iavi AIDS Vaccine Q&A

The world faces one of the greatest public health threats in six centuries: HIV/AIDS. Scientists and public health experts believe that only through a combination of prevention, treatment and care plus broad global access to a preventive vaccine can the global epidemic be ended.

What is a vaccine?

A vaccine is a substance that teaches the body to recognize and defend itself against organisms that cause disease. A vaccine causes a response from the immune system, the body's defense system, that prepares it to fight, and leaves a memory of how to fight, in case of exposure to a specific infection. A vaccine is not a cure but rather prevents infection or slows the progression of a disease in the event infection occurs.

Why are vaccines important?

Disease prevention through immunization is not a new concept; vaccines have been around for hundreds of years. The first modern vaccine was developed in 1796 by Edward Jenner to prevent smallpox. Every year, vaccines prevent up to 3 million deaths and save 750,000 children from disability. With the exception of clean drinking water, no other human health intervention has had the impact of vaccination on reducing infectious diseases. Through vaccination, smallpox, which once killed about a million people a year in Europe alone, has been eradicated globally. Polio is close to elimination, thanks to vaccines. Other vaccines—including those for rabies, tetanus, measles, mumps, and hepatitis A and B—when used as part of national immunization campaigns, save millions of lives and millions of dollars in health care expenses. What's more, immunization has been documented as one of the most cost-effective means of improving public health.

Are vaccines 100% effective in preventing disease?

No vaccine is 100% effective. In fact, most vaccines protect between 70% and 95% of those vaccinated against the targeted disease. This is the concept of partial efficacy. A vaccine does not have to be 100% effective to have a large impact on public health in a community if a significant segment of the population receives the vaccine. Some statistical modeling suggests that, for example, an AIDS vaccine with 50% efficacy given to 30% of the population would avert 5.6 million new infections in low- and middle-income countries between 2015 and 2030.

Successful mass vaccination programs also create so-called herd immunity. If enough people in a community are vaccinated with an effective vaccine, there are statistically fewer chances for an infectious disease to be transmitted, thus lowering the risk of infection for people who have not been vaccinated and for individuals for whom the vaccine is not effective.

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What is the difference between a preventive and a therapeutic AIDS vaccine?

In common parlance, "vaccine" typically refers to a preventive vaccine. A preventive vaccine is designed for individuals who are not infected with the targeted pathogen, for example, HIV. The vaccine would either prevent the individual from becoming infected when exposed to the virus, or if infection occurs, the vaccine would slow the progression of disease. A therapeutic HIV vaccine would be designed to reduce the impact of HIV/AIDS in individuals already infected with the virus.

Why is there a need for a vaccine to prevent HIV/AIDS?

Data from countries with ongoing HIV/AIDS prevention and/or treatment and care programs demonstrate that these initiatives alone are not enough to end the global epidemic. Today only 42% of those who need life-prolonging antiretroviral (ARV) drugs have access to them. And for every two people who receive ARVs, another five people become newly infected with HIV. History suggests that with major epidemics of infectious diseases, like smallpox and polio, only mass immunization programs with an effective vaccine can bring an end to epidemics. Today's medicines against HIV/AIDS are not cures. They are highly expensive, in part because they must be taken every day for life. A vaccine should be seen as part of a comprehensive response to HIV/AIDS. In order to curb or stop the global epidemic, both short-term and long-term solutions must be used. Short-term solutions include scaling up prevention campaigns such as education on safer sex, making male circumcision available and safe, ensuring treatment of the millions already infected, and mitigating the socio/economic impacts of the epidemic. The long-term solutions depend on developing new prevention methods including a preventive AIDS vaccine. As the World Bank emphasizes, investment in cost-effective interventions that prevent transmission of communicable disease—specifically vaccines—is one of the best uses of scarce public funds. What's more, we know from history that no major viral epidemic has been defeated without a vaccine.

How would an AIDS vaccine work?

An effective AIDS vaccine would teach the body to recognize the human immunodeficiency virus (HIV) that causes AIDS and provoke an immune response that would defend against the virus if it entered the body. The information on how to defeat the virus would become part of the immune system's memory; the immune system would be prepared to fight back every time it encounters the virus.

Why do scientists believe a preventive AIDS vaccine is possible?

Data from a recent Phase III AIDS vaccine trial in Thailand showed for the first time that an AIDS vaccine can reduce the risk of HIV infection in humans. Previously, the field had evidence of feasibility for an AIDS vaccine in animal models—but now we know that an AIDS vaccine candidate can also provide benefit in humans. The trial, conducted by the U.S. Military HIV Research Program and the Thai Ministry of Public Health, indicated that a prime-boost combination of two AIDS vaccine candidates reduced the risk of HIV infection by about 30%, but did not have any effect on the amount of virus in individuals who became HIV infected after vaccination. These results will help guide ongoing and future AIDS vaccine design and development efforts.

In addition, researchers know that the immune systems of some individuals have a natural ability to prevent infection with HIV. In other individuals, the immune system appears to control the progression of the disease. What's more, some HIV-infected individuals produce antibodies that are capable of neutralizing the majority of strains of HIV circulating in the world today; these antibodies, injected into non-human primates, work like an effective vaccine.

Why isn't an AIDS vaccine currently available?

Developing a vaccine is never easy; it took 47 years from the discovery of the polio virus to the development of a polio vaccine. With chicken pox it took 34 years. The vaccine for rotavirus, which causes diarrheal disease, took 25. HIV was discovered in 1983 and we've only had a serious AIDS vaccine effort for about a decade. To date, only three experimental AIDS vaccines have completed efficacy testing.

