

# When it Mattered

## Episode 42: Dr. Paul Offit

Chitra Ragavan:

When Dr Paul Offit was five years old he was sent to a polio ward to recover from clubfoot surgery. He spent six weeks in the ward surrounded by young children suffering from polio. That formative childhood experience put Dr Offit on the path to becoming one of the most renowned vaccine advocates in the world.

Chitra Ragavan:

Hello everyone. I'm Chitra Ragavan, and this is When it Mattered. This episode is brought to you by Goodstory, an advisory firm helping technology startups find their narrative.

Chitra Ragavan:

Joining me now is Dr Paul Offit, Professor of Pediatrics at the Children's Hospital of Philadelphia. The recipient of many awards and honors, Dr Offit is a physician scientist, and co-inventor of a vaccine that is estimated to save hundreds of lives a day. He has published more than 180 papers in medical and scientific journals, and is the author of five books, including *Autism's False Prophets: Bad Science, Risky Medicine, and the Search for a Cure*. Offit is a tireless advocate for children, both in the books he writes, and his willingness to take on the anti-vaccine movement, which has only made him a controversial figure. Offit currently is a member of a group put together by Dr Francis Collins who is the Head of the National Institute of Health. The group is called Accelerating COVID-19 Technological Innovations and Vaccines, or ACTIV, and it consists of industry reps, as well as representatives from the CDC, FDA, and academia.

Chitra Ragavan:

Dr Offit, welcome to the podcast.

Dr Paul Offit:

Thank you Chitra.

Chitra Ragavan:

You has surgery at age five for clubfoot, what is the condition, and how is it fixed?

Dr Paul Offit:

Right, so it's a condition that you're born with, it's congenital, and the way it looks is that your feet are sort of turned down and inward, much as a horse's foot would look. So it's usually treated simply by casting both feet, for the first few months of life, and that usually straightens things out. In my case, my father felt that the foot wasn't straight enough when I was five years old and so he insisted that something be done. So what

my mother did was she called the Clubfoot Clinic at Johns Hopkins University, because I grew up in Baltimore, and she couldn't get an appointment. So what she did then was she called my grandfather's brother, my great-uncle, who was a bookie. Sort of Baltimore's frankly most important major bookie. Meaning he booked bets, not made books.

Dr Paul Offit:

The guy who was the head, the doctor who was the head of the Clubfoot Clinic at Hopkins apparently was a gambler, and gambled through my great-uncle. So with that, my great-uncle called the clinic and was able to get me an appointment within a week. Within that, when we saw the doctor, the doctor said that, "Whatever you do," he said to my mother, "Don't operate on this foot." Because there was no, frankly, repair for clubfoot surgery. But my father was insistent and he was able to find through a friend of my grandfather, ie, his father son had recently finished an orthopedic residency and he was anxious to do surgery, and so he operated on my foot badly. As a consequence, I ended up being in this chronic care facility, which was a polio ward, in Children's Hospital in Baltimore, Maryland for six weeks.

Chitra Ragavan:

Did the surgery eventually actually work, or did it not?

Dr Paul Offit:

No, it didn't work. I mean clubfoot repair surgery was perfected in the mid-1990s, roughly 40 years after I had my surgery. No, I suffered severe, osteoarthritis with my right foot ever since I was a child. So it's really been painful since then, but I can live with the pain, it's not like something I can't live with.

Chitra Ragavan:

So what was that like, being in that polio ward for six weeks, right? That's a long time for a young child in a hospital.

Dr Paul Offit:

It was hell. This was the mid-1950s, it was a polio ward, people were scared of polio. There was one visiting hour a week on Sundays from 2:00 to 3:00. My mother was pregnant with my brother and had a complication, so she was unable to visit. My father who traveled often as a salesman, he tried to visit me actually on one of the hours that wasn't permitted, and from then on he wasn't allowed to visit me. As a consequence, no one visited me, and you know, I just remember that ward, my bed was right next to a window that looked down onto the front door of the hospital. I just remember staring out that window waiting for somebody to come and save me.

Dr Paul Offit:

I remember that ward. I mean here were these children who often had no one visiting them. I mean this was 1955, there weren't any TVs in the ward, there wasn't a play therapist. There weren't sort of animals, pet dogs to sort of make children feel better.

You just lay there for what seemed like forever. The nurses were not all that kind, as I recall, and you just stared out that window looking for people to come get you. You know, when I was a medical student at the university of Maryland we actually rotated through that hospital. I remember that, walking into that room, which was no longer a ward, it was just administrative offices. But you know, that window was still there, and I just remember walking over and looking out that window, and looking to the front door and crying.

