



PODCAST TRANSCRIPT

What is a Partial Protection

July 22, 2020

Jeanne Baron [00:00:01] AVAC is launching a new series on our podcast Px Pulse, *Research Fundamentals*. In addition to our regular schedule of programs covering advances and challenges in HIV prevention research, Research Fundamentals will explore scientific concepts in research, one at a time. In our debut episode, we explore the concept of partial protection. I'm joined by David Evans, science and advocacy consultant for AVAC, formerly of Project Inform, Penny Moore from South Africa's University of Witwatersrand and National Institute for Communicable Diseases, and Sandhya Vasan of the US Military HIV Research Program. Together, we explore the meaning of partial protection. Whether it's condoms, a flu shot, oral PrEP, or the Dapivirine vaginal ring, proven products fall short of 100 percent protection against disease. And there's a lot to know about how and why an intervention may offer imperfect but still useful protection.

Jeanne Baron [00:01:12] From COVID-19 to HIV, fighting contagious disease involves research and development in treatment and prevention that can bring real results that help a lot, but don't fix the whole problem. Medical breakthroughs can be important. They can improve public health dramatically, even if they fall short of perfect. This episode explores the meaning of partial protection. And we start by talking about two studies. One is Uhambo and the other RV144.

Uhambo or HPTN 702 brought disappointment in early 2020 when the vaccine being tested was found to be safe but not protective against HIV.

David Evans [00:01:57] Researchers will be studying this data intensely because an earlier trial using a similar vaccine did offer some protection.

Jeanne Baron [00:02:05] That was in 2009. It was a study in Thailand officially known as RV144. And it offered a spark of hope that an effective vaccine might be within reach.

Sandhya Vasan [00:02:16] The RV 144 efficacy trials— 16,000 people at the end of three and a half years. It looked like it was 31 percent protective.

Jeanne Baron [00:02:27] Those given the vaccine were 31 percent less likely to become infected compared to a placebo. Experts describe this as partial protection against HIV infection. And in this episode, we're going to talk about partial protection.

David Evans [00:02:45] The head of HIV research at the US National Institutes of Health, the NIH, Dr. Anthony Fauci, says even a partially protective vaccine could be good enough to alter the course of the entire epidemic around the world.

Jeanne Baron [00:02:58] Oh, and we should point out, this is the same Anthony Fauci so many of us now know as almost a household name. The Anthony Fauci who's one of the most visible members of the White House Corona Virus Task Force.

David Evans [00:03:12] Exactly. And in this case, we're talking about models just like we're talking about models with COVID. And when we look at the models for HIV around the kind of impact on the epidemic a partially protective vaccine would be, we're hoping for at least 60 percent effective. But Fauci's said—he's been quoted as saying— he'd settle for 50 to 55 percent [protective against HIV]. But keep in mind, no vaccine is ever 100 percent protective.

Jeanne Baron [00:03:41] Even the strongest, most protective vaccines like measles, still fall short of 100 percent effective. So what does partial protection mean, say, in the case of RV 144? And it's 31 percent protection.

Sandhya Vasan [00:03:53] How about the partial protection question?

David Evans [00:03:56] Does that mean it works all the time in some people, but not others? Or does it mean that the same person was protected in some instances, but not others? Or could it mean both?

Penny Moore [00:04:08] So this is tough to explain. So to me, partial protection implies that in every encounter that people have with the virus.

Jeanne Baron [00:04:19] So using 30 percent protection as an example:

Penny Moore [00:04:22] In one of every three of those encounters, the immune system will be able to send that virus off.

David Evans [00:04:27] It means it works in my body in some instances, but not every instance. For example:

Penny Moore [00:04:33] The extent of your risk is determined by whether you also, for example, have an STI, in which case the risk of becoming infected is much higher. And the bar that the immune system has to protect against is much higher. And in that case, a partially effective vaccine is less likely to fail to protect you.

Jeanne Baron [00:04:52] So in the same body, it might work sometimes, but not others. Like if you have a sexually transmitted infection, it might not work as well.

Penny Moore [00:05:01] Yeah, yeah. But, you know, the opposite, your second possibility is also equally possible.

Jeanne Baron [00:05:09] The second possibility that it works better in some people or populations than others. So partial protection means both a partially protective vaccine might be more likely to work in me than someone else. But it might not always work in me either.

Penny Moore [00:05:25] Yes. Thanks for clarifying that.

