integrase inhibitors for microbicide use. As with oral ARV therapy, the potential for drug resistance exists, and scientists need to test several combinations of drugs.

The challenges in developing an efficient microbicide go well beyond the basic science. The ability to block or kill HIV is only a first step. The products need to be not only effective, but also safe and acceptable. Safety for frequent use, especially when reapplied before each sexual contact, is essential. Like condoms, microbicides are most effective when used consistently and properly. Importantly, women must be willing to embrace their use. Issues include method of application,

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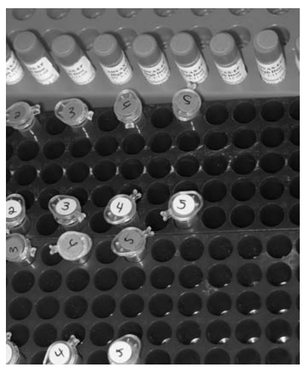
ADARC *Discovery*



ADARC Clinical Trials

The Clinical Program is a vital part of The Aaron Diamond AIDS Research Center's mission. Through clinical trials, scientists put research into practice. Trials conducted in the Clinical Program take place at The Rockefeller University Hospital.

ADARC's trials have benefited millions of people worldwide who are living with HIV. The Center leads studies that include HIV-positive patients, as well as healthy volunteers.

The decision to participate in a clinical trial is an important one. ADARC staff ensure participants receive as much information as possible, providing help and support through the duration of the trials.

Dr. Martin Markowitz, Clinical Director, leads studies that test the safety and efficacy of new drugs or treatments in HIV-positive patients, or seek to understand how the virus interacts with the host.

For more information on trials open to HIV-positive patients, please contact Don Garmon at 212.327.7290 or dgarmon@adarc.org.

Dr. David Ho and his colleagues conduct clinical trials in healthy, HIV-uninfected volunteers to develop potential vaccines against HIV. Participation in HIV vaccine clinical trials provides an opportunity to become involved in the fight against HIV/AIDS safely, at a very personal level.

For more information about vaccine trials, please contact Daniel Dugin, Clinical Trials Assistant/Recruiter at 212.448.5016 or aidsvaccine@adarc.org.

ADARC *News In Brief*

www.adarc.org
ADARC's website has been redesigned and will go live soon with fresh and timely information about our scientists and their research. Please visit us online and let us know your thoughts at info@adarc.org.

Former ADARC Scientist Wins AIDS Walk Africa Youth Scholarship

Talia Rosenberg, who is departing Dr. David Ho's laboratory to attend Yale Medical School, will trek across Swaziland this summer, the recipient of the first-ever AIDS Walk Africa Youth Scholarship awarded by the Elizabeth Glaser Pediatric AIDS Foundation. Supporters can help Talia raise awareness about the effects of HIV on mothers, children and families by visiting pedaids.org/awascholarship.

Gina Chu Joins ADARC Board

Gina Lin Chu, a civic leader whose passion and dedication are known to many, has been elected to the Board of Directors of The Aaron Diamond AIDS Research Center. "Gina's commitment to social good evokes the spirit of community service that moved Irene Diamond to found ADARC 17 years ago," said Dr. David Ho. "I am absolutely delighted that she has joined our board."

As an Asia Society trustee, Ms. Chu has taken leadership roles in many programs that promote multi-cultural awareness. She is a recipient of the Philanthropy/Community Service Award from the Committee of 100 and was honored as Philanthropist of the Year by the Asian American Federation of New York. She also serves as a trustee of The Asia Foundation, the Eisenhower Fellowships and the Bhutan Foundation, bringing energy and conviction to each.

Ms. Chu is working to raise ADARC's profile in the community and to foster understanding of the Center's vaccine programs that target HIV, avian flu and other pathogens. She has been instrumental in ADARC's efforts to advocate greater support and compassion for those affected by AIDS in China.