Our Best Shot

The key to developing an effective preventive and therapeutic vaccine lies, in part, in advocating for increased spending on vaccine research. POZ *editor-in-chief Regan Hofmann talks with Seth Berkley, MD, president, CEO and founder of the International AIDS Vaccine Initiative (IAVI), about what we need to find a vaccine.*

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It's clear that treatment and prevention efforts alone can't end the AIDS pandemic. Treatment delivery fails to meet the global need, and more people than ever before are living with HIV. But a vaccine—preventive and/or therapeutic—has eluded scientists for nearly 30 years.

On the heels of some hotly debated good news from a recently concluded vaccine trial in Thailand, Seth Berkley, MD, who heads the New York City–based International AIDS Vaccine Initiative (IAVI), sheds light on whether we're getting any closer to developing an AIDS vaccine. The news is surprisingly good—including for those of us already living with the virus.

Given the debate about whether to spend money on prevention, treatment or vaccine development, how do you make the case for increasing spending on vaccine research?
For every two people on treatment there are five new infections. As long as that number is out of whack it's going to be a problem to provide treatment for everyone who needs it. No matter how successful we are in raising resources, we're going to have continually more people who need treatment and we're going to end up with increasing numbers of people who require second line therapy and/or who have problems with toxicity.

No matter how committed you are to treatment—which we all must be—if you continue to have many more infections, you're going to overwhelm any system that you put in place. So it isn't an either/or situation for treatment versus vaccine research. Both must get prioritized. The challenge is to keep a short-term focus that includes treatment and prevention while making make better tools to fight the epidemic long term.

Why is developing a vaccine for HIV so hard?
HIV has characteristics that make it really a tough virus. The virus is constantly changing, which means it can get around any type of pressure that's put on it. The virus has also found a way to coat itself with sugars that make it [impervious to the body's] immune response. (The virus has a bunch of decoys that stick up where most of the immune response is targeted.) If HIV gets into the body and into the cells and really takes hold, it's very difficult to get rid of. That being said, we can

fully protect animals with vaccines, and we know that [some] people's bodies can hold the virus in check for long periods of time. The challenge is converting the knowledge we have into a vaccine that's practical and usable.

Who funds IAVI's research?
IAVI is [a social venture capital firm and is] supported by 12 governments, a number of philanthropies, companies and individuals. We're trying to diversify that funding further—especially at a time like this when there's a financial downturn. For the first time in nine years, funding for vaccine research is down—falling by 10 percent from 2007 levels.

Are we any closer to finding a vaccine?
People believe we've been working on [an HIV] vaccine for 25 years. That's not really true. We had an initial burst of activity, and then we had a low level of effort for some time. We're just beginning to have a serious effort again. When we started, we thought we would follow the normal pathways of development. That didn't work. This is a difficult virus. We've had to go back and really understand the problems that have blocked HIV vaccine development. What's exciting about the breakthroughs announced recently—including the results of the research in Thailand—is that we've begun to understand some of those problems. We're in a renaissance of AIDS vaccine development. We're going to have a lot more scientific breakthroughs.

It's still very hard to predict exactly when a solution is going to come—when we will have that eureka moment—but we are solving problems that are necessary [to address] to get there. The recent finding of broadly and very potent neutralizing antibodies is an example of my point. If people have those antibodies before they are exposed to the virus, they're likely to be protected. Knowing that humans can make those antibodies tells us that if you could stimulate [the body to produce] those antibodies through an artificial means—say through a vaccination—you would be able to get the type of protection that you need. That's really where the field is going.

Are researchers looking for a therapeutic vaccine as well as a preventive one?
We're working on multiple candidates simultaneously. There's been more financial interest in developing therapeutic vaccines because you can charge a lot more money for them. That being said, there's not a precedent for [developing] therapeutic vaccines. As we understand how to get really robust protection through vaccination it will affect treatment. [For example,] if you could put populations [of positive people] on maximum antiretroviral therapy to get [their] viral loads to nonexistent levels and then somehow reinstate the immune system and get specific HIV immunity and then remove the drugs…you might be able to hold [the virus] in check.

You have said it is difficult to test vaccines among the population of HIV-positive people. Why is this so?
If you test [a vaccine] among people who are HIV positive and the vaccine doesn't work, you have to ask whether it's because it doesn't work or whether the immune systems of people living with HIV are compromised. That's why testing vaccines first in those that have intact immune systems and understanding what protection is required [to prevent infection] is scientifically a better way to work.

What are the ethical challenges of conducting vaccine trials—especially in the developing world?
I don't think that AIDS vaccine trials really are an ethical challenge. People say it is unethical to expose people to HIV, but vaccine trials don't do that. What we do is go into a population that's at risk and give them the maximum amount of counseling possible and the necessary tools to prevent infections.

