Scientists see AIDS vaccine within reach after decades

REUTERS

By Julie Steenhuysen | Reuters – 2 hrs 57 mins ago

CHICAGO (Reuters) - At an ill-fated press conference in 1984, U.S. Health and Human Services Secretary Margaret Heckler boldly predicted an effective AIDS vaccine would be available within just two years.

But a string of failed attempts - punctuated by a 2007 trial in which a Merck vaccine appeared to make people more vulnerable to infection, not less - cast a shadow over AIDS vaccine research that has taken years to dispel.

A 2009 clinical trial in Thailand was the first to show it was possible to prevent HIV infection in humans. Since then, discoveries have pointed to even more powerful vaccines using HIV-fighting antibodies. Now scientists believe a licensed vaccine is within reach.

"We know the face of the enemy," said Dr. Barton Haynes, of Duke University in Durham, North Carolina, and recent director of the Center for HIV AIDS Vaccine Immunology (CHAVI). The research consortium was funded by the National Institute of Allergy and Infectious Diseases (NIAID), founded in 2005 by the National Institutes of Health to identify and overcome roadblocks in the design of vaccines for the human immunodeficiency virus, which causes AIDS. NIAID's funding of CHAVI ended in June.

Unlike many viruses behind infectious disease, HIV is a moving target, constantly spitting out slightly different versions of itself, with different strains affecting different populations around the world. The virus is especially pernicious since it attacks the immune system, the very mechanism the body needs to fight back.

"The virus is far more crafty than we ever thought," said Haynes, who will outline progress in vaccine research at the International AIDS Society's 2012 conference being held in Washington from July 22-27.

FIRST SIGN OF HOPE

Thanks to drugs that can control the virus for decades, AIDS is no longer a death sentence. New infections have fallen by 21 percent since the peak of the pandemic in

1997 and advances in prevention - through voluntary circumcision programs, prevention of mother-to-child transmission and early treatment - promise to cut that rate even more.

Still, as many as 34 million people are infected with HIV worldwide. And with 2.7 million new infections in 2010 alone, experts say a vaccine is still the best hope for eradicating AIDS.

Teams have been working on a vaccine for nearly three decades, but it wasn't until RV144, the 2009 clinical trial involving more than 16,000 adults in Thailand, that researchers achieved any hint of success.

The test of a combination of two vaccines followed several big failures, including the stunning news that Merck's vaccine may have increased the risk of infection among men who were both uncircumcised and had prior exposure to the virus used in the vaccine.

"It had an extremely chilling effect on the whole field," said Colonel Nelson Michael, director of the U.S. Military HIV Research Program at the Walter Reed Army Institute of Research, which led the RV144 trial.

The Thai study tested Sanofi's ALVAC, a weakened canary pox virus used to sneak three HIV genes into the body, and AIDSVAX, a vaccine originally made by Roche Holding's Genentech that carried an HIV surface protein.

Both vaccines had poor showings in individual trials. Researchers were so convinced the Thai trial would fail that 22 scientists wrote an editorial in Science calling it a waste of money.

Then came the shocker. Results of the study published in 2009 showed the vaccine combination cut HIV infections by 31.2 percent. According to Michael and many other experts, the result was not big enough to be considered effective, but its impact on researchers was huge, says Wayne Koff, chief scientific officer of the International AIDS Vaccine Initiative (IAVI) based in New York.

An extensive analysis of the Thai trial published this year in the New England Journal of Medicine offered clues about why some volunteers responded.

The study, led by Haynes, scientists at Walter Reed and 25 other institutions, found men and women who were vaccinated made antibodies to a specific region of the virus's outer coat, suggesting this region provides an important vaccine target.

Preparations are under way for a follow-up trial testing beefed-up versions of the vaccines among heterosexuals in South Africa and men who have sex with men in Thailand.

Once again, the trial will use a Sanofi vaccine, but instead of AIDSVAX, researchers will use a different vaccine candidate with a boosting agent from Novartis.

Michael said it has been a major effort to secure new research partners and funding, including support from host countries, as well as to persuade rivals Novartis and Sanofi to work together. The teams still need to retool the vaccines to work in South Africa, where the strain of HIV is different.

"We're really working as fast as we can," said Michael, who expects large-scale effectiveness studies to start in 2016.

The hope is to have at least 50 percent effectiveness, a level that mathematical modelers say could have a major impact on the epidemic. Michael thinks this might be the pathway for getting the first HIV vaccine licensed, possibly by 2019.

Vaccine experts are equally excited about a vaccine that Michael's team is developing with Harvard University and Johnson & Johnson's Crucell unit, which uses weakened versions of a common cold virus and a smallpox virus.

A study published in February showed this vaccine protected monkeys from a virulent strain of HIV. Animals that did become infected after repeated exposure also had low levels of virus in their blood. Safety studies in human patients are just starting, with large-scale efficacy studies slated for 2016.

NEXT-GENERATION VACCINES

The current crop of vaccines is largely designed to train immune system cells known as T-cells to recognize and kill cells already infected with HIV. While these trials progress, scientists are working on even more advanced vaccines that activate powerful antibodies to prevent HIV from infecting cells in the first place. Both would be administered before a person becomes exposed to the virus.

Most modern vaccines use this antibody approach, but HIV's extreme skill at mutating makes it difficult for specifically targeted antibodies to identify and neutralize the virus.

Teams led by Dr. Dennis Burton of the Scripps Research Institute in La Jolla, California, Dr. Michel Nussenzweig at Rockefeller University in New York, Dr. Gary Nabel of NIAID's Vaccine Research Center, Haynes at Duke and others have focused on rare antibodies made by 10 to 20 percent of people with HIV that can neutralize a broad array of strains.

Researchers think a vaccine that can coax the body into making these antibodies before HIV exposure would offer a powerful foil to many forms of the virus.

Such antibodies seek out and latch on to regions of the virus that are highly "conserved," meaning they are so critical to the virus that they appear in nearly every HIV strain. By attaching to the virus they make it incapable of infecting other cells.

Until 2009, scientists had identified only a few broadly neutralizing antibodies, but in the past few years teams have found dozens.

So far, scientists have isolated the antibodies, identified what part of HIV they target and even know the exact shape they make, Koff said. Researchers are now using this information to design vaccines that prompt the immune system to make them.

"We're not there yet," Nabel said.

NIAID this month said it will spend up to $186 million over the next seven years to fund the Centers for HIV/AIDS Vaccine Immunology & Immunogen Discovery. The new consortium is focused on making vaccines that induce these protective antibodies, with major grants going to Duke and Scripps.

Nabel said no vaccine being tested today "is likely to hit it out of the park," but many researchers do feel advances in broadly neutralizing antibodies are key to developing a highly successful HIV vaccine.

"It's really a new day when we start to think about where we are with AIDS vaccines," Nabel said.

(Editing by Michele Gershberg and Prudence Crowther)