

Season 3 - Episode 3 - Dr. Deepali Kumar

Transcript

BTB

Welcome to Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian Côté and joining us on the podcast today, Dr. Deepali Kumar, an award winning clinician investigator at UHN's Toronto General Hospital Research Institute. Dr. Kumar is director of Transplant Infectious Diseases at UHN's Ajmera Transplant Center. Her pioneering research is improving vaccine responses and protection for transplant patients and in 2021 led to the world first discovery that a third shot of the COVID 19 vaccine provides safe and effective protection against the virus for immunocompromised patients. Dr. Deepali Kumar, welcome to behind the breakthrough.

DR. DEEPALI KUMAR

Hello, and thanks for having me.

BTB

Let's start with the basic issue of vaccines and transplant patients. Historically, vaccines don't provide the same benefit as for non-transplant patients. Help us understand why that is?

DR. DEEPALI KUMAR

When a patient gets a transplant surgery, whether it's liver transplant, kidney, heart or lung, they have to take medications for the rest of their lives to suppress their immune system. And this is in order to prevent organ rejection from happening. So what these immunosuppressive medications do is that they blunt the response to vaccines, and we know that from previous work that's been done in the vaccine world with influenza vaccine, with hepatitis vaccine, etc..

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Right, so take us back to 2020 as the development of vaccines for COVID 19 start to look promising. What are you thinking when it came to, how well might these COVID vaccines work with transplant patients?

DR. DEEPALI KUMAR

We were wondering how well these vaccines would work. We weren't sure because this was a brand new platform with COVID vaccines. We had MNRA vaccines, we had adenoviral vector vaccines, and these vaccine platforms in human vaccines had not been used with human vaccines in the past. So we weren't sure how well they would work with transplant patients. But we had an idea that they may not work as well as they would in the general population.

BTB

So as the COVID 19 vaccines begin to roll out to the public late in 2020, what was known at the time from the trial data about their efficacy for transplant patients?

DR. DEEPALI KUMAR

We didn't know very much from trial data because trial data did not include transplant patients. And this was a huge gap in our knowledge. So we had some assumptions from previous vaccines, but we really didn't know how well these vaccines would work because they were brand new platforms.

BTB

So you set out to close this gap to determine what protection transplant patients actually will get from the COVID 19 vaccine after one shot and after the second shot. So talk to us about the study you constructed?

DR. DEEPALI KUMAR

So immediately when the vaccine announcement was made that we would be giving vaccines to the population, we constructed a study, and this was an observational study that would help us to learn how well vaccines would work, specifically how the antibody responses would be, how the T cell responses would be. So we constructed a study at UHN and immediately got ethical approval and started enrolling patients.

BTB

So what were your findings with regard to the antibody response produced by the vaccine in transplant patients?

DR. DEEPALI KUMAR

We found that the vaccines were not working very well. So the antibody response was quite poor. In fact, we found a five percent antibody response after the first dose of MRNA vaccine

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and a 34.5 percent response after two doses. And compared to the general population, this was quite low. The general population responses were in the order of 80 to 100 percent. So it was actually quite disappointing to see this.

BTB

So after two doses of the COVID 19 vaccine, transplant patient really remained quite vulnerable to the coronavirus. So what were you hearing from patients in clinic?

DR. DEEPALI KUMAR

So patients were very concerned. When these numbers were released, patients were wondering, you know, how protected they were. They were wondering if they should be getting their antibodies checked. You know, there was a lot of anxiety with this, and understandably so. I mean, COVID was, you know, was quite rampant in the population and we were in a big wave of COVID at that time, so very understandably, people were very anxious about this.

BTB

Was there almost a sense of defeatism, like why even bother getting vaccinated?

DR. DEEPALI KUMAR

Well, you know, we tried to combat that sense. There was a little bit of that, but we tried to tell people that antibodies are not the only arm of the immune system that protects you. We have other arms of the immune system like cellular immunity. And in fact, our study actually showed that for cellular immunity, you could actually make protective T cells, even if you did not have antibody. So I think that provided a little bit of reassurance to people that antibody was not the whole story.

BTB

I imagine, though, the disappointment with the efficacy levels of the vaccine for transplant patients, I guess, did that become a bit of an impetus for you to move on and construct a new trial in 2021?

DR. DEEPALI KUMAR

It did. And you know, we were hearing a lot from our patients and really, it's the patients that were the impetus for us to try to think of ways to improve vaccine responses. We were concerned about our patients. We were seeing our patients get COVID. We were seeing them have breakthrough infections even after having two doses. So this was very, very concerning. And so we had to do something and we had to think of ways to improve vaccine responses. And I think our team was actually in a very good situation because we had 20 years of experience working with vaccine responses in the transplant population. So I think we were well situated to find these better ways to improve vaccine response.

