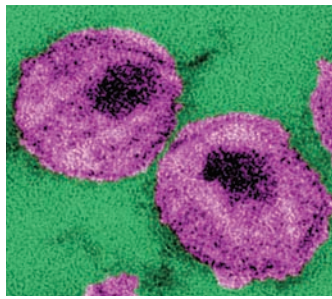


30 YEARS

OF AIDS VACCINE RESEARCH



1981

In a chilling prologue to one of the worst pandemics in history, the US Centers for Disease Control issues a report on June 5 of an unusual spate of *Pneumocystis carinii* pneumonia (an infection seen in severely immunocompromised individuals), among “five gay, otherwise healthy men.” In July, 26 more cases are reported in California and New York. Those affected are now also developing Kaposi’s sarcoma, a cancer caused by the herpes virus, which becomes a hallmark of this new disease.

1982

At a July 27 meeting in Washington, DC, the new disease is named acquired immunodeficiency syndrome (AIDS).

1983

US researchers publish the first report of eight infants who had a “disease complex comparable to AIDS.”

French researchers from the Pasteur Institute isolate a new retrovirus from the lymphoid tissue of a gay Caucasian patient that may be the cause of AIDS. They later call the new virus lymphadenopathy-associated virus (LAV).

1984

Scientists in the US confirm the discovery of a new retrovirus, but call it human T lymphotropic virus (HTLV) type III. This discovery prompts US Health and Human Services Secretary Margaret Heckler to proclaim that an AIDS vaccine candidate would be ready for testing within two years.

1985

Researchers from Uganda report a new syndrome in 63 people that is strongly associated with HTLV-III. The researchers dub the condition Slim disease because it results in severe weight loss, and note that it seems to be occurring predominantly in the “heterosexually promiscuous population.”

1986

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

French researcher Daniel Zagury inoculates himself with a vaccine candidate containing a genetically engineered version of an HIV protein inside a viral vector based on the vaccinia virus (the same virus used in the smallpox vaccine). Zagury also vaccinates nine HIV-uninfected children from Zaire (now the Democratic Republic of the Congo), making this the first unofficial preventive AIDS vaccine trial. Researchers and ethicists criticize Zagury because the trial is conducted without French regulatory approval and without adequate preclinical testing.

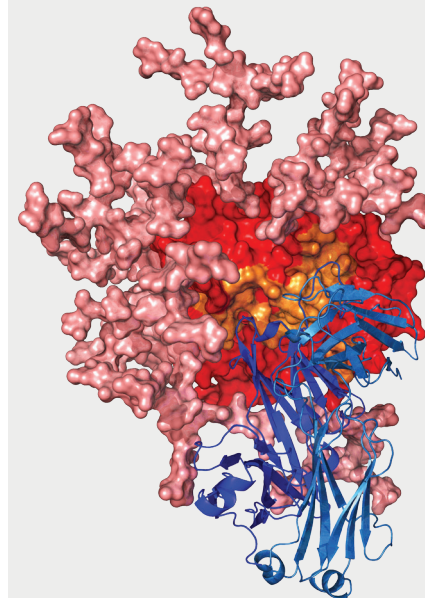
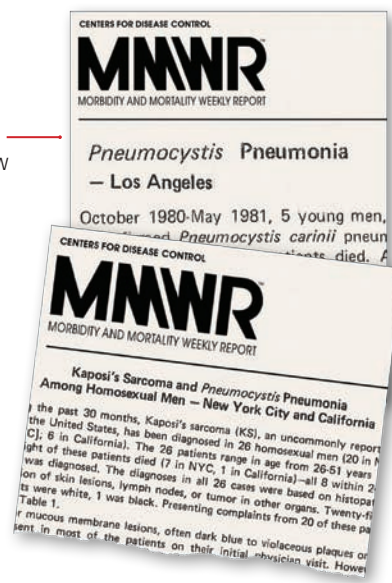
1987

The first preventive AIDS vaccine trial in the US begins, involving 81 HIV-uninfected volunteers, mostly men who have sex with men (MSM). The study’s collaborators are the National Institute of Allergy and Infectious Diseases (NIAID) and the biotechnology company MicroGeneSys, which developed the vaccine candidate containing a genetically engineered version of an HIV protein.

Efforts to protect chimpanzees from HIV using an experimental vaccine candidate fail. The candidate also used a vaccinia virus as a vector to deliver fragments of HIV.

1988

The UK Medical Research Council and the Uganda Virus Research Institute in Entebbe form Africa’s first research unit focused on the determinants of HIV infection and disease progression.



Vaccine Research Center at NIAID

1992

Researchers report that rhesus macaques vaccinated with a live, attenuated simian immunodeficiency virus (SIV), the monkey equivalent of HIV, are protected against infection, raising hopes that this might be a feasible approach to HIV vaccine development.

1994

NIAID refuses to fund the first efficacy trial of an AIDS vaccine candidate that was developed by California-based biotechnology company Genentech. The candidate, AIDSVAX, contains a genetically engineered version of HIV’s surface protein.

Researchers isolate a human antibody known as b12 from the bone marrow of an HIV-infected man who was asymptomatic for six years. In laboratory tests, b12 is able to neutralize more than 75% of HIV strains, making it a broadly neutralizing antibody (bNAb).

1995

Highly active antiretroviral therapy (HAART) is introduced. “From 1985 to 1994 it was all gloom and doom when it came to therapy,” recalls AIDS researcher David Ho, who pioneered the use of a class of drugs called protease inhibitors. “Two years later, everything turned around.”

The AIDS Vaccine Advocacy Coalition is formed on World AIDS Day.

1996

The International AIDS Vaccine Initiative (IAVI) is created as a non-profit, public-private product development partnership to ensure the development of a safe and effective preventive AIDS vaccine.