Developing a vaccine to prevent HIV/AIDS is particularly challenging given that HIV is one of the most complicated viruses ever identified. HIV targets and destroys the very immune system that a vaccine traditionally triggers. And the genetic instability of HIV is daunting: millions of viruses are constantly produced and their mutation rates are spectacular. The immune system is presented with an endless stream of new forms of the virus that it is unable to recognize and control.

There are other scientific challenges to AIDS vaccine development, including the lack of a fully adequate model for early testing of candidates in animals. There are questions of what will be the most effective approach or combination of approaches to triggering an immune response to HIV: cellular, humoral or mucosal. And finally, it is yet unknown whether a single universal vaccine can create immunity against the different subtypes, or clades, of the HIV virus, or if a different vaccine must be developed against each clade.

For private sector vaccine developers, a major disincentive for capital investment in AIDS vaccine research is the fact that the primary markets for a vaccine would be in the poorest countries in the world—those least likely to have the resources to ensure a reasonable return on investment.

Can an AIDS vaccine cause AIDS?

No. The preventive AIDS vaccines currently in human trials do not contain any live virus that could result in HIV infection, thus they cannot cause AIDS. These vaccine candidates contain only harmless particles or copies of particles of the HIV virus—enough to trigger the body's immune system but not cause disease. They are so-called recombinant vaccines that use genetically engineered components of HIV. These vaccines are something like a motor car with the engine removed. They are still recognizable as a car but can't drive.

How is an AIDS vaccine tested?

Vaccines and other pharmaceutical products are tested in stages, each taking a number of years. Initial laboratory work—to establish a scientific concept or platform for research—is followed by animal studies to establish overall safety. Only then can human clinical trials take place. During the human trials, the candidate vaccine is tested in volunteers to continue to evaluate safety and effectiveness.

There are three stages or phases of human clinical trials. For an AIDS vaccine specifically, Phase I involves a relatively small number of healthy HIV-uninfected adult volunteers at low risk of HIV infection. Phase I tests for safety. Phase II involves about 200 to 500 healthy HIV-uninfected adult volunteers, some of whom are at higher risk of HIV infection. Phase II tests for safety, an immune system response, as well as early information on required dose and route of administration of the vaccine. Phase III trials involve several thousand adult volunteers at high risk of HIV infection to assess the efficacy of the vaccine in preventing HIV infection and AIDS.

Who participates in AIDS vaccine trials?

Adult volunteers who meet the health and risk criteria outlined in the trial protocol and who give informed consent can participate.

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Who is involved in obtaining approval to conduct a vaccine trial?

To obtain approval to study a vaccine candidate in humans, a comprehensive package of preclinical and manufacturing data must be submitted to the appropriate national regulatory agencies for review. In the United States, for example, the Food and Drug Administration must review and approve every investigational new drug (IND) application. Each participating institution or trial center also must obtain study approval from its institutional review board or ethics committee. Depending on the country, the review process can take several months or more. Often the vaccine developer will have to supply additional information or revise sections of the proposed trial protocol.

How are the rights of volunteers in AIDS vaccine trials protected?

There are established international guidelines for ethical treatment of all volunteers in pharmaceutical and vaccine trials. These guidelines are reinforced by an independent review system on a national and trial-site basis. All potential volunteers must be counseled on informed consent—a written agreement to participate in a trial based on the volunteer's complete understanding of all relevant information. Sponsors of clinical trials must demonstrate that they will employ only competent and highly trained research staff and will take all the steps needed to maximize the confidentiality of volunteers. Throughout the trial, volunteers in an AIDS vaccine trial receive extensive counseling on how to reduce their risk of exposure to HIV as well as access to prevention methods such as condoms. A volunteer can decide to leave the study at any time without explanation.

Does every volunteer in a trial recieve the vaccine candidate?

Usually, no. To test the effectiveness of the candidate vaccine, most trials are designed to include a control group. Volunteers in the control group receive a placebo, which is a substance that looks just like the vaccine but is inactive. Assignment to the vaccine or placebo group is done randomly and neither the volunteers nor the researchers know who has been given the placebo or the vaccine until the end of the trial; this is known as blinding. Blinding is done to minimize the chances that volunteers will alter their behavior because they've received the vaccine, for instance, or that researchers will make assumptions about how volunteers are faring based on whether they received the vaccine or placebo.

What sort of side effects might an AIDS vaccine trial volunteer experience?

Some volunteers may experience pain, tenderness, redness or swelling at the injection site, or mild flu-like symptoms such as headache and fever. Some volunteers may experience no side effects at all. Vaccine trials are carefully monitored to ensure the safety of the participants.

How many AIDS vaccine trials are ongoing today?

Today, there are approximately 30 AIDS vaccine candidates undergoing clinical testing in humans. For detailed information about ongoing and past AIDS vaccine trials, including a candidate's design, composition, and manufacturer, we encourage you to visit the IAVI Report trial database, available at http://www.iavireport.org/trials-db.

This information was developed in collaboration with the International AIDS Vaccine Initiative and the Kaiser Foundation. This Q&A is a part of the "HIV/AIDS Reporting Guide" produced by the Kaiser Family Foundation, November 2009. The full guide can be found online at http://www.kff.org/hivaids/ReportingGuides.cfm.