Edited transcript of interview with Associate Professor Aniruddh Deshpande, Paediatric Urologist and Clinician Researcher

A/Prof Deshpande was interviewed by Imelda Wilde and Deirdre Pinto of Chronic UTI Australia on 6 September 2024. This is record of the interview has been edited and some material re-arranged under the relevant headings. This transcript is shared with Dr Deshpande's permission.

Improving recognition of chronic UTI

Chronic UTI Australia: What can we do to improve recognition of chronic UTI in Australia?

A/Prof Deshpande: We need a precise definition of what chronic UTI is. Doctors don't like imprecision. Because we're still understanding it, doctors don't have a clear understanding of chronic UTI.

People who are at the coalface of science are understanding the processes, but the different lab findings have to be reconciled into one tight definition that we can apply to people with symptoms.

Chronic UTI Australia: A clear definition is possibly challenged by the fact that it [UTI] is a spectrum [that can range from a simple, acute infection through to recurrent and then chronic symptoms]. And the symptoms aren't easy to see or measure. What we say, just to make it simple, is that once that infection starts embedding into the bladder wall and into cells, then it's turned chronic.

A/Prof Deshpande: Yes, but that will be hard to prove at a population level. We know what we're talking about, but not everyone does. We need a solution around that, and we are working on that. A starting point would be a good sellable definition, something that is nice and tight, that people can identify with, latch onto.

Your group [Chronic UTI Australia] has had a big role in improving recognition of chronic UTI. So, push on. Because the definition is loose does not mean the patients don't suffer. But I think it's nice to acknowledge up front [that the definition needs to be tightened] because that will win over the sceptics a little bit more.

Chronic UTI Australia: It's unfortunate that anything related to the urinary tract seems not to be talked about – it's not glamourous. Let's make it glamourous!

A/Prof Deshpande: I agree. It's in everyone's best interests – men as well as women – to make sure women don't have UTI. But people don't want to talk about their urinary problems. We need to reframe it.

Attitudes are already changing. It's different now even compared with four or five years ago. I think that Natasha's article [the feature article on chronic UTI, written by Natasha Robinson and published in The Weekend Australian in February 2024] will change the landscape forever.

Improving diagnosis of chronic UTI

Chronic UTI Australia: When did you first realise that dipsticks and urine cultures were failing to pick up infection in some of your paediatric patients? Was there a point at which that happened, or has it been more of a gradual thing?

A/Prof Deshpande: It's been a gradual thing, because I was noticing these patients in my practice, and then I happened to be doing a stint in the US [United States]. My interest is functional urology, which is bladder-related functional problems, and I had a semi-sabbatical in the US in 2016. As part of that sabbatical, I got introduced to Tom Hannan's work. Tom Hannan was the person in St. Louis who set up the first mouse model of chronic UTI. And now all his PhD students are spread out over the world and using this.

Tom Hannan first described this intracellular embedded infection in mice with uropathogenic E. coli. He saw the problem being unpredictable, in the sense that you can't predict which mouse will get it. And then unpredictable in its course; whether [the individual mouse] will clear the infection or not clear it.

When I started putting my clinical experience and his findings together, I realised that this is what some kids probably had. So, when I came back, I went to a person who had the ability to test this in the lab for me, who happened to be Malcolm [Dr Malcolm Starkey, now leader of the Urinary Tract Immunology & Microbiology Research Group at Monash University]. I said, "We should do this together." We succeeded with an NHMRC [National Health and Medical Research Council] Ideas Grant, which allowed us to model chronic UTI in young mice. That work is progressing well, with additional grant applications submitted and higher degree research students developing their careers in this area.

Chronic UTI Australia: Is that when you started looking into doing the confocal microscopy?

A/Prof Deshpande: Yes, that happened about two years ago. I worked with one of our infectious disease professors to get access to the [confocal] testing. The work [which demonstrated the presence of bacteria within the epithelial cells lining children's bladders] happened here in Sydney.

Chronic UTI Australia: Some doctors have asked why the confocal microscopy technique can't be rolled out on a larger scale [to overcome the current difficulties in diagnosing chronic UTI]?

