Research Update

Although the number of annual AIDS-related deaths has declined in the United States for the first time since the beginning of the epidemic, people continue to become infected with HIV. Prevention efforts have been successful in reducing rates of infection among some populations, but many people believe that developing a vaccine to protect people from HIV infection is the only way to stop the epidemic.

Historically, vaccines have been one of the most cost-effective and useful ways to control, if not eradicate, infectious diseases, including smallpox, yellow fever, measles, tetanus, diphtheria, and polio.\(^1\)

There is currently no vaccine proven to provide effective protection against HIV infection, but many researchers believe that one can be developed. There is evidence to support the feasibility of an HIV vaccine: experiments in which chimpanzees and monkeys were injected with vaccines similar to those targeting HIV have been somewhat successful; some people’s immune systems are capable of preventing HIV infection after multiple exposures or of delaying disease progression after infection, suggesting that a similar immune response can be induced in other people; and based on preliminary results of current HIV vaccine research, some vaccines have been able to induce partially effective immune responses in humans.\(^2\)

The potential ability of a vaccine to protect people from HIV infection for a fraction of the cost of treating the disease has also underscored researchers’ and government interest in developing an HIV vaccine. In the United States alone, caring for people living with AIDS costs approximately $15 billion annually,\(^3\) with the current cost of combination antiviral drug therapies ranging from $12,000 to $15,000 per patient each year.\(^4\)

Vaccine Basics

There are two main types of vaccines: a preventive vaccine protects people from HIV infection, but...
the body from infection, and a therapeutic vaccine strengthens an infected person’s immune system. This issue of PERSPECTIVES focuses primarily on preventive vaccines because research for this type of vaccine is currently at a more advanced phase than it is for therapeutic vaccines.

Effective preventive vaccines work by inducing the immune system to resist foreign and infectious substances, called “pathogens,” in the body. When the immune system encounters a pathogen, it can respond in two ways to protect the body: a “humoral immune response” produces antibodies in a person’s bloodstream to neutralize pathogens; a “cellular immune response” causes certain cells within the body to kill the pathogen or to kill the cells that have been infected by a pathogen.

HIV can exist in the body as either a free-floating virus in the bloodstream, which is detectable by antibodies, or within infected CD4+ cells, against which only a cellular immune response might prove effective. Some researchers believe that an ideal HIV vaccine would elicit both types of immune responses. An ideal HIV vaccine would also be relatively inexpensive, be easy to administer, require few doses, be able to induce long-term immunity to various strains of HIV, and have few side effects.

Vaccines can take many forms, including a weakened but live pathogen, a dead pathogen, or a protein section of the pathogen. Because of the nature and complexity of HIV, however, developing a vaccine has proven to be especially challenging.

First, scientists do not completely understand how the body’s immune system interacts with HIV, especially the mechanisms that cause the virus to elicit an effective immune response. In addition, HIV can mutate into different genetic variations, making it difficult for scientists to create a vaccine that effectively responds to this diversity. HIV can also enter the body through two major pathways: the blood, as in the case of infection through injection drug use, and through mucosal membranes, as in the case of infection through sexual intercourse. Little is known, however, about how to generate immune responses in mucosal membranes, such as in the mouth, rectum, and vagina.

Scientists researching and developing HIV vaccines incorporate findings from genetic engineering, biotechnology, and vaccine research for other infectious diseases. To date, there have been more than 40 different HIV vaccine trials that have enlisted more than 2,000 participants worldwide.

Vaccine Trials

As is true for drug treatments, once a potential HIV vaccine has proven its safety and ability to induce an immune response in the laboratory and in animal trials, it must successfully complete three phases of human testing before the U.S. Food and Drug Administration (FDA) can approve it for widespread use.

In Phase I, researchers recruit 20 to 80 participants who have little or no risk for HIV infection to assess safety and biological activity. Testing of large numbers of participants, usually in the hundreds or thousands, to determine the vaccine’s effectiveness and to further evaluate potential side effects and safety risks.

