

The Anatomy of an Epidemic

By Laura Stephenson Carter

An AIDS Directory

This is a sampling of DMS faculty and alumni, in addition to those in the feature below, who are involved in HIV/AIDS research and clinical care.

Alumni are in light blue Faculty are in dark blue

Samuel Katz, DMS '50, a longtime faculty member at Duke, has been widely lauded for his contributions to children's health—including pediatric AIDS research and care. He serves on the NIH Committee for AIDS Vaccines and headed a WHO panel on diagnosing pediatric AIDS.



John Modlin helped establish the NIH's Pediatric AIDS Clinical Trials Group and collaborated in the design of a study that demonstrated for the first time that maternal-to-infant transmission of HIV could be prevented by treating the mother with antiviral medication.

The story broke not with a bang but a whimper. Today, with 25 years of hindsight, it's easy to see that the emergence of AIDS was one of the biggest health stories of the 20th century. But back in the early 1980s, doctors hadn't yet put together scattered reports of unusual illnesses in New York, San Francisco, and other cities.

Young, previously healthy, gay men were complaining of fatigue, fever, diarrhea, unexplained weight loss, purplish lesions, respiratory ailments, and aggressive infections. Doctors were perplexed. Their patients were exhibiting symptoms normally found in immunocompromised patients. The purplish lesions were signs of Kaposi's sarcoma, a rare but nonlethal cancer more likely to strike elderly men. The patients' respiratory problems often worsened, turning into *Pneumocystis carinii* pneumonia (PCP), a rare disease first seen in orphanages in post-World War II Europe. Soon the men began exhibiting even more aggressive infections, including herpes; fungal growths; and toxoplasmosis, a parasitic infection of the central nervous system. They were getting sicker and sicker, wasting away, dying.

Laura Carter is DARTMOUTH MEDICINE's associate editor. Sources for the timeline below include The AIDS Reader, March 2006, Vol. 16, No. 3; American Medical News, July 2, 2001 (www.amednews.com); Newsweek, May 15, 2006 (<http://www.msnbc.msn.com/id/12663345/site/newsweek/>); <http://www.avert.org>; www.aegis.com/topics/timeline; and <http://aidshistory.nih.gov/>.

But the public health system was slow to react to these mysterious deaths. And peer-reviewed journals aren't designed to spread news quickly; during the six months or more that it takes an article to go through the review and editing process, authors are barred from leaking news to the popular press.

But Dr. Andrew Saxon, a DMS graduate, and his colleagues at the University of California at Los Angeles managed to find a way around this problem. Theirs was the first official published report on what we now recognize as the AIDS epidemic.

Breaking the silence

Dr. Andrew Saxon, DMS '70: now chief of clinical immunology and allergy and a professor of medicine at the University of California at Los Angeles (UCLA)

The patient had a "fungus ball on the end of his finger," recalls UCLA immunologist Andrew Saxon. He was awed. "You didn't see that except in bubble babies"—severely immunocompromised children who have to live inside a germ-free plastic bubble—"and in leukemics treated with intensive chemotherapy."

It was the fall of 1980. The patient was a young, previously healthy, homosexual man. Over the next few months, Saxon and his colleague Dr. Michael Gottlieb treated four more gay men, all strangers to each other but all diagnosed with unusual infections. The five also developed pneumonia, which lung biopsies confirmed to be the rare PCP.

June 2006 marks the 25th anniversary of the first published report about AIDS—a paper coauthored by a DMS alumnus. In the quarter of a century since then, the disease has swept the globe. But doctors and scientists—including many with Dartmouth ties—have been making progress, both scientifically and socially, against the wily virus that has killed 25 million people.

An AIDS Timeline

The following events are among the milestones that have marked the recognition, understanding, and treatment of HIV/AIDS.



AIDS has spread, it is later clear, to at least five continents—North America, South America, Europe, Africa, and Australia.

The June 5 *Morbidity and Mortality Weekly Report (MMWR)* publishes word of five gay men with *P. carinii* pneumonia (PCP).



U.S. Centers for Disease Control (CDC) coins the term AIDS (acquired immune deficiency syndrome) and names four risk factors: male homosexuality, Haitian origin, hemophilia A, intravenous drug abuse.

1978

Gay men in the United States and Sweden, and heterosexuals in Tanzania and Haiti, begin showing signs of a disease that is later determined to be AIDS.



1980

With the disease's spread unchecked by awareness or any preventive action, between 100,000 and 300,000 persons may have been infected by this point.



1981

The July 4 *MMWR* publishes a report on 26 cases of Kaposi's sarcoma in gay men in New York and California.

