

Science AMA Series: We're Drs. Michael Keefer and James Kobie, infectious disease researchers at the University of Rochester Medical Center in Rochester, New York. We're working to find new ways to develop a vaccine to prevent HIV. Ask Us Anything!

HIV_{Vaccine}Trials¹and/ScienceAMAs¹

¹Affiliation not available

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Hello from Rochester, NY!

To both: Do you think a breakthrough will be made that makes other hiding viruses (herpes, shingles) obsolete or do you think one modified B cell may work for one but the same principle won't work for another?

I'm envisioning a finding that makes a generic template for tailor made cells similar to this [genetically engineered T-cells](#) to soon become a broad way to attack illness.

Do you foresee a vaccine becoming a mandatory thing or a opt in for high risk patients? As someone who has worked with HIV in a lab setting and works with other diseases, I would love the opportunity to get vaccinated to as many things as possible. Thanks for your work, keep it up!

Dr. Kobie: Do HIV resistant people have B cells you use? How do find/separate out these cells?

Dr. Keefer: Would a person inoculated with antibodies need regular boosters? How long is the half life of these antibodies?

[Legnd](#)

Dr. Kobie here. In general much of the efforts and findings surrounding HIV vaccine research provide new insights into the basic mechanisms of how viruses hide from the immune system and allow new strategies to be developed to protect from them. Because of the precise and highly specific ways that B cells and antibodies recognize unique features of individual viruses (such as HIV or influenza), it is unlikely that a single B cell or antibody could be effective against different viruses. However there is a common principle that has been spawned at least in part by HIV vaccine research, that for other viruses that can mutate to escape the immune response, such as influenza, some parts of the virus don't mutate and by developing vaccines that can generate B cells and antibodies that specifically target those conserved parts better protection may be possible. This is currently being pursued in what has been referred to as a "universal flu vaccine" strategy.



Regarding use of genetically engineered T cells, similar to what is being used in cancer trials – referred to as CAR-T cells, is an interesting idea for fighting infections. These CAR-T cells are typically hybrids of a person's T cells and an antibody that targets a specific cancer protein. A similar concept might be effective in treat chronic infections, and is being explored by others for treating HIV infection. A difficulty in this approach is that it commonly requires using the person's own T cells, which may make performing this on a large scale very difficult.

Regarding B cells from HIV resistant people: People that are resistant to HIV, which is extremely rare, typically do not develop many B cells or antibodies against HIV. However, about 25% of people that have HIV develop antibodies that although ineffective against the HIV virus that is in their own body, are capable of neutralizing a wide range of HIV virus strains. This indicates that the human immune system is capable of producing broadly neutralizing antibodies against HIV, and if that process which is occurring in some HIV infected people, could be reverse-engineered through vaccination, perhaps such antibodies could be generated in HIV negative people and confer protection. Although it requires substantial advanced molecular biology and cell biology techniques to find the rare B cells that are producing the broadly neutralizing antibodies, several have been isolated and these antibodies have been extremely useful in deciphering the complex process by which they developed in the HIV patient. Additionally, several of these antibodies are now being used in clinical trials. Currently the AMP trial is evaluating the VRC01 antibody to determine if it can protect people that are at high risk for HIV infection from becoming infected. This trial is happening through the US, South America, and Southern Africa. <http://ampstudy.org/>

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OK, my turn (MK; boy PhD's can be wordy). Regarding whether vaccination will be 'mandatory', I guess we can learn from the experience with rolling out HPV vaccine, which still suffers from underuse for a variety of reasons, from controversial to practical. I do know that Hepatitis B vaccine uptake was really improved when it was made mandatory for infants. By the way, HBV is a sexually transmitted virus but that seems to not have caught on for the people who object to HPV from a moral perspective.

Finally, back to our AMP study. Yes, these infusions are given every 2 months, which I suppose is better than weekly. There are modifications that can be made to lengthen the half-life of new monoclonals and there is a lot of work underway on that now.

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[Legnd](#)

Hi everybody, looks like we have a lot of great questions! I'm Dr Keefer and we'll try to make it clear who is saying what. I'll give the honors for the first question to my colleague, Dr Kobie.

Why *has* it been so hard to develop an effective vaccine? And will solving that problem help you develop a more effective vaccine for any other viruses?