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Three Phases of HIV Vaccine Clinical Trials

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<td>Testing of a small number of participants, usually between 20 and 80, at low risk for HIV infection to assess safety and biological activity.</td>
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<td>Testing of several hundred to several thousand participants at high risk for HIV infection to further examine safety and immune effects of the experimental vaccine.</td>
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without producing significant adverse reactions in the body progression to Phase II trials. These trials enroll up to a few hundred people, some of whom are at higher risk for HIV infection than Phase I participants. The larger study sample allows researchers to further examine potential safety and immune effects of the vaccines. Phase II trials typically last between one and two years.6

Phase III vaccine trials enroll hundreds or thousands of high-risk participants to determine if the vaccine works, to what extent it offers immune protection, and if there are any side effects or safety risks that were not identified in previous smaller study samples. Because of the large scale of Phase III trials, they can take up to five years to complete.6

Vaccine trials are most effective when they are “randomized” and “double-blinded.” Randomized means that study participants are randomly sorted into control and experimental groups, and double-blinded means that, until the study is completed, neither subjects nor researchers know who is receiving the vaccine and who is receiving the placebo. A randomized and double-blinded trial helps to ensure that the results remain as unbiased as possible.6

Another important aspect of vaccine trials involves the process of obtaining “informed consent” from study participants. Ideally, informed consent allows participants to understand exactly what occurs in the study so that they may be aware of and comfortable with their risks. By giving informed consent, study participants acknowledge the potential risks, benefits, and procedures of the trial while reserving the right to withdraw from the trial at any time.7

The Current State of HIV Vaccines

The only experimental HIV vaccine to enter a Phase III trial is the AIDSVAX vaccine. In the coming years, however, many more potential vaccines are expected to advance to Phase III trials. A product of VaxGen, Inc., the AIDSVAX vaccine contains synthetic copies of two of the proteins found on the surface of HIV, which scientists hope will induce large-scale antibody production in trial participants. Because AIDSVAX does not contain any whole or live HIV, there is no risk of becoming infected directly from the vaccine. Although it is still unclear how effectively the vaccine-induced immune response can protect against the virus, or against how many strains of HIV this vaccine can provide protection, earlier Phase I and Phase II clinical trials have found that the AIDSVAX vaccine is generally well-tolerated and can produce an antibody response in some vaccine recipients.8

The AIDSVAX trial, which entered Phase III in the summer of 1998, is currently recruiting and enrolling uninfected gay and bisexual men and high-risk heterosexual women. Trial participants must be between the ages of 18 and 60 and must not have received other experimental HIV vaccines. Because the purpose of the trial is to determine the experimental vaccine’s effectiveness at preventing HIV that is transmitted sexually, injection drug users are not eligible to participate. VaxGen is conducting a separate trial in Thailand for injection drug users.3

VaxGen plans to enroll at least 5,000 volunteers for the U.S. AIDSVAX trial, which is being conducted in 40 to 50 cities in the United States, Canada, and Europe. Trial locations in California include Orange, Palm Springs, Sacramento, San Francisco, San Jose, and West Hollywood. Trial participants receive a series of seven injections into the muscle of the upper arm over the course of 30 months.3

Because the presence of a vaccine can cause the body to produce HIV antibodies, trial participants who test for HIV at test sites that are not affiliated with the trial might receive HIV-positive results without actually being infected.
response induced by the original vaccine injection.6

Throughout the study, participants receive risk-reduction counseling and HIV testing every six months with additional or more frequent counseling and testing available upon request.3 Because the presence of a vaccine can cause the body to produce HIV antibodies, trial participants who test for HIV at test sites that are not affiliated with the trial might receive HIV-positive results without actually being infected. Participants, therefore, must agree to test for HIV only within the trial.

Participating in Trials

People choose to enroll in HIV vaccine trials for different reasons. In a study of high-risk men and women, 77 percent of respondents reported that they were definitely or probably willing to participate in an experimental HIV vaccine trial. Many of these respondents indicated that finding an effective vaccine, giving back to their communities, and doing something to honor people who are infected with HIV or who have died of AIDS were important factors in their willingness to participate in a vaccine trial. On a more personal level, respondents indicated various benefits influencing their willingness to participate, including receiving current information about HIV research, increasing motivation to avoid risky behaviors, and the possibility of receiving protection from HIV infection.9

In a similar study, 91 percent of young gay men reported that they wanted to receive an HIV vaccine once it had been developed, but 37 percent of these respondents stated that they would not be likely to participate in a vaccine trial if given the opportunity. Reasons for this reluctance included fear of potential side effects, the possibility of receiving a placebo instead of the experimental vaccine, fear of risk of becoming infected, mistrust of the government and pharmaceutical companies, the possible temptation to have unsafe sex, and the possibility of testing positive for HIV antibodies without actually being infected.10

Related Issue: The Ethics of HIV Vaccine Trials

Now that VaxGen’s AIDSVAX has become the first experimental HIV vaccine to enter a Phase III trial, two ethical debates have emerged: “theorist” and “empiricist” researchers disagree about the appropriateness of human vaccine trials at this time; and some people believe that the methodology of the current AIDSVAX trial is flawed.