In July, *NY Times* publishes the first article about AIDS in the popular press—"Rare Cancer Seen In 41 Homosexuals."

In December, the first cases of PCP are reported in intravenous drug users.

1982

CDC announces that the virus that causes AIDS may be in the nation's blood supply.



Thomas Clark, DMS '01, is on the faculty at the University of California at San Francisco. In 2002, he founded Grassroot Soccer, an international AIDS education organization that trains professional soccer players to teach teenagers about HIV and AIDS prevention.



Alexandra Howell headed a Dartmouth Medical School research team that in 1997 was the first group to demonstrate that HIV infects normal tissues throughout the female reproductive tract. She currently studies HIV infection and the immune response to HIV proteins. *

Ann Collier, DMS '78, is on the faculty at the University of Washington and was the medical director, from 1987 to 1990, of Seattle's Harborview AIDS Clinic—one of the nation's first AIDS clinics. Her research interests include complications of HIV treatment, the epidemiology of cytomegaloviruses, and antiretroviral trials.

On June 5, 1981, Saxon and Gottlieb's article became the first published report on the emergent AIDS epidemic. A longer version of their article appeared in the *New England Journal of Medicine* on December 10 of that year.

* The effort to encapsulate in only a few words contributions by alumni and faculty to the fight against AIDS resulted in a few passages that don't fully reflect some faculty members' current work. Howell, since making the seminal 1997 finding described above, has studied heterosexual transmission of HIV, the influence of sex hormones on HIV infection, and the replication of HIV within the female reproductive tract.

They had a "profound T-cell deficiency," too, says Saxon. T-cells, a type of white blood cell that fights infection, had just been discovered in the 1970s. "We knew there was something going on."

By May 1981, Saxon and Gottlieb were sure they had an epidemic on their hands and were anxious to alert the medical community. They hoped to publish their findings quickly in the *New England Journal of Medicine (NEJM)*, one of the largest-circulation journals. But the *NEJM* editors were unwilling to accelerate their several-months-long review and editing process, and in the meantime they couldn't even guarantee that the article would be published. But if the physicians leaked their findings to the popular press, the journal would unquestionably pull their paper.

But then they thought of a way to get the news out quickly without jeopardizing their chances of being published in the prestigious *NEJM*. They sent their report on the cluster of five unusual patients to the Centers for Disease Control (which still goes by "CDC," even though "and Prevention" was later added to its name), for inclusion in the agency's weekly newsletter, the *Morbidity and Mortality Weekly Report (MMWR)*.

So on June 5, 1981, their article, "Pneumocystis Pneumonia—Los Angeles," became the first published report on the emergent AIDS epidemic. A longer version, "*Pneumocystis carinii* Pneumonia and Mucosal Candidiasis in Previously Healthy Ho-

mosexual Men: Evidence of a New Acquired Cellular Immunodeficiency," appeared in the *NEJM* on December 10 of that year.

In July 1981, the *MMWR* ran another AIDS-related report. This one told of 26 cases of Kaposi's sarcoma (KS) and other opportunistic infections among gay men. It was titled "Kaposi's Sarcoma and Pneumocystis Pneumonia Among Homosexual Men—New York City and California."

No one knew what was causing these infections. Some thought "poppers," a nitrate-based inhalant, were to blame. Although meant for heart patients, the drug was widely abused by gay men in the 1970s and '80s to enhance sex. Saxon and Gottlieb, however, suspected that an infectious agent—possibly cytomegalovirus, a herpesvirus that is normally harmless in healthy individuals—was to blame. But, Saxon admits, "we didn't recognize it as blood-borne at first."

Over the next few years, Saxon became immersed in the AIDS epidemic. (His research specialty was, and still is, B-cell immunity and allergy.) He read every article he could on the disease. In 1983, he started the first AIDS newsletter. He spoke frequently at medical meetings and was interviewed often by the media.

He believes the cause of AIDS might have been harder to find if Japanese researchers hadn't laid the groundwork in the 1970s by identifying the first human retrovirus, adult T-cell leukemia virus. "If that

U.S. Public Health Service (USPHS) recommends how to prevent AIDS transmission by sexual contact and blood transfusions.

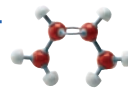
CDC adds a fifth risk category: female sex partners of men with AIDS.

World Health Organization (WHO) begins global surveillance of AIDS.



The CDC suggests that reducing needle sharing should prevent transmission of the AIDS virus among IV drug users.

LAV and HTLV-III are determined to be the same.



Atlanta hosts the first International AIDS Conference.

