

## partially effective vaccines

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**MOST PEOPLE HAVE HEARD** of vaccines. And most of them are taught that getting vaccinated against a particular disease-causing germ (*pathogen*) means they're protected from ever getting that disease.

There's plenty of truth in this simple equation *vaccine = protection*: Many vaccines do provide high levels of long-lasting protection to most people who get *immunized*. But in practice there is no such thing as a vaccine that provides 100% protection, 100% of the time. In this sense *all* vaccines are only "partially effective." Although that may sound worrisome, in practice vaccines are powerful tools for preventing disease, and they bring enormous benefits to individuals and communities.

Still, when it comes to AIDS vaccines, the concept of partial protection can be especially confusing. That's because there are two different ways of defining what we mean by this term.

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## what could a partially effective AIDS vaccine do?

The first, more easily understood definition of a partially effective vaccine is one that protects some people in a population, but not others. This is possible because many factors affect our immune systems and, by extension, our ability to respond to vaccines. It's in this sense that most licensed vaccines are partially effective. Many of them protect as many as 80 or 90% of individuals in a population. Others, like oral cholera vaccine, give lower levels of protection but still have a positive effect on health in communities where they are widely used. A textbook example is the original Salk polio vaccine, which is only about 60% effective. This may seem low, but within a few years of its introduction in the US—and even though many people didn't get vaccinated—it caused a dramatic drop in the number of new polio infections.

Vaccines that induce cellular immunity may not block infection but could help the body fight HIV after infection.

The second definition of partial protection describes a vaccine which doesn't completely prevent infection by a pathogen but helps reduce the severity of the disease it causes. An AIDS vaccine of this type would reduce the severity of HIV disease in vaccinated people who later became infected through blood or sexual exposure.

While either (or both) of these definitions could apply to an AIDS vaccine, the second, less well-understood one is now getting most of the attention. That's because most of the vaccine candidates being tested in *clinical trials* are designed to induce *cellular immune* defenses, which act against HIV only after it has entered the body and infected its target cells. So instead of preventing infection in the first place, these vaccines are more likely to improve the immune system's ability to fight the *virus after* infection. They would do this by slowing viral activity and protecting the immune cells (especially *CD4+ T-cells*) which HIV infects and destroys. These defenses could also help to control the amount of virus circulating in the body (*viral load*).

A vaccine that lowers viral load and helps people preserve their CD4+ T-cells could benefit them in several ways. It could allow them to live with HIV for longer periods of time without

getting sick. It could also prolong the time until they needed to start *antiretroviral therapy* (ARV). Each person reaches this point at a different time after infection, and an AIDS vaccine could help extend this period.

It could also have important benefits at the community level. People with low viral loads are less likely to transmit HIV to their partners during unprotected sex or to their infants during pregnancy and childbirth. If enough people in a community or country were vaccinated, these effects could help slow the spread of the epidemic in the region.

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#### how can we test for partially effective vaccines?

Even without a vaccine, people usually don't get sick for five years or more after HIV infection. So clinical trials that directly measure whether an AIDS vaccine extends this healthy phase would have to go on for ten years or even longer. To get faster answers, the less-than-perfect alternative is for trials to look at indirect measures of HIV's effects, especially viral load and CD4+ T-cell count, in volunteers who become infected through high-risk contact. Based on past history with natural infection and with patients on ARVs, these data should give an earlier indication of whether or not the vaccine will affect disease progression or infectiousness.

A vaccine that improved health for people who became HIV-infected would be a major breakthrough, and would probably get licensed for general use. But even after licensure, researchers would continue studies to answer crucial questions: How long does vaccine-induced protection last? How much of a reduction in viral load is needed to translate into long-term health benefits for the individual? How much of a reduction will reduce the risk of transmitting to another person?

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#### preparing for partial efficacy

Although imperfect, partially effective vaccines that reduce the severity of disease but don't prevent infection could be

powerful tools for fighting HIV. Their success depends on establishing realistic expectations and broad understanding of their benefits and limitations. At least two key messages will have to be conveyed:

- › Since these vaccines won't protect against HIV infection, they cannot be considered a replacement for other methods of prevention, including male and female condoms and a *microbicide* (if one is developed). It will be very important to convey this message so that people don't assume they are protected and increase their risk behaviors after being vaccinated.
- › This type of vaccine will not replace or even reduce the need for comprehensive HIV prevention and treatment programs. In fact, it will be most effective when it's promoted as one of several strategies for fighting the epidemic.

MANY GROUPS are already working on ways to convey these messages to different audiences, including governments, public health agencies, and people thinking about how an AIDS vaccine will be used. This involves thinking about ways to explain the concept—for instance, drawing a comparison between partially effective vaccines and family planning methods like condoms, hormonal contraceptives and diaphragms. No single method is 100% effective, but used in combination, these methods can provide very high levels of protection.

Clear understanding of these vaccines also involves studies designed to figure out where a partially effective vaccine would be most useful. For example, some statisticians and public health experts are working out different scenarios to model the impact of a partially effective vaccine in countries with well-established versus emerging epidemics, and in people with different types of risk factors for HIV.

A good, partially effective vaccine would be a huge advance towards controlling the epidemic and making an improved or combination vaccine that could do even better.