

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

[Dr Michael Dray] It is my pleasure today to talk with Dr Annabelle Farnsworth. She is a specialist gynaecological histopathologist and cytopathologist at Douglas Hanly Moir, Pathology, Sydney, New South Wales. Here she is, both director of cytopathology and medical director, a post she has held since January 2000.

Dr Farnsworth is well known throughout Australia and internationally for her contributions to cytology and gynaecological pathology. Oh, thank you, Annabel, for your time today. Cervical cancer is a preventable cancer, yet it is the fourth most common form of cancer among women worldwide.

Can you explain why this is the case?

[Dr Annabelle Farnsworth] Cervical cancer has been one of the most investigated and studied cancers over good 60 odd years, and it's interesting that we know a lot more about cervical cancer than we do about most cancers. For instance, we do know that it's an actual HPV related disease.

Many it's related to an infection with a human papillomavirus. Before there was a screening program or screening programs existed, it was the commonest form of death and called form of cancer in any country. And it was an absolute scourge because it affected young women often in the prime of their lives.

But it was realized many years ago in the 1940s that if you screen many if you look for the precancerous cells, you could actually find the precancerous, when the cancer was still in a precancerous phase it means it can be completely treated and cured.

And so that was really the beginning of cervical cytology. We were able to take cells from the area of the cervix and have a look at them under the microscope that allowed us to see those precancerous changes.

But, of course, to have the skill base and the knowledge base to do that surprisingly complex process was really only available in countries where there was well-developed pathology, medical laboratory science area. And so there were many countries in the world in the less developed countries, where the skill base and the technology literally just wasn't available.

And so we really have seen over the last 20 years this emergence of the countries that had access to a screening program. And in those days, it was just cytology the incidence of cervical cancer and the mortality from cervical cancer.

That's the rate of its occurrence. And the deaths have just fallen dramatically. Whereas in countries where there was not access to these technologies, basically the rates of cervical cancer in women stayed very much the same. So they stayed really high.

And we're talking about countries even in our neighbourhood. So places like Indonesia, Papua New Guinea, the South Sea Island countries right to this very day, they have incredible rates of cervical cancer and cervical cancer remains a common form of death in Indonesia and Papua New Guinea, for instance.

So it's actually one of the great tragedies of medicine. And I suppose the inequities that you see in medicine are really highlighted in this cervical cancer area. So, yes, in those countries, it's a real scourge. So that's really why it's happening.

And it also, I suppose, highlights how important cervical screening is. And it's like many things, you know, when it's not a huge issue, like cervical cancer is not a huge issue anymore in countries like Australia and New Zealand.

Then people forget that that it can be an absolute killer of young women.

[Dr Michael Dray] So that's a really amazing thing you've just said that there's been a huge impact on mortality of women worldwide, directly linked to the role of pathologists and cytologists with cervical cytology. That's that's quite an incredible statement.

[Dr Annabelle Farnsworth] Yes, it's actually true. And for instance, both Australia and New Zealand, it's I personally think it's one of the unsung kind of great success stories of both pathology, but also public health, because in both countries, it's treated as a public health program, meaning they're centrally organized by government.

And the other thing that we've learned about over the last 20 to 30 years is that for these programs to work, they have to be run with appropriate checks and balances. You have to have the equipment. And I think it's really interesting that both countries, both Australia and New Zealand, recognize this.

And so they have in place all of the quality assurance measures, all of the accountability measures. And these days, they understand the risks that are involved in a cervical screening program and have had a risk based analysis and quality programs that are now becoming absolutely the norm in all areas of pathology.

But, you know, I like to think that cervical cytology led the way in many of those areas as well. And certainly pathology and pathologists have been well, right at the very centre. And as I said earlier, it was the lack of their skill base that created this kind of script between the well developed and the underdeveloped countries.

[Dr Michael Dray] And we now come into this latest phase of cervical screening with the development of what's called the cervical screening test, replacing the pap smear not too long ago. Can you describe the difference between the two?

[Dr Annabelle Farnsworth] Yes. Well, because this disease, as I said, has been so well studied. And I suppose it's because there's been screening program and because we've also had scientists involved in looking down the microscope at these cells. The discovery that this was a viral caused cancer is also quite spectacularly interesting and really that the knowledge about that emerged because the cancer was behaving like a sexually transmitted disease it occurred more commonly in women with more sexual partners who onset of sexual activity was earlier. And in fact, people were looking for the victor or perhaps the causative agent, I should say, right back in the 1970s.