Chitra Ragavan:

It's like something Charles Dickens would write.

Dr Paul Offit:

No, I think the scars of our childhood invariably translate to our passions as an adult.

Chitra Ragavan:

What did that teach you, do you think, that experience?

Dr Paul Offit:

I think it taught me to care for children. I think what it taught me was that children are so often sort of vulnerable, alone, and as a consequence, and helpless. I think as a consequence, the drive to become a pediatrician. The drive to work on a vaccine that could save children and help them from suffering. The drive to write all the books that I write, which invariably have as a theme, child advocacy, trying to protect children from sometimes the irresponsible acts of their parents. I really do think, as I said before, I just think that the scars of your childhood translate to the passions of your adulthood, and I think that's what happened to me.

Chitra Ragavan:

Your parents went kind of against the grain of the medical recommendation at the time. I guess one could argue they weren't, perhaps, skeptical enough, or they were convinced by what they believed would be the right thing to do, they were acting in your interest. Did you ever discuss with your parents down the line what that experience was like that you went through? Did they ever regret doing it?

Dr Paul Offit:

I remember my mother said that when I came home after that ordeal that I insisted on staying in their bed. That I was depressed, sort of clinically depressed. Weeks went by before I sort of finally snapped out of it. My mother had told me that. They did what they thought was right, they were trying to do the best by me. I just don't think children were thought of in the same way then. If you ever saw the television show Mad Men, I think the theme of that show, because it really gets so much right, is children were basically ignored, right? I mean they sort of should be seen but not heard. The way we treat our children today is so different, we are so much more involved in their lives, and dote on them. I just think that wasn't true then. It was a different time.

Chitra Ragavan:

I think in *Mad Men* you also learned that children were taught to make cocktails for their parents, which might be helpful today when we're all cooped up at home, I guess. So clearly the polio ward was an early experience that taught you the human toll of not having vaccines, right? How did that interest in vaccines develop over time, and got you to where you are today?

Dr Paul Offit:

When I was a medical student there was a woman who was head of the division, or part of the Division of Infectious Diseases at University of Maryland named Ellen Wald, who also, when I went to Children's Hospital in Pittsburgh to do residency happened to go with her family at the same time. So she was a big influence on me. I mean she just made infectious diseases interesting and fun, and logical, and thoughtful, and I was drawn to that. So then I did a fellowship in infectious diseases at Children's Hospital in Philadelphia, and my boss was Stanley Plotkin. What I remember of first meeting him is I walked into his office, and he was sitting there reading a journal called *Morbidity and Mortality Weekly Report*, which was published by the Center for Disease Control and Prevention.

Dr Paul Offit:

What he was looking at is he was looking at the instance of so-called congenital rubella syndrome in the United States and in the world. He was the inventor of that vaccine. So rubella is a virus that when it infects women in the first trimester causes about 85% of those births to have severe, permanent abnormalities of the eye, ear, and heart. So-called congenital rubella syndrome. He was looking at that to see what the incidence was. He'd invented the rubella vaccine that had been used the previous year. He had done it in '79, I came there in 1980. It just struck me, here's a guy whose report card is looking at *Morbidity and Mortality Weekly Report* to see the incidence of congenital rubella syndrome.

Dr Paul Offit:

I had just come off a residency where I was taking care of one patient at a time, and here he was taking care of entire populations of children. It was a dramatic moment. It certainly got me interested in the power of vaccines.

Chitra Ragavan:

One of your greatest accomplishments, I guess, you are a co-inventor of the rotavirus vaccine, which is credited with saving hundreds of lives of children every day. So you were kind of able to do what your mentor did. What is a rotavirus, and how did you become involved in its vaccine development?

Dr Paul Offit:

Right, so rotavirus is a virus that primarily infects children between six and 24 months of age. It causes fever, vomiting, and diarrhea, and is a common cause of dehydration. In the United States at the time that we were working on this it accounted for about 75,000

hospitalizations a year, primarily in children less than two for dehydration, and about 60 to 75 deaths a year. But in the world rotavirus killed 2,000 children a day, roughly, before there was a vaccine. I was just fortunate enough to be in the right place at the right time. Dr Plotkin obviously had already made a vaccine, he understood what it took to get from bench to bedside.

Dr Paul Offit:

Also very fortunate enough to work with a man named Dr Fred Clark who was a PhD DVM, he was a veterinarian who had done extensive work with animal models and pathogenesis. Meaning how viruses cause disease. He was just a brilliant, thoughtful mentor, and I just was lucky to be able to be affiliated with those two people so that we could create the strains that became that vaccine.