USPHS issues recommendations on how to prevent HIV transmission from pregnant mothers to their unborn children.

International Committee on the Taxonomy of Viruses rules the AIDS virus be called human immunodeficiency virus (HIV).

HIV-2 is discovered among commercial sex workers in West Africa.

1983

Researchers at Pasteur Institute in France isolate virus that causes AIDS and call it lymphadenopathy-associated virus (LAV).



Both *Time* and *Newsweek* run cover stories about AIDS.

1984

Dr. Robert Gallo at the National Institutes of Health (NIH) isolates a virus that causes AIDS and calls it human T-cell lymphotropic virus type III (HTLV-III).

Gay bathhouses begin closing in cities all across the United States.

1985



President Reagan mentions AIDS at a press conference.

Blood banks in the United States start screening for the AIDS virus.

Actor Rock Hudson dies of AIDS.

In Indiana, 13-year-old Ryan White, after contracting AIDS from a blood transfusion, is barred from school.

1986

Needle exchange programs open in Boston and New Haven, Conn.

U.S. Surgeon General Koop issues a report calling for AIDS education and condom use.



Ruth Connor researches the transmission of HIV from mother to child during breastfeeding, evaluating various strains of lactobacillus bacteria that colonize the infant gastrointestinal tract for their ability to protect against HIV infection acquired through breastfeeding.

Judith Currier, DMS '85, is on the faculty of the University of California at Los Angeles, where she directs AIDS clinical trials. Her influential articles, including the "Female Face of AIDS: Preventing HIV Infections in Women," have helped expand AIDS research to include women.



Charles Wira (also DMS '70) investigates how hormones affect immunity in the female reproductive tract. He heads an NIH Program Project Grant on heterosexual transmission of HIV and is a member of two task forces at the NIH Office of AIDS Research. He is also a course director for DMS's DARDAR Project in Tanzania. *

hadn't happened, we would have thought we had the plague," he says. Instead, within two years after the seminal MMWR report, Dr. Luc Montagnier at the Pasteur Institute in France and Dr. Robert Gallo at the National Institutes of Health in the United States independently discovered that AIDS was caused by a retrovirus. Montagnier called it lymphadenopathy-associated virus (LAV), and Gallo dubbed it human T-cell lymphotropic virus type III (HTLV-III). By 1985, researchers had determined the two were the same, and the virus was renamed human immunodeficiency virus (HIV).

By the early 1990s, Saxon had suspended publication of his AIDS newsletter and returned to his allergy research. He still pays attention to what's happening in the AIDS field, though. He's pleased that so many antiviral drugs have been developed to combat AIDS, but he's surprised that an AIDS vaccine is proving elusive. "The virus is very clever in its ability to shift and hide" from the immune system, he concedes. "It mutates all the time."

Crusading for acceptance

Dr. C. Everett Koop, Dartmouth College '37: former U.S. surgeon general; now a professor of surgery, of community and family medicine, and of psychiatry at Dartmouth Medical School and senior scholar of Dartmouth's Koop Institute

C. Everett Koop spent most of his career as a pediatric surgeon, so a disease that appeared to affect only gay men was far outside his ken. Nevertheless,

when the first MMWR reports came out, he recognized that these unexplained infections spelled trouble. The problem was that he'd been appointed but not yet confirmed as U.S. surgeon general, so he felt powerless to speak out. Even after his confirmation in November of 1981, he had little influence at first over how the Reagan administration communicated to the country about AIDS.

Koop says that in the early 1980s, President Reagan didn't realize the implications of AIDS. "One thing that was absolutely obvious was that members of the cabinet and members of the domestic policy council kept Reagan and me apart," Koop contends. "They didn't keep him informed. It made him look as though he didn't care, or didn't know what to do about it, or was a heartless guy—all of which are wrong."

But other governmental agencies were acting. "Even if people like me are muzzled and not allowed to say what they want to, the momentum of the CDC, NIH, FDA . . . keeps rolling on," says Koop.

There was momentum in AIDS research, too. "We learned as much about AIDS in six years as we learned about the hepatitis virus in over 40 years," Koop says. "Largely that was because we had done so much bench science on cancer. A lot of the research was applicable to AIDS, and that's why we made the progress that we did." Soon, researchers had identified the virus's antibodies. "We also began to identify the virus itself," says Koop.

"We learned as much about AIDS in six years as we learned about the hepatitis virus in over 40 years," former Surgeon General Koop says. "Largely that was because we had done so much bench science on cancer."