Some scientists and public health advocates believe that it is too early for potential vaccines to be tested in human clinical trials. These theorist researchers argue that because so much is still unknown about HIV, including how it affects the immune system, further laboratory and animal research and testing is necessary before conducting large-scale human trials.14 The underlying assumption behind this argument is that it is unethical to allow people to enroll in vaccine trials when available knowledge of HIV is so limited.

In opposition to the theorist argument, empiricist researchers and other public health advocates believe that it is too early for potential vaccines to be tested in human clinical trials. These theorist researchers argue that because so much is still unknown about HIV, including how it affects the immune system, further laboratory and animal research and testing is necessary before conducting large-scale human trials.14 The underlying assumption behind this argument is that it is unethical to allow people to enroll in vaccine trials when available knowledge of HIV is so limited.

In opposition to the theorist argument, empiricist researchers and other public health advocates claim that, because of the unyielding nature of the epidemic, scientists should proceed with cautious and practical Phase III testing of experimental HIV vaccines. Although a specific vaccine trial may not be successful, the knowledge and experience gained from human testing, the empiricists claim, will increase the likelihood of developing an effective HIV vaccine in the future.14

HIV vaccine trials also pose ethical challenges to the method scientists use to determine if potential vaccines work. Researchers evaluate the effectiveness of the vaccine they are testing by comparing the rates of new infections within the experimentally vaccinated group to those in the control group, who received placebos. If a vaccine is effective, there should be a significant decrease in the rates of new infections within the experimental group. Some people consider this practice to be unethical because determining the vaccine’s effectiveness requires participants to be exposed to HIV.4 Researchers, however, cannot legally expose vaccine trial participants to HIV infection or intentionally place them in situations with high risks for infection. In fact, VaxGen’s Phase III trial requires all participants to undergo extensive HIV risk-reduction counseling throughout the trial.

On the other side of this debate is the belief that mandatory counseling provided by the trial may taint study results because counselors would discuss ways to reduce participants’ risks, thereby artificially decreasing the number of HIV exposures and interfering with researchers’ efforts to assess the vaccine’s effectiveness. Researchers state that any vaccine that may result from this trial would have to be used as a prevention tool in conjunction with, not instead of, HIV risk-reduction counseling.15
Uninfected vaccine trial participants who test positive for HIV antibodies face potential social and personal ramifications, such as discrimination from co-workers, family, insurance companies, and employers and travel and immigration restrictions. Some people may assume that because a person is in a vaccine trial, he or she is at high risk for HIV infection. In addition, a person’s current enrollment in a vaccine trial may affect his or her eligibility to participate in future vaccine trials. It is also unknown how well a person who receives an experimental HIV vaccine now will respond to new vaccines that may be produced in the future.

Some researchers and public health advocates fear that people currently enrolled in or considering enrollment in experimental vaccine trials might incorrectly believe that participating in these trials will protect them from HIV infection, which may cause them to engage in behaviors that place them at greater HIV risk. In a study of high-risk men and women, 74 percent of participants felt that the possibility of gaining some protection against HIV was one of several important factors that would influence their decision to participate in a vaccine trial. A separate study of high-risk gay and bisexual men reported that 37 percent of respondents agreed with the statement that some people might become more sexually active because of their participation in a vaccine trial.

Implications for Counseling

Over the years, many clients have asked counselors about the prospect of a vaccine that would protect against HIV infection. Now that the large-scale trials for the experimental AIDSVAX vaccine are recruiting volunteers, clients are likely to have increased awareness of HIV vaccines, and counselors may need to address questions about vaccines more frequently. It is essential to emphasize that, despite recent progress, there is no evidence of any vaccine’s effectiveness in protecting people from HIV infection, and there is no reason to expect a vaccine to be widely available in the near future.

Counselors are likely to work with clients who are aware of the AIDSVAX trial because advertising to attract volunteers is prominent in many places across the state, and posters and other literature about the trial may be present at sites where clients receive HIV counseling and testing services. Researchers from VaxGen, Inc., which is producing the AIDSVAX vaccine, are targeting their advertising to reach people at high risk for infection, but clients who are not eligible to participate in the trial may also be exposed to AIDSVAX advertising.

Many clients are likely to be curious about HIV vaccine trials, particularly because people who test for HIV are generally those most concerned about HIV. It is the test counselor’s responsibility to answer basic questions and to provide referrals for additional information or counseling support.