Chitra Ragavan:

You saw the human impact of the rotavirus I think in the case of an Appalachian mother that you were telling me about.

Dr Paul Offit:

Yeah, that was sort of, at some level I always had the image of that mother in my head during the roughly 26 years it took us to create this vaccine. I was a resident at Children's Hospital in Pittsburgh when a mother had come into the emergency department at night with a child who clearly was severely dehydrated. The child was about a nine-month-old girl who had been well, perfectly well, up until being infected with rotavirus. The mother was great. She called the doctor, the nurse the night before and was told to give frequent sips of fluid containing sugar and minerals, which she tried to do. But you know, it's very hard to rehydrate children who are vomiting.

Dr Paul Offit:

So by the next morning, or the next evening, the child was severely dehydrated. So when the child came into the emergency department we quickly whisked her back into the treatment room, and we tried to put an intravenous line into a vein in her arm or leg. But she was so dehydrated that we couldn't find one. So we called the surgeon to come down, the general surgeon to come down, and essentially do a so-called cut-down in her neck to try and at least get a line catheter into a vein in her neck, so we could give her the fluids that she so desperately needed. While we were waiting for him to come down we basically took a bone marrow needle and sort of bored into the bone right below her knee to try and at least put fluids into her bone marrow, in the hopes that it would be reabsorbed into her circulation. In the hopes that it would then prevent what was the impending shock that we were sure was happening.

Dr Paul Offit:

We tried to do that without success. The child went into shock, and then her heart stopped beating. We tried desperately to revive her, but couldn't. So here was a child who two days earlier was perfectly normal, who now was dead from shock caused by severe rotavirus disease. Then comes the hardest moment in your life in the world of

medicine, which is you now have to walk out of that treatment room, into the waiting room, and tell this mother, whose child was well two days before, that she was dead. It just still gets me how hard that is to do, and the look on her face has never left me.

Chitra Ragavan:

So when you look at your accomplishments, where would you sort of place your co-invention of the rotavirus vaccine, in the context of everything else you've done?

Dr Paul Offit:

Well I think I was just really fortunate enough to be part of a team at Children's Hospital Philadelphia that created this. I would say that was number one. I would say number two, interestingly, was the work I did on the polio virus vaccine. I was asked to be on the Advisory Committee of Immunization Practices in 1998. I was on that committee for about four or five years, and was asked to be head of the polio vaccine working group. You know, my interest at the time was, because I'd actually just written a book about the polio vaccine called *The Cutter Incident*, which was this tragic event associated with the birth of Jonas Salk's polio vaccine.

Dr Paul Offit:

So I had a very good sense of the polio vaccine and its weaknesses. At the time we were using the oral polio vaccine, the one that was initially dropped on sugar cubes and put into people's mouths, then now at that time was just sort of squirted into people's mouths from a little plastic vial. That was a great vaccine, it eliminated polio from the western hemisphere, but it had a side effect which was intolerable, which was that that vaccine could actually cause polio. It was rare, roughly one in 2.4 million doses, but it was real. So although we eliminated polio from the United States by the late '60s early '70s, every year in our country we would have polio caused by that vaccine. There would be eight to 10 children who would be paralyzed permanently, some of them would die because they got that vaccine.

Dr Paul Offit:

At the time there were other countries that had used only Jonas Salk's inactivated vaccine were able to eliminate polio from their country using that vaccine. So I thought why don't we switch to that vaccine? So I brought actually a guy whose son had gotten polio from the polio vaccine, a guy named John Salamone. I brought him onto that committee, and for those two years that we tried to move this country away from the oral polio vaccine, which was much cheaper and easier to administer to the inactivated vaccine, I think that was an accomplishment. So as a consequence, we don't have anymore cases of vaccine associated paralytic polio, which we had had for decades. There hasn't been a single case since the year 2000.

Chitra Ragavan:

So much of your early career was steeped in sort of medicine and science, and the invention of vaccines, but something happened to turn you into a much more assertive, perhaps aggressive vaccine advocate. You've kind of gotten involved in the politics of

vaccines, and the anti-vaccination, taken on the anti-vaccine movement very aggressively. What happened to kind of turn you in a new direction?