* The effort to encapsulate in only a few words contributions by alumni and faculty to the fight against AIDS resulted in a few passages that don't fully reflect some faculty members' current work. Wira heads a National Institutes of Health Program Project Grant designed to increase knowledge of immune protection in the human female reproductive tract and provide information regarding the prevention of local infection in the genital mucosa; such knowledge will be useful in managing sexually transmitted diseases and in understanding heterosexual HIV transmission.

U.S. Food and Drug Administration (FDA) approves zidovudine, AZT, the first anti-retroviral for the treatment of AIDS.

Entertainer Liberace dies of AIDS.



The AIDS Memorial Quilt is started in San Francisco (it comes to Hanover in 1991).

A summary of Surgeon General Koop's report, *Understanding AIDS*, is mailed to every U.S. household.



More celebrities die of AIDS, including choreographer Alvin Ailey and photographer Robert Mapplethorpe.



Congress passes a resolution to create the National Commission on AIDS.

The Americans with Disabilities Act is passed; it prohibits discrimination based on disability, including HIV/AIDS.

Ryan White dies and Congress approves the Ryan White CARE Act to provide community-based AIDS care.

1987

Princess Diana shakes hands with AIDS patients without gloves to show the disease can't be spread by normal contact.

AIDS is the first disease ever debated on the floor of the UN General Assembly. The body resolves to mobilize the UN against AIDS, under WHO leadership.



1988

WHO declares the first World AIDS Day. U.S. NIH establishes the Office of AIDS Research as a separate agency.

The U.S. bans discrimination against federal workers who are HIV-positive.

1989



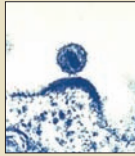
A drug trial shows that AZT can slow the progression of AIDS. U.S. Secretary of Health Louis Sullivan calls this "a turning point in the battle to change AIDS from a fatal disease to a treatable one."

1990

The CDC reports the possible transmission of HIV to a patient during a dental procedure. The dentist had been diagnosed with AIDS three months before performing the procedure.



Susana Asin investigates when HIV-1 infection occurs in women following the heterosexual transmission of cell-free or cell-associated virus through the semen of an infected partner. *



Peter Kilmarx, DMS '90, is an official with the Centers for Disease Control and Prevention's Global AIDS Program. He previously worked for three years in Botswana as head of the U.S. government's anti-AIDS programs there, and before that for six years in Thailand.

Richard Waddell heads the New Hampshire AIDS Education and Training Center. He also is active internationally through the DARDAR Project, as director of a course to train Tanzanian researchers and as coinvestigator of a clinical trial in Tanzania to test a new vaccine aimed at preventing TB in HIV/AIDS patients.

In 1986, Koop prepared a report on AIDS that he calls "the most frank report that was ever put in the federal register. I used four words which I thought, talking about AIDS, you couldn't avoid using . . . penis and vagina and rectum and condom."

* The effort to encapsulate in only a few words contributions by alumni and faculty to the fight against AIDS resulted in a few passages that don't fully reflect some faculty members' current work. Asin studies heterosexual HIV transmission, the influence of sex hormones and of inflammation triggered by sexually transmitted pathogens on HIV infection, and viral replication in the female reproductive tract.

"We couldn't see the virus, but we could see the footprints of where it had been. That was of great help, because knowing about the virus enabled us to clean the blood supply up." By 1985, just four years after the first MMWR report, U.S. blood banks were able to screen for HIV.

In 1986, Koop prepared a report on AIDS that he calls "the most frank report that was ever put in the federal register. I used four words which I thought, talking about AIDS, you couldn't avoid using . . . penis and vagina and rectum and condom." Back in those days, many people worried that AIDS could be transmitted by cats, mosquitoes, doorknobs, toilet seats, and even casual social contact. "My job as a health educator for the government at that time was not only [to explain], 'This is how you get AIDS,' but perhaps even more important, 'This is how you do not get AIDS.'"

Koop made it clear that AIDS was spread by the transmission of specific body fluids—semen and blood. "I went to tremendous lengths" to emphasize that "you didn't get it from kissing a girl goodnight, and you didn't get it from driving a car that an AIDS person had driven," he says. "That was very important because people were being kept out of school because it was thought that they would contaminate other children."

Then in 1988, a flyer titled *Understanding AIDS*, a summary of Koop's 1986 report on the disease, was mailed to all 107 million U.S. households.

"I did a lot to help educate people," says Koop. "Essentially, what the country needed was a frank, charismatic leader who was not afraid to talk about AIDS." The fact that Koop had come into the Reagan administration as an acknowledged conservative made his forthright approach to AIDS all the more powerful.