A/Prof Deshpande: It's not very viable. It's a very expensive test. The confocal microscopy shows bacteria with colours. You need to administer a dye for the bacteria to light up, which means you will need a different dye for every bacterium, because chronic UTI is often polymicrobial. And that adds to the expense. When you're looking at a human sample under a normal microscope it's a one-stop shop, whereas this [confocal microscopy] is very iterative. I am very fortunate in being able to setup a team at the Children's Hospital at Westmead and The University of Sydney where we have passionate researchers who are willing to do this and further.

Chronic UTI Australia: So, it's not suitable for rolling out on a large scale?

Chronic UTI Australia: No, at least not in the form in which we are testing it in the lab.

Chronic UTI Australia: Do you ever look at the urine for white blood cells and shed epithelial cells in your clinic, like they do in the late Professor James Malone-Lee's clinic in London? The Professor uses cells counts to monitor patients' response to treatment. Diagnosis is based on the history and symptoms.

A/Prof Deshpande: Yes, we draw on Professor Malone-Lee's research. We try to correlate what we find on simple urine test to what we find on concomitant microbiome tests and confocal microscopy.

Chronic UTI Australia: It [diagnosis of chronic UTI] is not easy. When you've got a respiratory infection, for example, you might have a cough, you'll have phlegm, you can have a wheeze. There's more evidence that's easy to observe and a lot of different things you can do to check the diagnosis: you can auscultate the lungs, do spirometry. With a UTI you might have blood in

the urine, but that could be other things besides infection. And not all chronic UTIs will have bleeding.

A/Prof Deshpande: We need to look at different pieces of information that may indicate chronic UTI… [for example] the point that Dr. Helen O'Connell [President, Urological Society of Australia and New Zealand] makes about epithelial cells in urine samples of adults not being just plain epithelial cells [typically reported as contamination in by pathology labs], but possibly eutrophic cells loaded with bacteria. Our findings in our lab certainly are supportive of this suggestion even in children.

We need to tease out the science, understand the science and the process of [chronic UTI development and persistence] and simplify the findings into a clinical application to diagnose chronic UTI.

One of the big challenges for you [Chronic UTI Australia] is to get the pathologists on board. Involving them [the Royal College of Pathologists of Australasia] is something the group [the expert clinicians and researchers who attended Chronic UTI Australia's roundtable in May 2024 and who have since maintained contact in a WhatsApp group] is talking about. Like the article in The Australian, I think the next game changer for you – for us - would be that.

Need for research to better understand and treat chronic UTI

A/Prof Deshpande: Over time, I have been able to confirm it [chronic urinary tract infection] in my practice, but not with the precision that I'd like. It can be challenging to treat, and responses to treatment are unpredictable. There's a small proportion [of chronic UTI in children] that self-resolves, but it's all very unpredictable.

We need to do a lot [more] work [on understanding chronic UTI. But we're making good progress in our lab and we hoping to set up a clinic t the [Westmead Children's Hospital] soon.

It is very important to tease the science out – to understand the various factors – host factors, environmental factors – that contribute to chronic UTI. We are hoping to apply for some funding to get this science sorted. Chronic UTI is not just a simple infection.

Understanding 'host factors'

Chronic UTI Australia: Are you interested in studying the immunology of chronic UTI as well – what Malcolm Stakey calls 'host factors?' It's something we talk about quite a bit in our group – why some people seem to be able to clear acute infections easily – even without necessarily taking antibiotics – while others go on to develop recurrent and chronic UTI.

A/Prof Deshpande: Yes, yes, yes. There are definitely some immunological factors. One of the things that Tom Hannon said, all those many years ago, I think 12 years ago, is that if laboratory mice were given Nurofen, they did not develop chronic UTI [in an experimental mouse model of the condition]. Nurofen is non-steroidal anti-inflammatory, which works via COX-2 inhibition. But that was a serendipitous observation…and you can't give Nurofen to every child every day.