David Evans [00:05:27] So I was really addicted to Game of Thrones and some of the battles you'd have the bad guys attacking only one side of the castle, which was less effective. But when they were coming on all sides and up through the ground, it just worked better. And it's the same thing. One body, but it might work sometimes and not others if there are too many things going on.

Jeanne Baron [00:05:51] And let's say an example where somebody maybe has an STI, their body's busy fighting the STI and has less defenses against an attack, so to speak, from HIV.

David Evans [00:06:08] Yes, it is. It's partly that it's busy. And in addition to that, it's almost like it's hyped up. And the more immune cells that are directed towards that other infection, there are actually more cells that are available for HIV to infect.

Sandhya Vasan [00:06:27] What are the factors that might make something more protective in some people and not others? And it's probably a variety of factors that we're still trying to understand through research. But certain genetic subtypes at an individual level were associated with a higher or lower likelihood of being protected.

David Evans [00:06:46] Let's start off understanding that when we talk about genetic subtypes, we're really talking about our genes. And, you know, our genes can differ. For instance, between men and women, between people with long ear lobes versus short ear lobes, or even people who get allergies versus those who don't. And all of these differences arise from variations in our genes.

Sandhya Vasan [00:07:13] So, you know, that is a kind of a hardwired genetic difference.

Jeanne Baron [00:07:18] But exactly what genes support a strong immune response remains a mystery. It's still unknown.

David Evans [00:07:27] You're right. We're learning a lot. But as far as the genes that help our immune systems respond to HIV, a lot is unknown. To make sense of it, you know, I was always more of a library kid than a jock growing up. But team sports do help me wrap my head around how my specific genes could affect a vaccine in fending off HIV. So imagine each exposure to HIV as a match between my immune system and the virus. The vaccine is like a coach and it's teaching and telling my immune system how to face off against what we'll call team HIV. Let's say the players on my team, because of my genetic makeup have flat feet and they run slower. A great coach may struggle to help my team overcome a deep bench of clever and relentless players on team HIV. It is not impossible for my team to win. It's just a lot harder. But someone else may have different genes, so their players learn new footwork easily and can do more with the coaching that's offered to them by the vaccine.

Jeanne Baron [00:08:38] In those scenarios the coach may be able to get the job done, but maybe not every match.

Sandhya Vasan [00:08:45] So there are a number of factors that might affect our individual susceptibility. But one of them is something you're born with, just your innate genetic subtype. And we're just starting to understand that in more detail.

Jeanne Baron [00:08:58] But we're not done.

Penny Moore [00:08:59] Virus and HIV infection is complicated by many other factors.

David Evans [00:09:04] Yeah, other factors do contribute to partial protection.

Jeanne Baron [00:09:07] Whether you have an STI, what kinds of genes you have...

David Evans [00:09:11] And what kind of HIV you encounter and how often you encounter it.

Sandhya Vasan [00:09:15] But in addition, the type of HIV or the amount of HIV you're exposed to can also determine protective efficacy.

David Evans [00:09:24] Exactly. So let's make sense of this. If I stick with that soccer or football example, the type of HIV and the amount I'm exposed to would kind of be like having multiple matches in a row where my players never get a break. And Team HIV gets to keep cycling in fresh players with diverse skills over and over again. Even a fairly strong, partially protective vaccine, (which again, in this example would be like a really good but not invincible coach for a sports team) would see my well-trained players tiring out eventually. On the other hand, if people don't just rely on the vaccine and instead add layers of other kinds of prevention, like condoms or PrEP, it's like adding fresh players to the team over and over again.

Jeanne Baron [00:10:16] So then how is a 50 percent or 60 percent protective product giving me a benefit if it means, something like, one out of two times of encountering HIV it works. How do I translate that into a benefit?

Penny Moore [00:10:36] It's stacking the odds in your favor.

David Evans [00:10:38] You're layering up your defenses against HIV. That way, if one fails, another might work. Many tools, many options customized to you.

Jeanne Baron [00:10:48] And at the population level, it's really just math. It's cumulative.

David Evans [00:10:52] Yeah. So the more people vaccinated or the more men who've turned to voluntary male medical circumcision, both partially protective interventions, the less likely HIV is circulating in the population as a whole. It's an intervention on the job all the time in your community doing its part.

Jeanne Baron [00:11:19] Providing their expertise in this episode, AVAC thanks David Evans, science and advocacy consultant for AVAC, Penny Moore from South Africa's University of the Witwatersrand and National Institute for Communicable Diseases, and Sandhya Vasan of the US Military HIV Research Program.