

[Voiceover] Welcome to The Pathologist Cut podcast. This RCPA podcast highlights the critical work of pathologist and the integral part pathology plays in medicine and health care.

[Dr Michael Dray] As you all know, 2020 has been a weird and different year. Lots of us have faced many challenges along the way. Since the start of the pandemic, the pathology community has done so much to bring online the massive PCR testing for early diagnosis of the SARS-CoV-2 virus, thanks to timely, measured responses from governments on both sides of the Tasman. Both Australia and New Zealand have been among the world's best in their response to this pandemic.

We're joined today by Dr Mike Catton. Dr Catton is deputy director of Melbourne's Peter Doherty Institute and has been part of Australia's frontline response to COVID-19.

The Doherty Institute researches and treats viral infectious diseases and was the first place in the world to grow the COVID-19 virus from a patient sample outside China. Mike, thanks for joining us today. What were your first thoughts when hearing about these unexplained cases of pneumonia in Wuhan?

[Dr Mike Catton] I guess we were alert, but not alarmed. We heard in late December there was a cluster of something like 40 cases of pneumonia, apparently linked to a wet market in Wuhan, but without any deaths. And with that, and that is specifically said without any evidence of human to human transmission. So that sounded a bit like a bit of a rerun of SARs, but without the the mortality, and it sounded a bit like a point source outbreak, rather than something that might go on to transmit how wrong we were.

So something really to keep an eye on, but not necessarily to be concerned about. And then, of course, things changed.

[Dr Michael Dray] Mike, you mentioned a point source outbreak. I don't quite know what that means?

[Dr Mike Catton] Meaning that simultaneously a number of people are infected from a common source at the same time, rather than people being infected in dribs and drabs over time, which may be more consistent with human to human transmission. So a point source outbreak might be consistent with an environmental exposure in the market, so might be more limited than its potential to spread. And that was consistent with the early information apparently ruling out human to human transmission of that obviously turned out to be wrong.

[Dr Michael Dray] At what point did you realise this was transforming into something more serious, like a corona virus?

[Dr Mike Catton] With the news really came in dribs and drabs through January? I think it might have been as early as around the 10th 12th of January, something like that, but there had been deaths started to assume a more serious tone.

And then over the weeks after that, there was evidence of human to human transmission and that then became really concerning. W.H.O. reached out to our lab on the 10th of January, asking us informally if we had a test capable of detecting coronaviruses or novel coronaviruses.

So we put two and two together and made four thinking that this might be what was going on and it did indeed transpire. So that prompted us to go to a group specific coronavirus PCR that we hadn't got a whole suite of assays designed to detect should they arise, really things that we developed in the wake of the first SARS and avian influenza outbreaks. So we went to international sequence databases of human and animal coronaviruses and checked the tests we had against everything that was known. Not because it had been some years since we develop that test and we wanted to check against the latest information.

It seemed to be capable of detecting everything, at least on the computer. So we were confident that we had a test that could detect something new. And it was really only only days after that the Chinese authorities released the full sequence of the new corona virus, so we then had the opportunity to compare our tests to the actual virus. And also we might. We ordered some PCR primers that we knew would take some that specific virus. So it only takes days to get PCR primers manufactured these days. So we were pretty confident early on that we were well-placed should they be Australian cases.

[Dr Michael Dray] So, Mike, the data came out of China with the code for the virus. So what? What happened next in Australia?

Well, in in small numbers, ones and twos. People returning from Asia, China who had respiratory illnesses and various state jurisdictions began to be tested quietly. Some of those made the media, and they were fairly overblown headlines about such and such person and such and such a hospital being tested.

And then finally, the the Friday night before Australia Day weekend of all pathologists know it's always a Friday night. We were actually just sitting down in the meeting room to plan the roster for working through the weekend, and there were two scientists hovering at the door looking serious.

And with the news that we had what looked like a first positive case, which was a return traveller who was being cared for in Monash in Melbourne. So we went on through that evening till about 4:00 in the morning doing more tests and sequencing the PCR products because it's the first case in the country. So to be surer than sure. But I think covertly

about 6:00 head scientist Julie inoculated some cell cultures with as big a volume of that sample that was positive on the PCR as we could muster. And part of our preparedness was at all times having some flasks of cells ready to go should they be something interesting or of concern. And so really, the sample went from its initial tests to into cell culture really quickly, and that was probably part of the story of the success.

[Dr Michael Dray] So it just seems staggering that then by the end of that, we had diagnosed the first case in Australia. You had got a live cell culture up and running and viable, and you'd done and you'd sequenced it. That's unheard of, really. And is that the way for future pandemics and future viruses?

[[Dr Mike Catton] I think this pandemic is in so many ways, a pandemic of firsts, but how the next generation sequencing has been used epidemiologically study the virus, the speed with which vaccines and tests are being developed. Linfa Wang, actually a very famous virologist, was giving a presentation contrasting the timelines with SARS one in this outbreak and how much more compressed the time was obviously reflecting technological development, but also greater preparedness and experience. You know, we're just able to respond quicker and more effectively. So look its the way of the future.

[Dr Michael Dray] So virus in the lab, then you started being very generous and the true Australian way and antipodean way. So so what was the what was the altruism there? What was the motive for getting it out there?

It was an experience that, well, some notably with SARS-CoV-1, but that other subsequent outbreaks as well with SARS-CoV-1, the lack of willingness of institutions to share particularly isolates of the virus, but reagents in general was notable, and it was a real barrier to scientific collaboration. And we noted that strongly and had a view that things would be much better if it wasn't like that. So the Chinese had the virus, but they were clearly some barriers internally there to sharing, and we now have it.