Another lab, in Colombus, is taking a slightly different approach [to understanding host factors]. They are looking at cohorts of children who have higher chronic UTI incidence, such as children with obesity or diabetes. They are trying to understand why these groups are getting more infections than the normal population and working backwards from there. They have some expertise in antimicrobial peptides.

Better understanding of the science of chronic UTI will lead to better diagnostics and treatments. We are not yet there.

Researching treatment interventions

A/Prof Deshpande: The therapeutic windows are also interesting because this is not simple infection. Biofilm and other things [can complicate treatment].

Chronic UTI Australia: Do we need to bring in strategies other than antibiotics alone?

A/Prof Deshpande: Yes. It's going to be a good, interesting journey.

Chronic UTI Australia: Are there strategies? I know Professor Malone-Lee was a little bit cynical about biofilm busters. Because biofilms are not just in the urine.

A/Prof Deshpande: Yes, biofilms are everywhere in the body. They are a normal part of the body that can play a protective role in many situations. But biofilms can potentially compromise treatment success in many different situations – in wounds that don't heal [for example].

There can be 'super menace' biofilm. There is a lot of people doing very good biofilm research. I think the Scandinavians are leading the pack, but there's Americans, there's Australians. So, I think we will have to work with them.

The other aspect is immune therapy. We need to understand which 'host factor' is being switched on or off. Is there a window, or a couple of windows of opportunity [for effective treatment to eradicate the infection}? We are studying that. All our patients get immunological assays.

Chronic UTI Australia: I wonder about the impact of diet when we talk about environmental factors? I remember reading a study about some Scandinavian country where people like drinking sour milk, such as kefir, with the good microbes in it. They said there was a reduced incidence of UTI in women who regularly drink sour milk products. And when we talk about kids having UTI, it's particularly kids who are obese and kids with diabetes, and kids who are eating a lot of refined carbohydrates.

A/Prof Deshpande: The important thing is that it is probably the easiest thing to fix. If there is a dietary modification we can make, everybody will agree. You know, there was a very interesting study at the John Hunter Children's Hospital. Families coming into the hospital, whether for a child's fracture or whatever, were given a survey, and it was found that 90% were already doing something to improve their child's diet. [Getting them to] eat less carbohydrates, more protein, less peanuts…some kind of change, based on no medical recommendation]. Whether it was the right thing or not, there's a lot of interest in that area.

Chronic UTI Australia: So, if we were to come up with a dietary recommendation, there would be high compliance?

A/Prof Deshpande: Yes.

Immediate strategies to prevent and treat chronic UTI

Chronic UTI Australia: Do you have any thoughts on what we could do right now that could make a difference to chronic UTI patients? We've talked about getting a concrete definition of chronic UTI, but are there other things we could do now [to improve recognition, diagnosis and treatment of chronic UTI]?

Primary care education

A/Prof Deshpande: The first thing I'd say is that you [Chronic UTI Australia] have come a long way in just six years. We're seeing some success already through increasing awareness. We will see some change happening. Apart from lacking a tight definition of chronic UTI, I don't see

huge ongoing scepticism about chronic UTI. Once we educate them [doctors], they'll latch on quickly.

Our solutions have to go through a certain pathway, starting with primary care education. Capacity building in primary care is critical, so GPs can pick up red flags. But capacity-building needs to be an ongoing thing and it should keep up with the science.

Ensuring acute infections are fully resolved

Chronic UTI Australia: In the survey we did with people experiencing chronic UTI symptoms, the average time between participants' first UTI and chronic UTI symptoms was 8.5 years. It occasionally happens that people get a big infection, and it turns chronic very quickly, but the more normal pattern seems to be a longish period of repeat UTIs before the infection becomes embedded and chronic. Do you have any views on preventing UTIs from turning into chronic UTIs?

A/Prof Deshpande: Well, nobody calls me in their first UTI. It's the GPs and [other] primary care people who do it [treat straightforward UTI]. But this question is 'what happens if my friend gets it.' Based on what I've seen in the lab, if there is any hope of stopping this turning into an embedded infection, I would grab it.