When mandatory AIDS testing was proposed in 1987, Koop and other public health officials worried that it would result in widespread discrimination against those who were HIV-positive and might drive people with HIV/AIDS underground, away from help and counseling. AIDS testing has remained voluntary and anonymous. Koop thinks it's time to change that policy, however, so that public health departments can use contact tracing to stem the virus's spread, as they do for other sexually transmitted diseases.

Today, a few months shy of his 90th birthday but still active as senior scholar of the Koop Institute at Dartmouth, Koop continues to be a relentless advocate for public health and health education.

Reaching around the world

Dr. C. Fordham von Reyn, DMS '69: now a professor of medicine (infectious disease) at Dartmouth Medical School and chief of the infectious disease section at Dartmouth-Hitchcock Medical Center

In the early 1980s, AIDS was exploding in the nation's cities. But it was also quietly making its

Basketball star Magic Johnson announces that he has HIV and retires from playing.



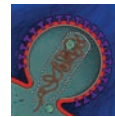
The CDC recommends that infected health-care workers should be barred from performing certain procedures.

AIDS becomes the number-one cause of death for American men aged 25 to 44.

The first clinical trial of multiple-drug AIDS therapy gets under way.



CDC expands the definition of AIDS to include additional opportunistic infections, as well as HIV-positive adults with a CD4 count of under 200.



AIDS has become the leading cause of death for all Americans aged 25 to 44.

The FDA approves the first non-blood-based test for HIV.

The USPHS recommends the use of AZT by pregnant women who are HIV-positive to reduce prenatal transmission of HIV.

1991

The red ribbon is introduced as the international AIDS symbol. Two new drugs become available as monotherapy and increase the survival of AIDS patients. But doctors soon realize that they provide only 18 to 24 months of protection against the disease's progression.



1992

Tennis star Arthur Ashe announces that he has been infected with HIV via a blood transfusion.



1993

A new scientific technique, quantitative polymerase chain reaction, allows patients' viral load to be accurately assessed.



Ballet dancer Rudolf Nureyev dies of AIDS.

1994

The CDC launches a series of AIDS advertisements that focus on condom use.



John Mellors, DMS '78, is a member of the faculty at the University of Pittsburgh. He studies antiretroviral therapy for HIV/AIDS, viral variants that are resistant to antiretroviral drugs, viral load as a predictor of disease outcomes, and salvage treatment regimens. He also conducts clinical trials of new antiretroviral combinations.

Richard Zuckerman studies the interactions between HIV and herpes simplex virus (HSV) because over half of persons with HIV are also infected with HSV. He also does research to clarify clinically important interventions that may prevent HIV transmission and/or progression.



Victoria Johnson, housestaff (HS) '82-86, is on the faculty at the University of Alabama. She studies HIV resistance and co-authored a 2003 *New England Journal of Medicine* study on the effectiveness of a specific combination of anti-HIV drugs.

way to rural New Hampshire and Vermont, too.

“The earliest patients we saw with AIDS in New Hampshire were gay men who had moved back from urban areas and were dying of the disease, and hemophiliac men who were living locally and had been receiving concentrated blood products from hundreds of donors,” says infectious disease expert Fordham von Reyn. “I saw my first patient in 1983. He came back from New York City almost terminally ill. At this point, the stigma was tremendous. His family, who owned a local business, didn’t want to be taking him out of the house. I made house calls. I didn’t have anything much to offer other than treating complications and symptoms and trying to provide some comfort.

“It was wonderful in the late ’80s when we had the first drug to treat HIV,” von Reyn continues. “But unfortunately we treated people with serial monotherapy—one drug at a time. When one failed, we switched to another, and later realized that this was an ideal recipe for introducing resistance. So when multiple-drug treatment became the standard in the 1990s, then we really saw a tremendous difference in how people did. Patients who were sick in bed, dying, . . . perked up, gained weight, went back to work,” after taking what came to be known as the AIDS “cocktail.” By that time, for patients in the U.S., AIDS was no longer a death sentence but a manageable chronic disease.

Yet no one predicted that AIDS would spread

the way it has—that Africa and the Indian subcontinent would see infection rates well into the double digits and that heterosexual men, women, and children would far outnumber gay men in the ranks of the HIV-positive. Today, the typical AIDS patient is a young, married, monogamous woman in Africa. But the disease continues to have social, medical, and economic implications for developed and undeveloped nations alike.