Researchers report that an attenuated SIV vaccine caused disease in infant macaques. These findings, along with other data in humans, dash hope that this would be a safe approach to test in humans.

1997

During a May 18 speech at Morgan State University in Baltimore, Maryland, US President Bill Clinton announces a national goal to develop an AIDS vaccine within a decade. Thereafter, that day is known as World AIDS Vaccine Day.

1998

VaxGen, a spinoff of Genentech, launches a Phase III efficacy trial of AIDSVAX, with the help of private investors. This is the first efficacy trial of an AIDS vaccine candidate. The trial enrolls 5,400 volunteers, mostly MSM, in the United States, Canada, the Netherlands, and Puerto Rico. A year later, another arm of the trial begins in Thailand, involving nearly 2,500 injection drug users.

1999

After a decade of planning, Africa’s first AIDS vaccine trial starts in Uganda, testing ALVAC vCP205, a canarypox viral vector-based vaccine candidate (made by the French company Pasteur Mérieux Connaught, now Sanofi Pasteur), in 40 volunteers.

The Kenya AIDS Vaccine Initiative (KAVI) is established in collaboration with the University of Nairobi, Oxford University, and IAVI.

NIAID establishes the Vaccine Research Center (VRC) at NIAID, with a primary focus on AIDS vaccine development.

The HIV Vaccine Trials Network (HVTN), headquartered in Seattle, is formed by NIAID to test preventive AIDS vaccine candidates.

The South African AIDS Vaccine Initiative is formed by the government with the goal of coordinating and supporting the development of a safe and effective AIDS vaccine.



Andreas von Bubnoff

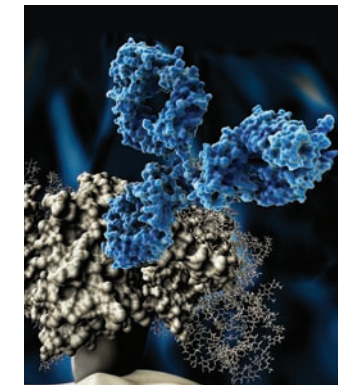


Jean-Marc Giboux/Getty Images

“There are still basic questions to answer, and at the same time we have to save the lives of patients and try to reduce the duration of treatment.”

I think this is key if we are to beat this disease in the 21st century.

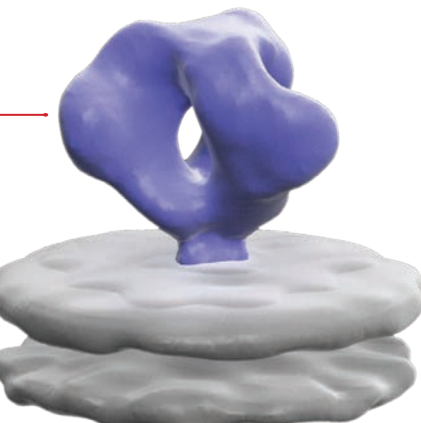
—Luc Montagnier



Christina Corbaci at The Scripps Research Institute



US Military HIV Research Program



Sriram Subramaniam, US National Institutes of Health

2003

Preliminary data from VaxGen’s two Phase III trials show that AIDSVAX is not effective.

Twenty-four leading AIDS vaccine researchers publish a paper arguing that the scale of research is insufficient for solving the major scientific challenges impeding development of an AIDS vaccine. This leads to the creation of the Global HIV Vaccine Enterprise, an alliance committed to accelerating the development of an AIDS vaccine.

An efficacy trial known as RV144 begins in Thailand with funding from NIAID and the US Army. The trial, conducted by the Thailand Ministry of Public Health, tests a combination of two vaccine candidates (Sanofi Pasteur’s canarypox vector-based vaccine candidate ALVAC-HIV vCP1521 and VaxGen’s AIDSVAX) in 16,000 volunteers.

2004

Twenty-two prominent AIDS vaccine researchers publish an article questioning the scientific rationale for pursuing the RV144 trial, arguing that other candidates have a greater chance of success.

A Phase IIb test-of-concept trial known as STEP begins in North and South America, the Caribbean, and Australia. The 3,000-person trial tests the efficacy of Merck’s MRKAd5 vaccine candidate in either preventing HIV infection or in reducing viral load among volunteers who become infected despite vaccination.

2005

NIAID announces US\$300 million in funding over seven years to establish a virtual consortium known as the Center for HIV/AIDS Vaccine Immunology (CHAVI).

2006

The Bill & Melinda Gates Foundation awards \$287 million to establish the Collaboration for AIDS Vaccine Discovery (CAVD) that supports 16 AIDS vaccine development centers.

2007

Vaccinations in the STEP trial are discontinued after a data safety monitoring board determines that the vaccine didn’t work. Subsequent data shows that MRKAd5 may have increased the risk of HIV acquisition among a subset of volunteers. Vaccinations in the Phase IIb Phambili trial of the same vaccine candidate, which launched in South Africa in February, are also halted.

2008

Researchers obtain an improved 3D image of the structure of HIV’s surface protein.

The Neutralizing Antibody Center, a partnership of IAVI and The Scripps Research Institute in California, where the center is based, is established to develop vaccine candidates that can elicit bNAbs.

2009

The Ragon Institute, a research collaboration dedicated to finding an AIDS vaccine, is launched with a \$100 million gift.

Results from the RV144 Phase IIb trial in Thailand show that the vaccine candidate reduces the risk of HIV infection by about 31%, providing the first evidence that a vaccine candidate can protect against HIV infection in humans.

For the first time in a decade, researchers isolate several new bNAbs against HIV from the blood of infected individuals.

2011

Results from analysis of immune responses in RV144 expected in September.

1980s

1990s

2000s