If you're testing the urine of someone, a child or an adult, who has had a UTI recently and has been treated with antibiotics, the numbers [culture cells counts that indicate infection] have to be different. So, when we talk to the College of Pathologists, that's what I would be pushing for – changes in the way urine test results are reported. If you're testing a person walking on the street with no problems, you can apply whatever [definitions] but if you're treating an adult or a child who's had a urine infection in the last few weeks, the definitions have to be different. The end of treatment should not be a negative culture test. I think the end [goal] of treatment is to have no epithelial cells, no pus cells. As the science advances, we may agree on different end points that include metabolomics, proteomics and state of the art microbiological paradigms.

Chronic UTI Australia: What about symptoms?

A/Prof Deshpande: Symptoms may go away quite quickly. If you start antibiotics [for an acute infection] just now over coffee, tomorrow morning at breakfast you will be asymptomatic. But the infection may not be fully resolved. That is the problem. It's not a good thing.

Chronic UTI Australia: That's why we need new [testing and treatment] guidelines.

A/Prof Deshpande: Exactly. I agree.

UTI and chronic UTI in children

Chronic UTI Australia: We hear you're slammed with referrals for children who have suspected chronic UTI.

A/Prof Deshpande: Yes, it's largely girls that we're seeing. Under six months of age, 90% of kids with UTI are boys. Once you get past six months, the girls take over. As you go from six years to 14 years, the oestrogen climbs up and the rates of problems climb up. These kids are suffering.

Importance of UTI research in paediatric populations

A/Prof Deshpande: The advantage we have in paediatrics [from a research perspective] is there is no sexual activity, no menopause and those sorts of factors coming in. There's no endometriosis. These 'confounders' are not there.

We're trying to build the scientific understanding of chronic UTI in kids [so we can get] better diagnosis and treatment. All our patients who are getting confocal [analysis of their urine], they're also getting urine immunological assays to understand which urine cytokines are going up and down.

Very few labs worldwide are doing chronic UTI research One lab, at Columbia University in the U.S., is looking at cohorts of children who have higher chronic UTI incidence, like kids with obesity and diabetes, and examining the role of antimicrobial peptides. They're trying to understand why these kids are getting more UTIs than the norm.

In some ways these [different research approaches] are parallel roads and they'll converge somewhere.

Recognition and treatment of chronic UTI in children

Chronic UTI Australia: You mentioned in [your interview for] The Australian magazine that a lot of your colleagues are still not accepting of the idea of chronic UTI in children. We are fascinated to kind of understand what the barrier is. As we touched on before, not having a clear diagnostic definition is probably part of that. Do you think there are other barriers too?

A/Prof Deshpande: We need streamlined pathways for management of paediatric chronic UTI, including specialised clinics and lab support, is important to enable primary carers to feel supported and hence confident.

I think doctors want to treat their patients. But the eye doesn't see what the mind doesn't know. That's the number one thing. So, they'll treat it as a recurrent UTI and go down that path forever. Once we make them aware of chronic UTI, I think they all latch on pretty well. I don't see a huge ongoing scepticism. But it's our duty to give them a tight product that they can identify with.

Chronic UTI Australia: What's your opinion on treatment of acute UTI in children to avoid the potential of developing recurrent and chronic UTI later?

A/Prof Deshpande: In paediatrics, there are some things that we do differently to adults. One is we always do boys and girls differently. Physiologically they are different: nature has made them different. You can't apply the same science to boys and girls.

With boys, I wouldn't fret too much if they got a UTI, I would just treat them using the [existing treatment] guidelines. But a girl getting an acute e. coli UTI would worry me [about making sure it was fully treated]. If there is any hope of preventing this turning into a chronic UTI I would grab it.

A/Prof Deshpande: Chronic UTI Australia: Are different treatment approaches in children compared with adults?

A/Prof Deshpande: There are some things we do with adults that would be very difficult to do with children. Giving adult women estrogen can help prevent and treat UTIs but giving seven-year-olds estrogen is going to be very complex in a society like ours.

There may be a role for probiotics too.