Basics about the AIDSVAX Trial

When discussing a subject as complicated as HIV vaccines, it is important for counselors to be as clear as possible and to let clients know that the answers to many questions remain unknown, especially whether or not the AIDSVAX vaccine can effectively protect people from HIV infection. It may be useful to explain that clinical trials, by their nature, involve experimentation with unknown technologies, and that such trials seek to provide clarity to previously unanswered questions. The current AIDSVAX trial is one step in a larger process of determining if the vaccine protects against HIV infection, how it works, and against which strains of HIV it may be effective.

Because of the complexity of the subject and the limited scope of the HIV counseling and testing session, it is particularly important to offer written information and referrals to clients who have questions about HIV vaccines. Test counselors may obtain such information from the HIVInsite web site (see page 3), maintained by the Center for AIDS Prevention Studies (CAPS) at the University of California San Francisco, or by contacting VaxGen, Inc., the company that is developing AIDSVAX, at 650-624-1000. If clients have relationships with physicians or other medical providers who are knowledgeable about HIV vaccine trials, encourage clients to discuss the subject with these providers.

Test site counselors should maintain a neutral stance when

A Counselor’s Perspective

“Clients sometimes incorrectly believe that a vaccine is just around the corner because there is already a large-scale vaccine trial and that, as a result, they can be less concerned about engaging in unsafe behaviors. I clarify this misinformation and explore what it means for them to continue avoiding high-risk behavior.”
discussing with clients the possibility of entering a vaccine trial. It is not the counselor’s role to encourage clients to or discourage clients from entering a trial. Refer clients who express interest in volunteering for a trial to the trial site, and encourage them to obtain and carefully consider information about vaccine trials before deciding whether or not to participate. Also encourage such clients to discuss the subject with their primary health care provider.

One of the conditions of enrolling in a vaccine trial is to agree not to test for HIV at facilities not affiliated with the study because, in doing so, uninfected participants who have developed vaccine-induced HIV antibodies could receive an HIV-positive test result. Such a result could affect the extent to which a person engages in risk behaviors. For instance, receiving a positive test result could affect a person’s level of concern about avoiding risk behaviors based on the belief that he or she is already infected when, in fact, he or she may not be infected. In addition, testing positive for HIV antibodies may lead some trial participants to assume that they have received the vaccine rather than the placebo and that they are therefore protected from HIV infection.

Counselors should know that clients enrolled in an HIV vaccine trial who are seeking testing from a state-funded counseling and testing site are likely doing so against the study’s protocol. If clients seek antibody testing and disclose that they are in the vaccine trial, test counselors should explain that the antibody test may be of limited use and that it will be more effective for clients to test through the study in which they are enrolled.

Counselors should not refuse testing services to a client who is in a vaccine trial, but it may be helpful to explore such a client’s reasons for seeking services at the counseling and testing site. A client who has recently engaged in risk behavior, for example, may be concerned about risk of infection. A client in a vaccine trial may also want to test in order to determine if he or she has received the vaccine or a placebo. In this case, counselors should explain that an HIV antibody test cannot accurately determine this because the vaccine has not been proven to induce antibody production in everyone who receives it.

**Prevention Challenges**

The AIDSVAX trial presents numerous prevention challenges. Perhaps the most difficult is that the trial enrolls only people who are engaging in high-risk behaviors and that the trial makes a splash while humble canarypox Phase II plods along uncelebrated. However, the trial’s success for the HIV vaccine is not yet clear.

**A Counselor’s Perspective**

“Personally, I’m skeptical about the chances of success for the HIV vaccine trial, but if a client wants to participate in the trial, I express neither skepticism nor optimism. Remaining neutral, I provide basic information and referrals and encourage the client to learn more before deciding whether or not to volunteer for the trial.”

### References

at the time of entering the trial; despite the fact that trial staff provide risk-reduction counseling, researchers can determine the vaccine’s effectiveness only if there is a significant rate of HIV infection, which can occur only if trial participants engage in unsafe behaviors.

When clients who are participating in the vaccine trial believe they can engage in unsafe behaviors without becoming infected, explore this belief. Are they seeking to rationalize their behavior? Are they misinformed? Are they informed but being unrealistic? Explore the context of the client’s HIV risk behavior, validate that the information is complicated, provide or clarify information about vaccines as needed, and listen to clients’ responses.

Prevention challenges may also apply to people not involved in vaccine trials. Some clients may incorrectly believe that they no longer need to engage in safer behaviors because of the relatively advanced stage of the AIDSVAX trial. When clients ask about the potential effectiveness of the AIDSVAX vaccine, explain that a consistently effective and reliable vaccine has yet to be developed and is many years from becoming a reality.