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So, Dr. Kumar, describe then the scope, say of the trial, you know, the premise that you came up with in response to this lack or low vaccine efficacy for transplant patients?

DR. DEEPALI KUMAR

What we decided to do at that point was to see if a third dose of COVID mRNA vaccine would increase these antibody responses and T cell responses. And the reason we did that was because we had experience previously from the flu shot. You know, a few years ago, we had done a flu shot study where we compared a high dose flu shot with a standard dose flu shot in the transplant population. And we actually found that the high dose flu shot worked a lot better. So in drawing parallels with the flu shot, we thought, well, maybe a higher dose or a third dose of, of the mRNA vaccine would also work better. And so what we did was we designed a randomized trial, which was placebo controlled. So which this meant that half the patients in our trial would get a third dose of mRNA vaccine and the other half would actually get placebo.

BTB

And talk about sort of the timing and intervals and the dosage throughout the trial?

DR. DEEPALI KUMAR

So the patients we enrolled had received two doses of mRNA vaccines one month apart. So the third dose in the trial was given at two months after the last dose of vaccine, so we followed what we would call a zero, one, three month schedule. So half the patients received the vaccine and half the patients received the placebo. And I have to say I'm very grateful for the patients who agreed to be in this study because they knew that there was a 50 percent chance of receiving placebo, and many of them were actually very anxious to receive the third dose of vaccine. So it was something that I was very glad that patients agreed to do. So that was the basic study design of the trial.

BTB

And you finally published it back in August of 2021. What did you report?

DR. DEEPALI KUMAR

We were very excited with our findings. And what we found was that one month after the third injection, the patients who had received the mRNA vaccine had a significantly higher immune response than the patients who had received placebo. And from a p-value standpoint, this was a very, very significant p-value and also very significant in terms of numbers. You know, some of the, the antibody responses that we saw with the third dose were comparable to the healthy population, and that was actually very exciting. And so we also looked at T cells and we found that T cells also increased, as well as neutralizing

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antibodies, which also increased with the third dose. So overall, you know, when we looked at the overall immunogenicity of the third dose, it was quite good.

BTB

When you got those results, I'm just curious, did you stand back and actually go like, wow?

DR. DEEPALI KUMAR

Yeah, we were just super excited about these results because we felt that we had really found something that would help our transplant recipients and we submitted our results to a journal and we were just monitoring it daily, let's put it that way to see what would happen in terms of the publication.

BTB

And tell us like, this publication had quite a ripple effect, did it not?

DR. DEEPALI KUMAR

It did, when we submitted this for publication, we actually also contacted the FDA in the United States, as well as the provincial agencies, provincial vaccination agencies in Canada. And we actually presented this data even prior to publication because we knew that once the data was published and patients saw the results, that we would really have to be ready to implement third doses.

BTB

And it's happening, isn't it?

DR. DEEPALI KUMAR

It is. And the exciting thing was that our publication came out, and the next day there was a FDA release and the day after there were recommendations to give a third dose.

BTB

So it's become a standard of practice in do you know where so far now?

DR. DEEPALI KUMAR

So it has now been approved in the United States. Ontario has also recommended third doses, and I think it's just a matter of time where third doses are recommended in other parts of the world as well.

BTB

And we should clarify third doses for immune compromised transplant patients. Of course, there is a big discussion ongoing about third doses in general.

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DR. DEEPALI KUMAR

Right. So our study, I think, paves the way for third doses in transplant patients. But it also opens the door to third doses in other immunocompromised settings.

BTB

Right.

DR. DEEPALI KUMAR

Like cancer chemotherapy, like, you know, autoimmune diseases and so on. So I think it really opens the door for other populations as well. The third doses in the general population, I think that's a different story.

BTB

Right? And given the fact that this pandemic is likely, certainly the presence of COVID 19 is to continue for quite some time. Is this a study with a set of patients that you will continue to monitor over the months ahead to see how long the efficacy remains in terms of the antibody response?

DR. DEEPALI KUMAR

And that's exactly what we're doing. So we are following these patients in the trial and we're going to see how long antibody lasts. We're going to check them at six months and 12 months after having the third dose. So we'll see how long this antibody is actually lasting as well as the T cells.

BTB

What are you hearing from your patients now in the clinic?

DR. DEEPALI KUMAR

Well, patients are really excited and patients are just, you know, waiting to get their third doses. And I think, you know, this will be of great benefit to them.

BTB

From a personal standpoint, a moment like this, you know, such a sort of a world first essentially, in terms of the trial data that you came up with in terms of the impact on patients. Has it sunk in for you? Do you allow yourself to kind of pop a bottle of champagne and celebrate?