Interestingly, when this was first debated, some people said vaccine trials would be unethical because if you told people they'd be given a vaccine that might work, they would engage in high-risk behavior. The other side said if you taught people prevention strategies, there would be no infections. The best example of this is the original VaxGen trial that started off with an incident rate of about 3 percent. That rate went down to about 2.1. Slowly it began to climb during the trial but didn't [go above] 3. So the people in the trial benefited because the incident rates went down. They were trained; they were [educated]; and they didn't have higher risk behavior. And frankly, if that worked alone, we wouldn't need a vaccine. But not everybody can [use prevention measures] all the time. I think part of [what makes an ethical trial] is having informed consent. In the international setting, it's making sure the counselors are peers and making sure the people really understand what they're doing. What's interesting to me is people say it's [unethical to test vaccines in the developing world] yet those populations want to be part of this—they want to be part of the solution.

When we look at our failures on a prevention front, how big of a role does stigma play?
One of the challenges, especially in the developing world, is people won't step forward for treatment, for testing or to access prevention strategies. It would be much easier with a non-sexualized, non-stigmatized disease. So trying to reduce that stigma is important. Interestingly we've had a role in many countries in opening up dialogue [about HIV]. If you have a conservative government that doesn't want to talk about sex, risk factors and other issues, [then you have to talk to them in terms of science, which is acceptable]. Vaccines are non-stigmatizing. They could be for anyone. They're not targeted to a specific group like some of the other interventions might be.

In South Africa, we had a terrible problem with people being honest and talking about HIV/AIDS. It's now better there. In India it is much better. One of the critical things that is occurring is people are trying to destigmatize HIV/AIDS. And the more we can successfully do that, the more we can make HIV mainstream, [the easier it will be for us to pursue a vaccine].

Do you think that there's a rift in how the HIV vaccine research is portrayed in the media and what you're actually experiencing?
Absolutely. When IAVI started, vaccines weren't a priority. People weren't focused on them. The activist community was rightfully saying, "We're going to die if we don't have treatment." AIDS activists chained themselves [to buildings] and threw [fake] blood on the researchers and said, "You've got to focus money on [AIDS drugs]." We now have more drugs for HIV than any other virus. That's the power of science: If you focus a large amount of money and attention on a scientific problem, you are more likely to solve it.

Where has the media failed?
Because an AIDS vaccine is so important, when an HIV trial doesn't work it's front-page news. And people say that's the end of it. The development of most vaccines is a process. You expect failure after failure. In malaria I think we've tested 47 or 48 vaccines. I hope we don't have to go through 48 vaccines [for HIV], but it's crazy to think that we would have a successful one in the first shot…no pun intended.

One of the challenges is how we balance our short-term and long-term needs. For the world, there's no question the vaccine is the best single way to solve the problem of HIV overall. On the other hand, there isn't enough incentive to invest in it, and there aren't enough champions. Vaccine research hasn't become a rallying cry for parents who say [for example], "My children are at risk; we need a vaccine." [People are more apt to say], "I don't want to discuss it." That's the greatest problem that we have. Without a constituency [behind vaccine research], it is less likely to get funded.

If you could have three things happen in the next year to further your cause, what would they be?
Build a world of advocates that care about the long term. The goal is to end the epidemic. There are interim goals, like getting rid of stigma—but ultimately we want to wipe this epidemic off the face of the earth.

Second, we really need unrestricted long-term money. Long-term [support] is even more important than the amount because we need to focus on this as a long-term problem. You need to set the infrastructure, consortiums, studies and vaccine designs [to have success], and to do that takes a really long time.

Third, to get the best scientists all over the world working on this. At IAVI, we are making a real effort to bring innovation into the field. People must see HIV/AIDS as a real problem. We need the finances to [support the exploration of] high-risk ideas so the process can move forward.

What would happen with the major pharmaceutical companies if a vaccine proved effective? Would they manufacture it? How would people get it?
People who make drugs and people who make vaccines are often at different companies. So I don't buy the idea that people aren't making vaccines because they have a good drug market. The problem is the science is extremely difficult. It's politically controversial. It doesn't make sense for pharmaceutical companies to invest large portions of their shareholders' resources in [this field]. So they've moved away from it. In a situation where we do have success and products are looking promising, I believe they will come back.

It's expected that the HIV vaccine would have to be made available to all those who need it. And we don't necessarily have funding mechanisms to do that. We have to strengthen delivery of our other lifesaving vaccines, because they aren't necessarily getting to the people who need them. The more we can strengthen global health and global health systems, the more mechanisms we will have for delivery. You can't use traditional mechanisms. We haven't even begun to tackle that

aspect of vaccinating the world against HIV.

What do you consider to be your greatest accomplishment?
Empowering African scientists to do work that is as good, if not better, than the work in the West. People didn't believe that could happen. We're beginning to build [an impressive] network of scientists from the northern and southern hemispheres. This is not only important for HIV but also for how we are going to work in the future. I'm very proud of the women and men involved in that network.

Do preventive vaccines matter to people living with HIV?
I certainly hope everybody in the HIV community understands how important this is for them. It's critical that we get the best tools we possibly can and that we prevent [future] infections. The knowledge that is gained from understanding the body's [immune response to HIV] is going to [help] design better drugs, targets and therapeutic vaccines, which will be used to treat people and get them off drugs. That knowledge is going to be critical for sustaining the lives of those who are infected. I think that having an interest in vaccines is critical [for the whole world] and that those who are already infected can and should lead the charge.

For more information on IAVI, visit iavi.org*.*