Dr Paul Offit:

So I was in the midst of trying to make this rotavirus vaccine, and I think with that I saw exactly how hard it was to make a vaccine. How hard it was to prove that it was safe and effective. I mean our phase three trial, so-called pre-licensure FDA trial was a prospective, placebo-controlled, 70,000 children, 11-country, four-year, \$350 million study to prove that the vaccine was safe and effective. At the same time, that I was seeing how hard it was to make a vaccine. I was seeing how easy it was to damn them. Andrew Wakefield published a paper in 1998 when I first came on the Advisory Committee for Immunization Practices stating that the combination measles, mumps, rubella vaccine caused autism.

Dr Paul Offit:

I mean all that was was a ... It wasn't a study, it was just a case series of children who got the MMR vaccine, and within a month developed signs and symptoms of autism, which was in no sense a proof. All that did was show that the MMR vaccine doesn't prevent autism, it only prevents measles, mumps, and rubella infection. I mean subsequent to that 18 studies have been done in seven different countries on three different continents involving hundreds and hundreds of thousands of children showing you're no more at risk of getting autism if you got that vaccine than if you didn't. But the media ran with that story.

Dr Paul Offit:

Anti-vaccine groups were created because of that story. Our group, the Advisory Committee of Immunization Practices was asked to consider whether or not we should separate the MMR vaccine into its three separate parts to try and avoid autism. Because there was a Congressman who was on the appropriations committee who believed that MMR vaccine caused autism. It was a nightmare. I didn't really see a lot of people standing up in the media, scientists especially, saying that here is not only that the MMR doesn't cause autism, but here's all the reasons why it doesn't make sense that it would. I didn't see that, and so I started to get in the game, if you will.

Dr Paul Offit:

I wrote a book called *Autism's False Prophets: Bad Science, Risky Medicine and the Search for a Cure*. That was a book where I sort of took on the anti-vaccine movement. I tried to pull the curtain back to show here's who funds these people. Here's how the extent to which they're politically connected, to which they're media savvy, to which they're lawyer-backed. Here's what this is really about. This isn't just a group of sort of grassroots movement, this is a sort of, in many ways, a lawyer funded political campaign. With that, I put an X on my back and became I think probably the most hated person by the anti-vaccine movement.

Chitra Ragavan:

They've criticized you for being supposedly in bed with vaccine manufacturers. You've been called a liar, a profiteer, a millionaire vaccine industrialist. When you first started on this path was it difficult when you started to read and hear these things? How did you kind of respond to that criticism that you have a vested interest in the outcome of the vaccine adoption?

Dr Paul Offit:

Well I knew that wasn't true, so therefore, I mean I can live with myself. I mean we were the creators of the vaccine. When you co-invent a vaccine obviously we were the patent holders on the vaccine, but you know, me and my two co-inventors Stanley Plotkin and Fred Clark, were the intellectual property of our hospital. Our hospital owned that patent because they owned us. Therefore, they're the ones who essentially sold the license to Merck. Then when it became a vaccine they basically sold out to an asset acquisition company. So I mean everybody accuses me of being sort of in bed with Merck, I have no direct financial connection to Merck at all. It's my hospital that has that, because they own the patent. But you know, they sold that asset out a long time ago.

Dr Paul Offit:

Now I was, as were my two co-inventors, were subject to sort of the tech transfer policy of our hospital. So we did receive some financial remuneration, but that's okay. It's not like we created a better way to freebase cocaine, we created a vaccine that saves lives. I mean it was a 26-year effort, to some extent, I was compensated for that effort, I can live with that, it's too bad that they can't. I don't make any money, and didn't, and haven't made any money off the sale of vaccines since our hospital sold that patent, which was decades ago. So I can live with myself because I know what motivates me. I know why I did what I did, and it was all for the benefit of children.

Dr Paul Offit:

I mean nobody, no scientist goes into work day after day thinking, "Boy, if I can just figure out which of these two viral surface proteins evokes neutralizing antibodies, I can be rich." You're just trying to understand the virus. That it eventually came to be that we were vaccine inventors was surprising to me. It was nice, but it was never really the specific goal. We were just trying to understand the virus. If we became part of what became that vaccine, that was great. So in any case, I understand that they are going to target me, and because they don't have the data, they have to attack me personally.

Dr Paul Offit:

They have to make ad hominem attacks. Because when I say, "Look, here's 18 studies that show MMR doesn't cause autism." What they should do is if they have science, they should show, "Look, here are excellent scientific studies that show MMR does cause autism." But that doesn't exist. So therefore, they make ad hominem attacks. I've always said, again and again, I'm not their problem. The science that shows they're wrong is their problem.

Chitra Ragavan:



You said you're kind of the most hated person by anti-vaxxers, and you have been the subject of death threats. How did that begin to happen, and what's that experience been like? I mean how often and how many threats do you get?