“None of us realized at the beginning that this would become a worldwide pandemic,” says von Reyn. Today, he’s turned over the care of local AIDS patients to colleagues and is attacking the disease on a far broader front. He is one of the leaders of the DARDAR Project, based in the central African nation of Tanzania. The HIV infection rate in Tanzania is 10% in adults and 30% in pregnant women. DARDAR, a collaboration between Dartmouth Medical School and Tanzania’s Muhimbili University College of Health Sciences (MUCHS), includes a clinic for children with HIV/AIDS, a trial for a tuberculosis vaccine (tuberculosis being a common complication of AIDS), and a program to train Tanzanian researchers.

The term DARDAR was drawn from the first three letters of “Dartmouth” and “Dar es Salaam,” the city where MUCHS is located. In addition, the acronym is similar to the Kiswahili word “dada,” which means “sister.” The close relationship between the two institutions—and their commitment

“None of us realized at the beginning that this would become a worldwide pandemic,” says von Reyn, the chief of infectious disease at Dartmouth-Hitchcock. Today, he is the leader of a project based in Tanzania, where the HIV infection rate is 10% in adults and 30% in pregnant women.



The International Conference for People Living with AIDS is held in Africa for the first time ever.

President Clinton hosts the first White House Conference on HIV/AIDS.

Time’s 1996 Man of the Year is AIDS researcher Dr. David Ho.

FDA approves the first HIV home-testing kit.

The number of new U.S. AIDS cases declines for the first time.



AIDS-related deaths in the United States decline by more than 40% over 1996, thanks to the AIDS cocktail.



First large human HIV vaccine trial starts.

The first case of infection with a strain of HIV resistant to the most powerful antivirals is reported in San Francisco.

There are reports of treatment failures and side effects from HAART.

1995

Four new antiretroviral drugs are approved for clinical use in the United States.

The FDA approves a new class of drugs—protease inhibitors—that helps make the disease a more manageable illness for some patients.



1996

The Joint United Nations Programme on HIV/AIDS (UNAIDS) begins work.

Magic Johnson returns to play basketball. A triple “cocktail” treatment, known as highly active antiretroviral therapy (HAART), is announced. AIDS no longer means certain death—it is now becoming a chronic, manageable disorder.

1997



The U.S. Agency for International Development reports that it is estimated that 40 million children in developing nations will lose one or both of their parents to AIDS by 2010.

1998

Sub-Saharan Africa is home to 70% of the people worldwide infected with HIV.



J. Brooks Jackson, DMS '82, is on the faculty at Johns Hopkins. He ran a large AIDS clinical trial in Uganda in the 1990s which found that oral nevirapine significantly reduces the transmission of HIV from mother to infant.



Mary-Margaret Andrews (also HS '91-'97) is the director of Dartmouth-Hitchcock Medical Center's Family HIV Program, a federally funded program that provides care to women and children who are HIV-positive.

Peter Wright, DMS '65, is on the faculty at Vanderbilt University. In 1987, he created Vanderbilt's HIV vaccine program, which is part of an international HIV trials network. He also established a research and development unit within WHO's Expanded Program on Immunization.

In 1984, Saykin was offered the opportunity to work on a mysterious new disease. AIDS represented uncharted territory. "The etiology was just emerging," says Saykin, now a neurologist at DHMC. "It was a fatal disease." He was touched by how cooperative and motivated the AIDS patients were.

to address AIDS together—was broadened six months ago to be a Dartmouth-wide project called the Global Health Initiative. Von Reyn expects to focus on those efforts for some time to come.

Investigating implications

Dr. Andrew Saykin: now a professor of psychiatry and of radiology at Dartmouth Medical School

In 1984, Andrew Saykin was a junior faculty member at the University of Pennsylvania when he was offered the opportunity of a lifetime—to work on a mysterious new disease. Dr. Robert Janssen, a CDC neurologist who had trained at Penn, asked for Saykin's help in assessing the neurological effects of early-stage AIDS. Late-stage AIDS patients often developed dementia, but "the big question was 'What about all the people who had been exposed to whatever was causing HIV?'" explains Saykin. "As a recently minted neuropsychologist at Penn, I was in the business of designing cognitive test batteries to try to be sensitive to subtle cognitive dysfunction."

So Saykin became a consultant to the CDC and had a chance to "go with the CDC team to the International AIDS Conference and present data." His research up to that point had focused on diseases with "a long research tradition behind them . . . epilepsy, schizophrenia, and Alzheimer's." But AIDS represented uncharted territory. "The etiology was just emerging," he points out. "It was a fa-

tal disease. It was also very poignant in terms of working with these patients. We gave them about a three-hour battery of detailed cognitive tests, tests for anxiety and stress and depression, and so on." Saykin was touched by how cooperative and motivated the gay men he worked with were.