[firedrops](#)

Dr Keefer here. Developing a vaccine to prevent HIV infection has been seen as the 'ultimate challenge' for vaccinology as the virus infects the very immune cells that we depend on to make a vaccine work. Plus, as mentioned below, no one has cleared the virus once infected, although there is the 'Berlin patient' and cure research is a very active area at this time. But as practically everyone knows, HIV mutates at an astonishing rate and the challenge has been how to deal with this without developing a vaccine for every strain (which is similar to what is currently done for influenza vaccine). A good way to grasp this is by comparing HIV's diversity to that of humans compared to our closest relative, the chimpanzee. Humans and chimpanzee genetic makeup is 99% the same, but for HIV there can be up to 40% difference between strains seen in different part of the world or even within Africa. The good news is that in spite of all this variability, we know that there are still a number of spots on the envelope of the virus that cannot be mutated without the virus losing it ability to infect CD4 cells and produce disease. That is where the broadly neutralizing antibodies comes in that we are testing in the AMP study. That study will provide incredibly important information to the HIV vaccine field and if we see positive effects we know that pursuing vaccines that can induce these antibodies will be the way to go. Finally, as Dr Kobie said, much of what we learn from HIV vaccine research already directly informs vaccine development for other infectious agents such as Zika, Ebola, malaria and TB. Also, work on cancer vaccines can further inform vaccines for HIV and vice versa.

How close are we, in terms of years, to successfully curing HIV? Also, about these so called superbugs, what do you think will be the cure for these kind of antibiotics resistant bacteria?

[superneilneil](#)

Dr. Kobie here. We are certainly closer than we were 10 years ago. The pace of gaining new insights is accelerating. For HIV vaccine research, several years ago there were modest, yet encouraging results from the RV144 "Thai Trial" HIV vaccine study, which showed for the first time that a vaccine can lead to protection from HIV infection in some people. Substantial efforts have been devoted to improving

this vaccine strategy and several trials underway, including seeing if the strategy can be extended to southern Africa. Additionally, novel strategies trying to sequentially evolve protective antibody responses through vaccination, mimicking what might be occurring in HIV-infected patients that develop broadly neutralizing antibodies are entering into early phase clinical trials soon, and should provide important insights to advance us closer to having an effective vaccine. Critical to ensuring we can successfully end HIV is continuing to encourage the development and testing of new ideas, so that we can develop multiple ways to tackle the HIV epidemic, from prevention to cure.

Hi, thanks for the AMA!

My question is for Doctor Keefer. You talk about giving antibodies directed toward HIV, so this would be a form of passive rather than active immunization. What situations do you envision this being used in, as it is not a permanent protective vaccination?

[superhelical](#)

Hi Superhelical! Dr Keefer here. Yes, you are exactly correct, this is a form of passive immunization and there are several examples of this being used in the medical field for a variety of infections including rabies, varicella zoster, hepatitis B, tetanus, respiratory syncytial virus and more. So HIV passive immunization could conceivably have a role in controlling the epidemic but to date monoclonal antibodies/passive immunization has been too expensive to be feasible in a large scale public health setting. That said, there are some areas that they could be useful for such as protection of newborns of HIV infected mothers who didn't take ART and/or during breastfeeding. Also, if their half-life can be lengthened to the point that an injection is needed only once or twice a year it could become a viable alternative for PrEP, as PrEP really is not intended to be a life-long measure for most people.

How are you developing dead HIV cells for vaccines and what precautions do you take in the lab?

[HajaKensei](#)

Dr. Kobie here. Good question. The vaccines that Dr. Keefer and I work on do not involve using the HIV virus itself, even dead virus. The vaccines just use synthetic proteins that are manufactured using genes from the HIV virus, but in no way contain the whole virus and in no way can cause HIV infection. Although use of inactivated/dead virus is a common vaccine strategy, such as for influenza or polio vaccines, for HIV it is unlikely that it would be practical from a safety perspective and in my opinion not necessary.

Vaccines are a reaction. Physicians looking at diseases must consider the etiology, epidemiology and pathology of disease. Indeed the University of Rochester was the founder of the Bio-Psycho-Social approach to disease.

"The biopsychosocial approach was developed at Rochester decades ago by Drs. George Engel and John Romano. While traditional biomedical models of clinical medicine focus on pathophysiology and other biological approaches to disease, the biopsychosocial approach in our training programs emphasize the importance of understanding human health and illness in their fullest contexts. The biopsychosocial approach systematically considers biological, psychological, and social factors and their complex interactions in understanding health, illness, and health care delivery."

<https://www.urmc.rochester.edu/education/md/documents/biopsychosocial-model-approach.pdf>

I would like to see and hear the approach to diseases from the etiology, epidemiology, pathology

approach and how the BPS model is working at Rochester today.

Same Rochester?

[digital_angel_316](#)

Dr Keefer here. Yes, this is the same Rochester famous for the BPS model back in the day. Yes, we clearly recognize that there is much, much more to controlling the HIV epidemic than just developing effective medicines and vaccines. That is especially clear to us as technically we should be able to eliminate the epidemic in the US/developed world where there should be full access to HAART, which can decrease further transmission of the virus ("Treatment as Prevention"). But life is very complicated for many people and in my opinion the stigma associated with HIV has not been alleviated much, if at all, over the past 30 years in some of the communities that are impacted the most. As a result, here in Rochester, as well as all the HVTN sites around the world (www.hvtn.org) community engagement is as important to our research as anything else we do as we have a chance to reach people every day who can benefit from learning more about HIV and how to protect themselves. We are also doing a project here now with AMP study volunteers to help them identify and prioritize their challenges in everyday life, then work with them on solutions when they are seen at follow-up visits in the study.