Dr Paul Offit:

Well certainly when that book was published I would say it was on a daily basis. It's faded more to like, you know, I would say every week I get some sort of negative thing, either by email or snail mail, or comments on Facebook pages. So it's been a variety of things. One would be just sort of you know, just hate mail. Two would be sort of physical intimidation. There was a march once at the CDC, a rally during an ACIP, Advisory Committee for Immunization Practices meeting where I had to walk through that group. I had to walk, you know, the CDC in its infinite wisdom had policemen there, they had like helicopters flying overhead, but you still had to walk through this group, many of whom held signs with like your face on it, with like a slash through it, right? So that was fun.

Dr Paul Offit:

But when I was walking one guy grabbed me. He grabbed me by the arm and he wouldn't let me go. You know, I just kept saying, "Look Sir, you're going to have to let me go. Sir, please let me go. Sir, you're going to have to let me go." because you can't do anything other than that. You cannot push him, you cannot touch him. The minute you do that, you're in for a much longer road than you want to be. So eventually he let go of my arm, and I've had that where people take their iPhones and put it right up in my face while they're trying to film me, because they want me to touch them. Because if I touch them, all you have to do is touch somebody against their will, and that's battery. They know that, so you have to know that and to sort of be very patient.

Dr Paul Offit:

Then I've had death threats. I've had three legitimate death threats. Although death threats are made on the Internet every day, according to the FBI, there's thousands of death threats that are made, they don't consider it to be a true death threat unless 1) it's made more than once, it's sad that I actually know these criteria. 2) that it is specific. Meaning, "I am going to come to your office and shoot you with a gun." Not just, "Watch your back." 3) that it could be done by someone who they think could do it. Meaning, a paranoid schizophrenic. When that happens the FBI actually gets involved.

Dr Paul Offit:

So my hospital has a very good relationship with the Philadelphia FBI, and they coordinate with the national organization, they coordinate with other cities. So if I get a death threat, and there was one not too long ago, they then monitor that person. They monitor the person's emails. They monitor their comings and goings. They look to see what they buy, have bought a weapon that could kill somebody. They look to see whether they bought a plane ticket to Philadelphia or a train ticket, or whatever. So your idea, by the way, of civil liberties dramatically changes when you're threatened. My attitude is like if they threaten me, please, violate their civil liberties, I'm fine with that.

Chitra Ragavan:

Is it worth it? Is it worth taking on this movement, the death threats, and the criticism, and all of these battles you're taking on?

Dr Paul Offit:

I think it comes with the territory. I mean you know, I'm among scientists, and I'm most comfortable obviously presenting science in a scientific venue where you look at data and you try and analyze data. That's the most fun for me. The minute you cross the line though, the minute I took on this route by trying to, I think, expose their funding, expose what their motivations were, expose how were they getting paid, et cetera, that's politics. With the politics, comes this. It's ugly, it's dirty, it's mean-spirited, it's full of lies. You know, you're in or you're out. If you're in, just realize that that's what you've signed up for.

Chitra Ragavan:

Even though they're so highly politicized now, and you've written a lot about sort of the vested interest and all of that, but I guess early in the days it was probably a movement birthed in certainly the tragedy of sorrow of when kids don't take well to some of these vaccines. Is that kind of what we're dealing with here with autism? That there are some ... What's the issue here for people that don't track this? Why is there this conviction that the vaccines cause autism?

Dr Paul Offit:

Well because from the parent's standpoint, "My child was fine, they got a vaccine, now they're not fine, could the vaccine have done it?" It's a fair question. The good news is it's an answerable question. So if you wonder whether or not MMR vaccine causes autism, it's not that hard to look back retrospectively and see whose gotten this vaccine and who hasn't. Make sure that those two groups are alike in terms of their medical background, or socioeconomic background, or healthcare seeking behavior, so you can isolate the effect of that one variable, receipt of MMR vaccine. When that study has been done again, and again, and again, it shows that there is no difference.

Dr Paul Offit:

So that was an ill-founded concern, and most people are convinced by that. I mean I think if you asked a thousand people 20, 25 years ago, "Do you think MMR vaccine or vaccines can cause autism?" I think most parents of children with autism would say yes. That's not true anymore. 85% of parents, and this is just a recent study by the Autism Science Foundation, 85% of parents of children with autism do not believe vaccines caused it, but some do. 15% do. They are unconvinced. No matter how much data you show them, they're unconvinced because they believe that the pharmaceutical industry is just controlling everything. Controlling the medical establishment. Controlling the government. Controlling the journals who publish these papers. They're conspiracy theorists, and there's no getting around that.