Saykin and Janssen's studies—one of which was published in the *Annals of Neurology* and another in the *International Journal of Clinical Neuropsychology*—found that HIV-infected people who had not yet developed AIDS exhibited mild neuropsychological deficits: subtle changes in language capability (such as fluency and ability to recall the names of objects), attention span, ability to process visual and auditory information, psychomotor speed, and memory.

"In general, the cognitive effects were quite subtle during these very early stages," says Saykin. "In fact, it became somewhat controversial as to whether people who were [HIV-positive] but had no other symptoms at all really had cognitive abnormalities. It was only when people developed more advanced disease, with these constitutional symptoms and so-called AIDS-related complex, that people really began to show more measurable cognitive changes."

Yet Saykin's research had major policy implications. "After the early reports, the military decided to test everyone for HIV," he explains. They "decided that people who were [HIV-positive]



The AIDS virus is traced back to chimpanzees in Africa.

WHO reports that AIDS is the fourth biggest killer worldwide.

The International AIDS Conference (the 13th such gathering) is held in a developing nation (South Africa) for the first time.

President Clinton issues an executive order to help developing nations import and produce generic AIDS drugs.



President Bush appoints an openly gay man, Scott Evertz, as the director of the Office of National AIDS Policy but puts no extra money in the 2002 federal budget for AIDS prevention or treatment.

FDA warns AIDS drug-makers to lessen the optimistic tone of their antiretroviral ads.



About 50% of Americans still believe HIV can be acquired through everyday contact.

HIV is the leading cause of death worldwide among those aged 15 to 59.

1999

The infection rate in Uganda has dropped from 30% in 1992 to 12% in 1999, thanks to educational initiatives.

UNAIDS estimates that 33 million people are now living with HIV/AIDS and that 2.6 million have died this year. More women than men are infected with HIV in Africa.

2000



The U.S. and the UN Security Council declare HIV/AIDS a global security threat, fearing that it could topple governments, spark ethnic wars, and undo decades of work building up free-market democracies.

2001

China admits that HIV/AIDS threatens its public health and economic security.

AIDS is the leading cause of death in sub-Saharan Africa, and the rate of HIV infection is rising fastest in Eastern Europe and Russia.



2002

The number of children orphaned by AIDS has tripled in six years, to 13.4 million.

UN Secretary General Kofi Annan speaks out on World AIDS Day against HIV-related stigma and discrimination.

Timothy Lahey is both a clinician and a researcher. He does studies in the fields of immunology—tuning immune responses to HIV—and epidemiology—looking at the impact of living in rural areas on HIV outcomes. He recently received a five-year Mentored Clinical Scientist Development Award from the NIH.

Joyce Sackey-Acheampong, DMS '89, is a member of the faculty at Harvard Medical School. She founded a non-profit organization called Foundation for African Relief that trains African health workers who care for people with HIV/AIDS and runs an HIV/AIDS clinic in Ghana.



Bryan Marsh (also HS '90-'96) is medical director of DHMC's Regional HIV/AIDS Program. Alan Rozycki (also DMS '63) and Jeffrey Parsonnet have also provided care for many years for AIDS patients from all over northern New England.

should not be running sensitive equipment” like planes and computerized tanks.

Later, when viral load could be measured, “it became clear there was a correlation between viral load and . . . cognitive performance,” he says. Other studies showed that early antiretroviral treatments for AIDS patients with dementia helped them regain some cognitive function. “It was exciting to see a treatment developed and see a response on cognitive testing and brain imaging.”

Saykin doesn't do much AIDS-related research these days. Since joining the Dartmouth faculty in 1992, he has focused on cognitive testing and brain imaging in people with Alzheimer's disease and other dementias. But among those populations are occasional patients who are HIV-positive, reminding him of his early experience with the epidemic.

Tending to teens

Dr. Karen Kramer Hein, DMS '68: now retired; formerly a professor of pediatrics and epidemiology at Albert Einstein College of Medicine, executive director of the Institute of Medicine, and president of the William T. Grant Foundation

Karen Hein likens the early years of AIDS to a whale-watching expedition. “Everybody's looking at the tail,” she says, meaning where the epidemic has been evident. “Meanwhile, the ‘whale’ is going under the water—and where it's going to surface, where it's heading, is adolescents.”

Hein was savvy about adolescent health issues

partly because she had been medical director of a juvenile detention center in New York City in the 1970s. There, she had treated adolescents who had sexually transmitted diseases, were abusing drugs, and were engaging in other risky behaviors. The diseases among her patients at the detention center were “like a beacon for what's going to become news, or happen in the community on a larger level,” she says. “Long before heroin was known to be an epidemic for young people, we had kids who were using heroin detoxing in our infirmary.”