People who are partners of trial participants may have questions about vaccine trials. For instance, clients may have sex partners in vaccine trials who, as a result of these trials, test positive for HIV antibodies. Counselors should clarify any misinformation and explain to clients who are partners of trial participants that participating in a vaccine trial does not protect a person from infection even if he or she develops HIV antibodies. This is because the experimental vaccine’s effectiveness has not been proven and because the presence of HIV antibodies does not ensure protection from infection.

In addition, counselors should be aware that trial participants were selected for the trial because they were engaging in high-risk behavior and be prepared to discuss this with clients who are partners of trial participants. Beyond this, counselors should provide some of the basic risk-reduction counseling to these clients as they would anyone other client who engages in risk-related behaviors with a partner who has a history of high-risk behaviors.

**Case Study**

Marcia is a 30-year-old woman who in recent months has been engaging in unprotected vaginal sex with a man who has told her that he has received an “HIV vaccine.” She says that she will likely have sex with this man again, that he wants to have unprotected sex, and that she does not know whether or not to continue doing this. Marcia, who last received an HIV antibody test 18 months ago, says that her relationship with this man is not monogamous and that she believes he is having sex with other people.

**Intervention**

As with any client, assess Marcia’s knowledge of HIV transmission, her perception of her risks, and the sexual or injection drug using behaviors in which she has engaged. Learn about any other sex partners she has had in the past two years. Also learn more about the nature of her relationship with this man, if she is engaging in risk behaviors with other people, and whether or not she knows if her partner engages in risk behaviors with other people.

Ask Marcia what she knows about the context of her partner receiving an “HIV vaccine” and if she has considered the possibility that her partner may not actually be in this trial. Assess Marcia’s knowledge of the current vaccine trial, and clarify the facts of this trial, primarily that trial participants do not know whether they have received the experimental vaccine or a placebo. Explain to her that the effectiveness of the experimental vaccine is unproven, and there is no evidence to indicate that a person who has received it is protected against HIV. Also explain that in order for someone to be selected to participate in the trial, that person must have been engaging in high-risk behaviors at the time of entering the trial. If she was not previously aware of this information, ask how it affects her. Allow time in the counseling session for Marcia to contemplate these points.

Explain to Marcia that regardless of whether or not her partner is participating in a vaccine trial, engaging in unprotected sex with him can place her at risk for infection. Also learn from Marcia if practicing safer sex is something she has thought about and discussed with her partner. If not, ask how she feels about raising the subject with him. If appropriate, engage her in a role play in which she discusses safer sex with her partner.
Test Yourself

Review Questions

1. True or False: Effective vaccines work by inducing the immune system to resist foreign and infectious substances in the body.

2. True or False: HIV can exist in the body only within infected CD4+ cells.

3. True or False: A person participating in an HIV vaccine trial who has developed HIV antibodies is protected against HIV infection.

4. True or False: Vaccines must undergo testing in three phases of clinical trials before they can be approved for widespread use.

5. True or False: A double-blinded study is one in which only researchers know which study participants receive the experimental treatment and which participants receive placebos.

6. Which of the following are potential ramifications for uninfected vaccine trial participants who test positive for HIV? a) discrimination in terms of housing and medical and life insurance; b) discrimination by family and co-workers; c) travel and immigration restrictions; d) all of the above.

7. True or False: Scientists completely understand the mechanisms by which HIV affects the immune system.

8. True or False: Because Phase III clinical trials are so extensive and involve hundreds to thousands of people, it can take several years to process results or information from these studies.

Discussion Questions

1. How can counselors put aside their own biases, including personal ethical concerns, about HIV vaccines in order to provide objective information to clients who ask questions about vaccines?

2. How can counselors respond to clients who incorrectly consider large-scale vaccine trials to be a sign that an effective vaccine will very soon be widely available, and that, as a result, they no longer need to engage in safer behaviors?

3. Which basic facts should counselors know about HIV vaccines?

4. How can test counselors who struggle with scientific concepts gain a basic understanding of HIV vaccines?

5. How can counselors respond when clients who are in a vaccine trial seek services from an HIV counseling and testing program?

Answers to Test Yourself

1. True.

2. False. HIV can exist in the body as either a free-floating pathogen in the bloodstream or within infected CD4+ cells.

3. False. There is no evidence that vaccine-induced antibodies effectively provide protection from HIV infection.

4. True.

5. False. In a double-blinded study, neither the researchers nor the study participants know who is given the experimental treatment or the placebo until after the study is completed. This helps to ensure that results remain as unbiased as possible.

6. d.

7. False. One of the reasons developing a vaccine against HIV is so difficult is because scientists do not yet fully understand how HIV interacts with the immune system.

8. True.
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