Dr Paul Offit:

So you know, what can I say? I think that we in the public health or academic community have done a good job at trying to answer these concerns. But the true anti-vaccine activists hold onto a belief, much as one holds a religious belief. They believe that vaccines cause hyperactivity and autoimmune diseases, and autism, and diabetes, multiple sclerosis, and all a variety of things that vaccines don't cause. Which is not to say that vaccines don't have problems, including serious problems, one example being polio that was caused by the old polio vaccine. But that's not really what their concerns are. Their concerns have largely been addressed via scientific studies and shown to be ill-founded.

Chitra Ragavan:

Actually this kind of is a great segue way to coronavirus, because vaccines now are once more uppermost and on people's minds, right? When will there be a vaccine for coronavirus? With rotavirus it took 26 years, what's your prognostication on sort of where we are, and what it's going to take to get a vaccine for coronavirus?

Dr Paul Offit:

Right, so the 26-year timeline we had for our vaccine is not abnormal. I mean typically, you know, a timeline's around 20 years for the development of a vaccine. Meaning from having the strain to doing all the research, and then the research to development. So when Dr Fauci says he thinks we have a vaccine in 12 to 18 months, obviously there are going to be steps that are skipped or compressed. So what do I think about this? I think there will be a coronavirus vaccine. There's every reason to believe it. First of all, the Food and Drug Administration in the United States has received more than 120 investigations new drug licenses. There are more than 70 companies throughout the world that want to make this vaccine.

Dr Paul Offit:

BARDA, which is part of Health and Human Services has put up \$2.5 billion, \$500 million to each of five companies. The virus is stable, it doesn't mutate in a manner similar to say influenza virus, and we know the protein of interest. The protein that sits on the surface of that virus, that spiked protein, so-called S protein, that's the protein that attaches the virus to cells. So if you can prevent the virus from attaching to cells, then you're going to prevent infection. So that's the protein of interest. That's all good news. But I think it's going to be a dramatically compressed timeline. I think what's going to end up happening is that you're going to have companies doing very small prospective placebo controlled studies that will involve between 1,000 or 6,000 people.

Dr Paul Offit:

That is tenfold less, more than tenfold less, than what you normally see in a pre-licensure study. I think these aren't going to be licensed products. I think they're going to be so-called FDA approved, not FDA licensed products, due to so-called Emergency Use Authorization Act. I think we're going to learn about the real safety and efficacy of this vaccine after it's already rolled out to the public. When then tens of thousands of

people have gotten it, and tens of thousands of people won't have gotten it. So you'll see sort of what the safety and efficacy profile really is.

Dr Paul Offit:

So I think this is going to play out in one of two ways. There will be a vaccine. I think there will be a vaccine soon. I think not a vaccine, I think there's going to be several vaccines, or many vaccines, used in countries throughout the world. Then we'll learn about it, after it's already out there, I think then we'll learn about it. It'll play out one of two ways, it'll be remarkably effective, stop the spread of this awful virus. That is the only way to stop the spread. I mean population immunity will only be achieved by a vaccine. It's not going to be achieved by natural infection, because it never is. Either the vaccines will be a hero, much as in the movie Contagion, when the vaccine was the hero of that movie.

Dr Paul Offit:

Or because things have been compressed and pushed quickly, there will be a side effect that will be severe that people hadn't anticipated, and that could make people question whether we have done this the right way.

Chitra Ragavan:

So it kind of has that same sort of the risk issue, right? The shorter compressed timeframe, the higher the risk, and greater the risk of a backlash. But I guess you have to weigh the odds against people dying.

Dr Paul Offit:

Well that's exactly right. I think you're talking about trying to prevent a disease that's killing 2,000 people a day in the United States. So the risk/benefit ratio changes. You're willing to take a greater degree of uncertainty about safety, or greater degree of uncertainty about efficacy, because you are scared to death of dying from this virus. I mean you know, if this virus was killing two people a day in this country, you'd be far less willing to accept vagaries about safety or efficacy than you would now. So I think that's always true in everything in medicine. It's always a risk/benefit ratio. If you have cancer, you're willing to take chemotherapy that itself could kill you, because you fear dying from the cancer. I think this is similar.

Chitra Ragavan:

I think that's one of the hardest things for people to understand, how risk/benefit analyses work, and sort of the statistical modeling. But what works is human stories, right? So when you hear stories of people dying, neighbors dying from a vaccine or something, that tends to get greater prominence sometimes in people's minds, than doing sort of the statistical correlation, and trying to figure out the cost-benefit analysis.