As soon as researchers determined that AIDS was a sexually transmitted disease, Hein realized that adolescents were at risk. “Part of the rationale for concern,” she explains, “was that if teenagers were getting HIV, they probably look healthy, they probably wouldn't even know they were sick, and they wouldn't get sick until they were in their twenties.” But no one listened. “Then, lo and behold, people in their twenties started getting sick.”

In 1987, Hein opened the world's first comprehensive AIDS program for adolescents. Even by then, some of her colleagues were skeptical. “They made fun of us and called us the ‘emperor's new clothes clinic,’” she says. They thought “we were making a big deal out of nothing.” Before long, however, similar programs were started in San Francisco and Washington, D.C.

Hein worked tirelessly to build awareness about *continued on page 58*

In 1987, DMS alumna Hein opened the world's first comprehensive AIDS program for adolescents. Even by then, some of her colleagues in New York City were skeptical. “They called us the ‘emperor's new clothes clinic,’” she says. “Then, lo and behold, people in their twenties started getting sick” with AIDS.

WHO announces 3 by 5 Initiative, to bring treatment to 3 million people by 2005.

Vaxgen announces that its AIDS vaccine failed to reduce infection rates among clinical trial subjects who had been vaccinated.



FDA approves the first rapid oral HIV test.

HIV prevalence in Uganda has been reduced by 70% since the early 1990s. The drop is believed to be due to people limiting their number of sexual partners and to community-based prevention efforts.

It is clear that WHO's 3 by 5 Initiative will not achieve its goal. The head of the organization's HIV/AIDS program expresses regret for the failure of the ambitious plan.



UNAIDS estimates that worldwide, 25 million people have died from AIDS and 40 million people are living with HIV.

2003

Belgian researchers conclude that HIV-2 probably jumped from sooty mangabeys to humans in Guinea-Bissau in the 1940s.



2004

A survey of U.S. media shows that the number of AIDS stories peaked in 1987, increased slightly in 1991 when Magic Johnson spoke about his HIV status, and rose again in 1996-97 upon the introduction of combination therapy.



2005

The FDA approves the first generic AIDS drug made by a foreign company. AZT's U.S. patent ends. The FDA immediately approves four generic forms of the anti-retroviral for sale in the U.S.



2006

This year's International AIDS Conference is scheduled to be held from August 13 to 18 in Toronto, Canada.



IMAGES: TIME, NATIONAL INSTITUTES OF HEALTH, NATIONAL LIBRARY OF MEDICINE, UNITED NATIONS, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT, MORBIDITY AND MORTALITY WEEKLY REPORT, NEW ENGLAND JOURNAL OF MEDICINE

Anatomy of an Epidemic

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HIV/AIDS in adolescents. She published abstracts, articles, and book chapters; spoke at numerous professional meetings; and collaborated with the New York City Board of Education to expand AIDS education in the public schools. In 1989, she published an explicit book for teens titled *AIDS: Trading Fear for Facts*. “We became the ambassadors, or the Johnny and Joanna Appleseeds, for AIDS awareness,” she says.

In 1991, she met basketball player Magic Johnson—shortly after his public announcement that he had AIDS. Hein began counseling Johnson on his AIDS-education activities. Soon, with his star-power behind the effort, “the issue went from being invisible to high visibility,” recalls Hein. She also began training interested teens in how to talk effectively to the media.

But even though awareness of adolescent AIDS was growing, Hein was disheartened to see the familiar issues of denial, stigma, and discrimination play out on the adolescent stage. A few years later, the same issues would surface on the international stage.

Although now retired, Hein continues to be involved as a volunteer in HIV/AIDS initiatives around the world. In countries with effective education and outreach efforts—including condom availability—“HIV rates are plummeting,” she says. But in other countries, “when people die, they don’t say what they died of. So it’s almost like the 1980s all over again.”

Looking ahead

“There was no way of knowing that AIDS would sweep through the world like it did,” says Dartmouth faculty member Ford von Reyn. “But once you began to see that it was occurring by blood transmission, by sexual transmission, and by mother-infant transmission, and once it was recognized how common it was in central Africa, then it was really clear that the world was facing a huge international public-health crisis.”

“I don’t think in our lifetime that AIDS is going to go away,” alumna Karen Hein concludes sadly. “Skipping ahead 100 years, when they look back on our lifetime, . . . I think we’ll be known for a pandemic—and it’s not going to be bird flu.

“I think it’s going to be AIDS.” ■

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