Are the vaccines you're working on looking to be effective only pre-infection, or will they be effective if administered post infection providing the virus is moderately dormant at the time (like the rabies vaccine).

[Willmono7](#)

Dr. Kobie here. Dr. Keefer and I currently work on vaccines for preventing HIV infection. There have been several clinical trials to try using vaccines to treat/cure HIV infection in people with HIV infection. The weakened immune responses common in people with HIV infection, and the widespread distribution of the virus throughout their body makes curing HIV infection with a vaccine a substantial challenge.

What is the main market for this vaccination, geographically? How viable will it be for distribution to its intended market?

[Imadethisuponthespot](#)

Hi Spot--Dr Keefer here. Yes, the main market for HIV vaccines will mostly be the developing world, especially sub-Saharan Africa, but there are still a lot of people and communities that need one in the US and Western Europe. The latter has a chance to control the epidemic through 'Treatment as Prevention' and PrEP but there's still a ways to go with that. I agree that distribution of an effective vaccine to all the areas in the world that need it will be a challenge (but easier than distributing ART and PrEP to the same places) but I think we'll see groups like the Gates Foundation make it happen (actually Gates and a number of other non-governmental agencies are making big contributions today).

What do you like most about what you do?

[ezzyrd](#)

Dr. Kobie and Dr. Keefer here. Working with great study volunteers and colleagues to tackle a challenging adversary. This is global effort and we are glad to be part of it. You can be part of this work too!- we are always looking for study volunteers: <http://www.hvtn.org/en/participants.html>

Is it true that even if scientists came up with a 'cure' for AIDS and Cancer, it would not be published because of farmaceutic corporations making money off people with those desease, might br a stupid question and conspiracy but i just want your opinion on those topics. Cheers

[MisViolence](#)

Drs. Keefer and Kobie here: Important question. If scientists came up with an effective cure/vaccine for HIV it would get widely publicized. Big and small pharma have been valuable partners in this effort.

Hello. Is it easier to create a vaccine than a cure? Will there be age or gender limits on who can receive the vaccine? What motivated you to try to tackle such a huge disease?

[nosunshine33](#)

Dr Keefer here-- it's really hard to say that either will be 'easier' but I get what you mean. Right now both are huge scientific challenges but I am heartened that so many other medical advances have occurred through the work already done in both areas of AIDS research. Also, looking back at where biomedical science was 50 years ago compared to where we are today, I am certain that things will happen in the next 50 years that we can barely imagine now. The key is keeping our focus on understanding the basic mechanisms of the immune system and disease processes (where the PhDs work) and have enough clinical researchers (like myself) to bring them into people and communities when the time is right. As to why I got involved in this work, I kind of 'grew up' with the HIV epidemic from the perspective of my training. I was in medical school when the first cases were reported and took care of many HIV-infected patients in my ID fellowship training and early career, at a time we had only AZT and not much else and nothing really worked. I also got a chance to get involved in HIV vaccine clinical research at a time when there were only a few places in the world doing it and moving more into HIV prevention appealed to me after losing essentially all of my patients from the early days. More recently I've become very active in working with younger researchers (like Dr Kobie) who will finish this thing off. Regarding age or gender limits on vaccines, we now test them only in people 18-50 years of age and in our early phase studies for people who are at low-risk for HIV we are looking for all genders (even beyond the usual 2). Ultimately, it will be essential that vaccines are available to younger people (like what is done with the HPV vaccine now) in order to get the maximal benefit to control the epidemic. Also, it is possible that we'll find that some vaccines work better in some populations (for example, heterosexual women vs MSM) but that will depend on the study results and highlights the reason we need to enroll a diverse population (genders, sexual orientations, races, ethnicities) of volunteers into our studies to be sure they work for everyone.

Don't HIV tests look for the presence of antibodies in response to infection? And if so, would they be able to differentiate between an actual HIV-infected individual and someone who has been vaccinated?

[JhackOfAllTrades](#)

Hi Jhack--Dr Keefer here. Yes, you are right, we do want our vaccines to create antibodies and sometimes they can be confused with real infection on many of the licensed tests on the market today (a thing we call "VISP" or "vaccine-induced seropositivity"). Actually, it is pretty easy using direct viral detection techniques to tell the difference but people might not be aware of that. Gumbly621 has it right, we do encourage our volunteers to receive free testing at our research site for as long as they need. On the other hand, sometimes people forget about this and get tested away from our clinic but we have always been able to solve any problems through our testing process. Also, you might wonder "what if I decide to move away from Rochester (or another HIV vaccine site)"? We can solve that



problem too because there are many HVTN sites around the country and even if you aren't close to one, we can arrange for your blood to be drawn locally and sent to our lab. By the way, the package insert on all FDA-approved HIV tests states that a false positive test can occur in someone who has received an experimental HIV vaccine, but I guess no one spends much time reading package inserts.