Dr Paul Offit:

I think we're terrible at determining risk. I think the greatest risk of getting vaccines, frankly, is driving to the office to get them, if you look at it statistically. I think we're

scared of all the wrong things. We should be scared of things like fried foods and not the things that we're scared of. I just think we don't get it. But you're right, I mean it's the personal stories that are compelling. I mean how does the New York State Lottery get you to buy tickets when the odds of you winning are 14 million to one, against, because they say, quote, it can happen to you. That's good enough.

Chitra Ragavan:

So I'm curious, with all of your expertise in vaccines and viruses, when coronavirus first started to emerge in China, what were your thoughts? When did you start to pay attention to it?

Dr Paul Offit:

Yeah, I really didn't think it was going to be as big in this country as it is. I clearly was fooled by SARS and MERS, which has been one-year deals. I mean SARS caused 8,000 cases and 800 deaths. MERS caused about 2,500 cases and 1,000 deaths, and were one-year deals. One and off, and you know, SARS-1, the original SARS, was a bad coronavirus, that was this virus too. But that was not true. I mean as we very quickly learned in China, 80% of those cases were asymptomatic or mildly symptomatic, which was not SARS and MERS. I mean people who had SARS and MERS infections were sick, that's why it was easier to put a sort of moat around them and stop the spread. That wasn't true here.

Dr Paul Offit:

This virus also is weird. I mean it has neurological complications. It can cause kidney complications. It causes a lack in sense of smell and taste. This is not a typical respiratory virus, this is very different than flu. On the other hand, what's weird about it, another one of the weird things about this virus is it really does have a unique predilection for people who are older and have certain co-morbidities, like diabetes or Type 2 diabetes or obesity or hypertension, high blood pressure. But it spares the young. It really spares the young healthy person. That's not true of flu. I mean flu has killed 160 children this year in the United States. Whereas, I think this COVID-19, which has killed 60,000 people, I honestly think it's killed fewer than 10 children. So it spares the child, interestingly. I'm not sure why.

Chitra Ragavan:

You're a member of a working group put together by Dr Francis Collins. Tell us about this group, I guess it's called ACTIV, and what's your goal?

Dr Paul Offit:

Well the goal is to try and facilitate the industry who is making this vaccine, to find out what they need, and how it can be most quickly gotten to them. So for example, what is the critical, immunological determinant of protection? If someone for example is naturally infected with this virus, can we look in their blood, their serum and see just what kind of antibodies they have? I mean assuming then that they're going to be at least protected at least in the short-term. What's the nature of those antibodies. Did they

neutralize the virus? If so, how, at what titer did they neutralize the virus? That sort of thing. The kinds of things that help them in their development program, realizing it's going to be much compressed.

Chitra Ragavan:

You're seeing a lot of attention also being paid to potential anti-viral therapies, separate from vaccines. Do you have any thoughts on where we are with that? I know there are some promising ones, seemingly promising ones that have literally moved the markets in recent days. Where are we with sort of the development of anti-viral therapies?

Dr Paul Offit:

Yeah, I mean so Remdesivir, the news came out about a clinical trial sponsored by the National Institute of Health yesterday, of about a little more than a thousand people who were divided into two groups. One group received Remdesivir, the other one received a placebo, which is to say, nothing. Then looked to see what the progression of that was. Now the primary endpoint on that study was length of illness. What you found was that those who were not treated with Remdesivir had illnesses that lasted about 15 days, whereas those treated with Remdesivir had illness that lasted for 11 days. So that was a benefit, but there was no statistical difference in death. You were just, I think it was 11% that died in the placebo group, 8% that died in the ... Or 8.5% that died in the Remdesivir group, which was not statistically significant.

Dr Paul Offit:

So that's hopeful, but not what you would have really hoped for. There was also a study out of China yesterday showing that people who were severely ill, meaning in the intensive care unit, those who were treated with Remdesivir were just as likely to die as those who weren't treated with Remdesivir, which is basically what this other study found. So I mean it seems to me that the goal of Remdesivir is for people who come into the hospital and have say an oxygen requirement, can you keep them out of the intensive care unit? Can you keep them from being on a ventilator? Can you keep them out of the morgue? That's the goal of Remdesivir. I don't see that. I don't think that that is what's happening.