DR. DEEPALI KUMAR

You know, I have to say things have not really slowed down yet, and I'm waiting for that, you know, champagne moment. But, you know, I think what hit me was how research can

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make such a huge difference to policy and how quickly that can happen. I think this is what research is really all about, and I think that is what has after so many years, it's come to a head, I would say, and I think what has happened is truly amazing.

BTB

Well, and your discovery is quite amazing, and I think it probably also speaks to the body of your work knowing which questions to ask.

DR. DEEPALI KUMAR

Yeah, I think that, you know, having that background of working in the vaccine world and specifically working with immunocompromised patients, I think that really had us very well situated to do this trial and do it in a way that was definitive.

BTB

I'm just curious, with the advent of mRNA based vaccines, you know, my understanding is they can be tweaked very rapidly. They're cheaper to make than traditional vaccines, and there's some there's something like one hundred and fifty trials underway for other viruses and diseases. Is there hope that the discovery of these mRNA based vaccines could one day be, you know, pay off in terms of tailor made vaccines for transplant and immunocompromised patients?

DR. DEEPALI KUMAR

So, you know, there are other infections that transplant recipients get that would be amenable to prevention by an mRNA vaccine. So, for example, something like CMV virus, where we are looking for good vaccines for our patients with CMV and mRNA vaccine would be excellent for our patients.

BTB

What is CMV?

DR. DEEPALI KUMAR

CMV cytomegalovirus.

BTB

Okay.

DR. DEEPALI KUMAR

Similarly for Epstein-Barr virus EBV, which is the virus that causes mono. This also causes quite a problem in our transplant patients, and so a vaccine for, for that would also be very good.

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BTB

And we should make mention of the fact that the UHN foundation was in part, a contributor to helping to finance this study of yours, this world first discovery. Just talk to us, Dr. Kumar, about, you know, the role that UHN foundation and philanthropic dollars played in helping to provide seed money for your study?

DR. DEEPALI KUMAR

We could not have done this study without the support of the UHN Foundation and it was so important for us to have that support. You know, mainly because the study was done so quickly that we had no time to try to get external support like from a grant, for example. And because we had foundation support, we were able to do this study very, very rapidly. I think from start to finish, the study basically took us three or four months, and I'm so grateful to the UHN Foundation for their support.

BTB

You're listening to Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Today, we're in conversation with Dr. Deepali Kumar, award winning clinician investigator at UHN's Toronto General Hospital Research Institute. Dr. Kumar's pioneering research, as we just mentioned, is made possible, in part thanks to the generous donor support coming from the UHN Foundation. So if you would like to contribute to Dr. Kumar's groundbreaking medical research, please go to www.uhnfoundation.ca/podcast.

Deepali you are born and raised in Saharanpur. I hope I have that right in India, a city about 200 kilometers north of New Delhi and then age nine, your parents decide they're going to both pursue PhDs halfway across the world at the University of Manitoba in Winnipeg. Talk to us about the challenges you faced in those first years after the move.

DR. DEEPALI KUMAR

You know, I moved from a small town in rural India all the way to Canada, and it was a huge culture shock. I had never seen snow, I didn't know the language. I mean, English is not my first language. And in my first year, which happened to be in Winnipeg of all places, they put me back a grade and I had to actually repeat the fourth grade. And that was because, I guess I wasn't well versed in the schooling in Canada, but I have to say it was such an exciting time to learn new things. I was amazed at how friendly people were in Canada, and I made friends, you know, which was a great time.

BTB

Your parents complete their PhDs, move on to teach at Carleton University in Ottawa. I'm curious when you reflect back on what it must have taken for them to make such a life

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altering decision, change their careers, uproot their young daughters and move you across the world to essentially start over. What lessons do you draw from their courage to do that?

DR. DEEPALI KUMAR

You know, I think that is such a brave thing to do. And what I learned from that is to never be afraid to take risks and to follow your dreams. This is what my parents did. You know they wanted a better life for us. They wanted us to be well educated and they were brave. They were not afraid, and that's what I learned from them. And if you do that, if you are not afraid to take risks, you will certainly succeed.

BTB

You've mentioned in the past the critical importance of good teachers in helping to shape and guide your education and your career journey. How do you in turn, now mentor?

DR. DEEPALI KUMAR

You know, I've had amazing teachers and I've also had amazing students, which I've been very lucky to have. You know, I think as a mentor, it's important to always be there for your trainees, for your students. It's important to put your students first and make sure that they are learning. And it's very important to not only be there for your students at the time that you know they're with you, but also afterwards, you know, afterwards, when they go out into the world, they get new jobs, they're in their career and they want to talk or they just want some ideas for research. I think it's just very important to be there for your students now and also in the future.

BTB

I read actually a number of interviews that you've given over the years in preparation for our chat today and you've talked about work-life balance quite a bit and how important that is for you. Talk to us about your approach?