We were in a position where we could share. We really wanted to be seen to do that, to do it and be seen to do that and send a message how this pandemic should be approached. And I don't know that that was the reason it's the same was certainly taken up.

And it certainly has been an incredibly collaborative approach to this pandemic, which is a contrast to past serious outbreaks. So I think it's been a very, very positive evolution in the way people have responded.

[Dr Michael Dray] So it sounds like you have been planning for this outbreak for a long time. What's gone into the planning process for this?

[[Dr Mike Catton] First and foremost, our job is to detect the virus. So the preparedness

has been the tools that will enable us to detect the unexpected to diagnose new viruses. So is broadly reactive PCR tests, but also an automated workflow that would let us push through significant numbers of samples.

As it's turned out, we've we've ended up testing numbers of samples that we couldn't believe we were capable of. And then a frontend for that workflow of containment labs, because what we're presented with might be the moderate end of the lethality scale, or it might be highly lethal.

So we've got the physical containment level two labs like any sort of hospital diagnostic lab, but we've also got PC3 for treatable but dangerous viruses and then the PC4 suit lab for untreatable, dangerous viruses. So any of those frontends to the laboratory can receive and process samples and render them in in a state that we can then put into the automated PCR workflow. So that the logistics of getting samples from the front door through to the report at the end of the workforce facility, all of that issues pathologists will be very familiar with in any testing process. Preparing that with a mind to it being available to cope with an outbreak or anything that might be expected or unexpected.

[Dr Michael Dray] So how are we faring compared to other countries?

[Dr Mike Catton] Look, I think Australia was, of course, I'm biased, I think Australia has done really, really well. To all evidence, that first case at Monash Medical Centre was the first case in Australia that we detected. So there's no evidence that we had cases or transmission in the community before that.

So we were capable of quickly on a case definition grounds, detecting potential case testing and identifying that case, culturing the virus and going off to share it to characterize and confirm it. We pretty quickly over the weeks that followed that detection, had rolled out test capability in all the Australian states and territories and in New Zealand.

So we played a role in helping. And some like New South Wales and Queensland were already underway. Others access and activated control material from us so that by some primer sets for some like New Zealand where for a time we supported with diagnostic testing. Now there's sort of high throughput capability in New Zealand that was all done pretty quickly. And so all states and territories in Australia and New Zealand, so Australasia had test capability up pretty quickly. And if you compare that performance to the United States or Europe, it's very, very favourable positioning of our capability compared to what others achieved. So I think a real pat on the back for Australasia.

[Dr Michael Dray] So testing is sort of a point of difference as to how we've we've fared with managing the COVID pandemic?

[Dr Mike Catton] Yes. The public health responses has been very successful as well. Victoria and New Zealand have shown that even with an extremely successful testing and control strategy, how easy it is for a small cluster to develop and then the small cluster become a large number of contacts and spread. It's really showing us what the benchmark of how we need to achieve going forward to keep vigilance.

[Dr Michael Dray] And a lot of those decisions are guided by laboratory tests.

[Dr Mike Catton] Look at everything starts with the laboratory techniques that really does. You know, there aren't too many viral infections where you can stand at the foot of the bed and make a diagnosis. It just does not happen. It's all about the laboratory.

[Dr Michael Dray] We've been talking about the role of the laboratory and genomics at really helping contain and control and and just sort of monitor this whole pandemic. And we're looking at the future with genomics again. Do you have any sort of thoughts or messages or tips for junior doctors or trainees as to from your position? What would you like to say?

[Dr Mike Catton] Encourage people to consider a laboratory career in that it is. It's where everything begins. There's lots of rewarding areas of medicine, but everything begins with a laboratory diagnosis. Or at least I like to think so. I think it's a fascinating area.

It's an area very technically driven, and we're in a phase of incredible technical evolution at the moment with the evolution and I.T. capabilities like data crunching capability to to be able to manipulate and analyse data in ways and in close to real time and at scale, ways that we never could before.

So that makes an enormous range of things possible. Our ability to detect tiny quantities of quantitate as analytes, whether it's a molecule in a in a sample or a whole virus. That's very, very similar. And virology has morphed in my career from sort of like growing orchids and a greenhouse into this era where it's this big data, high throughput, incredibly penetrating analysis. There is an amazing opportunity to make a difference from the laboratory and there, particularly in areas like haematology and microbiology, where there is dual training that is becoming increasingly popular is the ability to play in the clinical, a very patient centric focus with a very laboratory centric focus and experience how those two things go together.

Generally, people, I think, gravitate within that to to one place or the other. So there are people whose calling is greatest in the lab and may have research interests that's based around the lab. And there are others that are more in the in the clinic and at the bedside.

But but you get to span both things. So I was going to put in a plug for virology because virology is as we're demonstrating an incredibly impactful area of pathology but has a tiny

workforce and and the clinical virologist workforces guys like me.

From, you know, from a we were talking about Jurassic Park before, from the dinosaur era who are going to be gone, so there are opportunities to be involved in clinical virology. And I think a real workforce gap in the pathologist workforce, and it's certainly an area that would be crying out for people that are fascinated in the lab and in the research and clinical and that blend you can put together.

[Dr Michael Dray] Well, you're a wonderful advocate for the clinical virologist, as well as the number cruncher, and it's wonderful just to share some of your passion and some of your stories directly out of Michael Crichton novel. And it's been great talking with you, Mike. So thank you very much.

[Dr Mike Catton] Thank you so much. Nice talking to you.

[Dr Michael Dray] Thank you.

[Voiceover] You have been listening to the Pathologist Cut podcast with RCPA President Dr. Michael Dray. For the latest RCPA updates, make sure you're following us on Facebook and Twitter.