Dr Paul Offit:

Which tells you that at the time that you're making the diagnosis, by the time they're already in the hospital, now getting intravenous Remdesivir, the degree to which viral replication is an important part of the disease pathogenesis, the process of the disease, is not so important. At that point, the replication, the degree to which the virus reproduces itself happens early in the illness, but as you move later in the illness it's the immune response that's the critical determinant of disease, not so much viral replication. So therefore, an anti-viral won't make much difference. So I think if you catch people early, and treat them with Remdesivir I think you have a much better chance of having a better outcome than the way we're doing it now, which is after they're already in the hospital.

Chitra Ragavan:

You're already seeing a lot of people rebelling against the shelter in place orders. People have congregated in large numbers in certain instances. Without a vaccine, and with people starting to come out to work and to play, I mean what's the prognosis?

Dr Paul Offit:

You know, I think two years from now we're going to look back on this and see what we should have done, and what we shouldn't have done. Because there's two parts of this public health disaster. The first is the virus, which is causing suffering and hospitalization and death. The second is the cure. I mean we're asking people to stay in their house, and not go out and work. Which means that now more than about 25 million people have applied for unemployment insurance, and assume that there are many who haven't applied because they can't figure it out, how to do it, or they're having trouble getting through the phone, or because they can't do it, because they're here undocumented.

Dr Paul Offit:

The original projection is going to be right, I think we're going to lose 20% of the workforce. I think 35 million people are going to be out of work. That's going to approach really depression level, meaning Great Depression, 1929 levels. I mean that's disastrous. With that level, that massive level of unemployment will come massive joblessness, massive homelessness, and all the things that come with massive homelessness, which is the food insecurity, and depression, and child abuse, and domestic violence. Which are invariant when you have this kind of level of massive homelessness and joblessness.

Dr Paul Offit:

So that's the second part of this. I don't think that's getting the attention it really needs. I think we should have been much better at getting out of the house and getting back to work, and that all depended on testing, and we just never had the testing. I think we're never going to have the testing. We should be doing five million tests a day, not 200,000. For that reason, we aren't getting out the way that European countries are getting out. Germany is really the model for this. They're knocking on doors, testing people, and getting people out. They also had half the number of deaths per million that we've had. We just were bad at this, in many ways. It's hard to watch a number of European countries doing so much better than we're doing.

Dr Paul Offit:

I do think the population density is everything, and the spread within a dense population is everything. So populations that are less dense probably can go back to work more quickly. We just are going to look back on this and see things that we could have done better. There's going to be heroes and villains in this story, I just don't quite think we know who they are yet.

Chitra Ragavan:

Is there anyway to overcome this hurdle of testing, and actually start to get more tests out and get people to work?

Dr Paul Offit:

If we haven't done it now, I just am losing hope we're ever going to do it. The administration's right when they say there is the capacity for testing, that's true. What the problem is, is that you need a lot of the ancillary stuff for testing, like swabs and viral transport media. That's what the federal government, through the DPA Act could have really co-opted industry to make that and distribute it, and they never did it. I don't get it. I don't get it. I mean the administration spends time telling you about what a wonderful job they're doing, and then they don't provide the tests.

Dr Paul Offit:

So I think at this point, we can assume we're not going to get them. What we're going to do is we're going to just start getting out there. Georgia's now getting out there, parts of Florida, Texas, are just saying, "Okay, we're just going back." Iowa, whether we think you should or not. We'll see what happens. I think we're about to a grand national experiment to see what we should have done, and what we shouldn't have done, because we don't have the testing, it's really a shame.

Chitra Ragavan:

Just looking back at your career, and looking back at that five-year-old boy looking out the window waiting for his parents to visit, and surrounded by kids who had polio. Looking at your journey, what would you say to that boy about where you are today and your contribution, and the world that you're seeing now, and all this conversation around vaccines?

Dr Paul Offit:

I think that I have served the children in that ward well. Those children who were suffering a disease for which only a couple of years later there would be a vaccine to prevent it. Those children who were largely felt, no doubt, abandoned by their parents, that things are better. That we live longer than we used to. That vaccines have, I think, made us have longer, and better, and healthier and safer lives. I think my charge from them, from the memory of them, has been at some level, fulfilled.

Chitra Ragavan:

Dr Offit, it's been a great pleasure talking to you today. Thank you so much for joining me.

Dr Paul Offit:

Thank you, Chitra.

Chitra Ragavan:



Paul Offit is Professor of Pediatrics at the Children's Hospital of Philadelphia. The recipient of numerous awards and honors, and a physician scientist by training. Dr Offit is the co-inventor of the vaccine that is estimated to save hundreds of lives a day. He also is a tireless advocate for children, both in the books that he writes, and his willingness to take on the anti-vaccine movement. This is When it Mattered. I'm Chitra Ragavan.

Chitra Ragavan:

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