DR. DEEPALI KUMAR

You know, I always put my family first, that's always been my main approach. My, I have three children that are the center of my life, and I put a lot of effort into work, but I always make sure I'm there for my family when they need me. So, you know, I know that a lot of people listening are very driven and, you know, want to succeed in their careers, and they certainly should. But I think, you know, what I would say is that your life outside of work is just as important as your work life. And so it's very important not to put off personal things because you think, for example, the timing is not right because of your career and so on. It's very, very important to be well grounded in life and to focus on your non-work life as well, because that is truly just as important as your work life.

BTB

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Well said, let's turn to your patients. As a clinician, you see patients a lot. You see the stakes involved in making things better for them. How do you balance that urgency with the fact that science takes time?

DR. DEEPALI KUMAR

So, you know, the science and patient care both inform each other if science is not done properly or methodically, then it will negatively impact patient care. So you definitely cannot cut corners in science because you're feeling this urgency to happen. And I think, you know, the case in point is the recent study that we did on third doses. We knew we had to do it quickly, but we did not cut corners in terms of the methods we used.

BTB

Do you ever feel pressure in this work?

DR. DEEPALI KUMAR

Well, pressure is built into transplantation, which is what I do. That is the nature of transplantation. Transplantation is a high stakes profession. And so yes, there is a certain degree of pressure. For me personally, I like a little bit of pressure and I think that really keeps me going personally.

BTB

How do you navigate failure? Because we're not really taught in school or in life, how to cope with failure, how to deal with failure?

DR. DEEPALI KUMAR

No, we're not taught how to deal with failure. And you know, many people deal with failure in a bad way. But, you know, I think it gets back to where your priorities are and if your priority is your family, if that is also a priority for you, then you are grounded. You know, you need to be, well, grounded to be able to deal with failures because in research, there are more failures than there are successes. And I think it's very important to be grounded in order to help, you know, in a healthy way, deal with your failures.

BTB

There's an author, Simon Sinek, who speaks and writes a lot about leadership and motivation, and he has a quote that I really love to read to people and it goes like this, "People don't buy what you do, they buy why you do it." Why do you do what you do?

DR. DEEPALI KUMAR

I'm motivated. I have a lot of internal motivation, and I think that's what really keeps me going. And the internal motivation comes from seeing a lot of patients and seeing them get better. Because when I see patients get better, I'm motivated to find that next cure. That

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next discovery, you know, doing that next study. So I think for me, seeing patients get better and science really go hand in hand.

BTB

What's interesting about the COVID 19 pandemic is it's raised medical research into the everyday consciousness of the general public. It feels like almost a once in a lifetime opportunity to demonstrate to Canadians that it's an essential service. It's intertwined with healthcare. I'm curious, though, as the pandemic hopefully fades, will medical science also fade back into the background?

DR. DEEPALI KUMAR

You know, COVID has really brought medical science right to the forefront. It's brought medical science into people's homes, into their daily lives. It's all over the news and, you know, as the pandemic fades. And I think that's a big if, it's if it fades. I don't know if we will really see medical science fade into the background because I think we've made a big impression. Patients have a lot of other medical problems that have nothing to do with COVID, and we still need to tackle those. So there is a lot of work to do in medical science.

BTB

And I'm curious, what do your parents think of their daughter and her achievements?

DR. DEEPALI KUMAR

You know, my parents are very humble people, and I think they are just enjoying the moment as any parent would, you know, with their child in medical science and working on COVID. So I talk to them every day and they always have a lot of questions for me about COVID. They want to know what I'm doing next, they want to know what other research is going on. They're very interested in COVID research because they're researchers themselves and I think a lot of curiosity that I get, I think I get it from them too.

BTB

So what's next for you, what you would be watching out for in the months to come?

DR. DEEPALI KUMAR

I've taken on the role of the incoming president of the American Society of Transplantation, which is a real honour and privilege. And this will really allow me to take transplantation internationally, and it will allow me to advocate for transplant patients at an international level. But in addition to that, I continue to do research and my research is continued focus on COVID and the project that we've started in terms of making sure that our transplant patients are protected from COVID will continue on and we will make sure that you know, we continue to make new discoveries that help our patients.

BTB

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Well, Dr. Deepali Kumar, award winning scientist at UHN's Toronto General Hospital Research Institute. Thanks so much for sharing your pioneering research with us and continued success.

DR. DEEPALI KUMAR

Thank you.

BTB

Dr. Kumar's research is made possible, in part thanks to generous donor support. If you'd like to contribute to her pioneering medical research, please go to www.uhnfoundation.ca. That's all one word uhnfoundation.ca/podcast. And for more on the podcast, go to our website uhn.ca or www.behindthebreakthrough.ca and let us know what you think. We love feedback. That's a wrap for this edition of Behind the Breakthrough, a podcast all about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.