And then with the development of molecular techniques, they discovered the human papillomavirus. And really, as they say, the rest is history, because they've actually done the all of the genetic work that actually shows how the virus integrates into the genome of the cell and switches on all of the cancer producing cellular mechanisms.

So, of course, what happened there was although when we looked down the microscope, we see the effect of this virus on the cells, the development also then came that we were able to detect the virus. Now, the virus was not able to be grown in laboratories which way it was discovered fairly late.

But you could detect it using advanced molecular techniques where you actually were able to look for the viral DNA and the development of those really accurate viral DNA tests. Then got everyone thinking that maybe a much more accurate way of doing this screening case would be to look for the virus.

So you could theoretically pick it up a little bit earlier at the same time. It's like everything there's no perfect test in the world, but of course, the cervical cytology screening test was a very good test, but it did not pick up all the cancers.

And so the human papillomavirus test is what we call more sensitive, meaning you'll detect more virus, which means theoretically you detect more disease. And that's been the theory behind the replacement of the what we call the cytology aspect with the HPV.

But I think the other thing and back to this conversation earlier was about the fact that you didn't have the scientists and the pathologist in underdeveloped countries to look down the microscope at the cells. But with the HPV testing systems that is available throughout the world, it's a much more robust it's a more device based test, which means that it can be transported more easily and can be interpreted. So there has been a great deal of hope that the availability of this particular HPV test will allow testing for this

disease in the underdeveloped countries where the rates of cancer are still really high.

[Dr Michael Dray] That's a really interesting concept, isn't it, that we've been able to bring a more advanced understanding of the ethology of cervical cancer and and hopefully reduce that disparity. You commented earlier that the cytology really led the way in setting up quality systems in the laboratory and how to treat those quality systems will carry over to the use of the actual HPV testing as well.

[Dr Annabelle Farnsworth] Yes. Well, I hope so, too. And of course, that's one of the issues with the you know, it's all very well to say you can generate a black box in inverted commas out into to do the kind of testing.

But you've got to make sure that it's accurate. And, of course, in pathology, it's very simplistic to think that you can just put a sample into a machine and out comes the answer. All of those analysers have to be quality assured in the same meticulous fashion as we do other things.

And certainly in Australia, where we have made the change, the change is still on its way in New Zealand. The quality assurance processes have been well thought out. And and we, you know, working in the area are very conscious of making sure that that is, in fact, the case.

The other interesting thing about HPV, certainly in the developed countries is that it's a more sensitive test. So whereas we were very worried about false negatives in the PAP smear screening program, in the new program, the issue of false positives, meaning over treating people becomes an issue that we also need to be conscious on.

[Dr Michael Dray] So is that where the someone with the positive HPV then goes on and has the cytology test? Is that how that felt?

[Dr Annabelle Farnsworth] Yeah, that's very much the case. And in fact, it's interesting that in Australia, that's proving to be an absolutely crucial part of the program. We meaning Australia, was really the first country in the world to move ahead with this.

And so we are lucky in the fact that we have a double testing regime so that if someone does test positive for HPV, they will then go on and have a cytology sample made. And that cytology result is proving to be very, very helpful in making sure that the HPV isn't just a commensal.

HPV is incredibly common. Every study shows about 80 percent of people will have an HPV infection sometime in their lives. But of course, the people that get diseases like only a tiny percentage of that and cytology is still such a good tool to it's really a biological marker.

I mean, people are looking for fancy molecular biological markers, but really cytology is a biological marker that you can actually see and is indicating that the HPV virus is actually affecting the cells in a particular way.

[Dr Michael Dray] Yeah, that's so true, isn't it? Coming back to the cervical screening program, both the Australian and the New Zealand one who should be getting tested these days?

[Dr Annabelle Farnsworth] Well, the current recommendations for women over the age of 25 and up to the age of seventy five, believe it or not, in Australia. And so that's really quite a long program. And I think that in days gone by, we screened younger women.

But the rates of high grade disease or cancers in young women is quite small, even though the rates of HPV infection is very high, because, of course, it's the HPV infection that you get when people are sexually active.

So at the commencement of that kind of time period of people's lives, the HPV rates are really high. But of course, it does take a while to develop disease. And so that's why, again, all the studies show that commencing testing in twenty five is quite safe.

In Australia, as I say, we've extended the screening recommendation to age up to seventy five, full stop, if you like. Women are living a lot longer. And of course, that is an area that's becoming very interesting in particularly some way, because there's a surprisingly higher rate of HPV in older women, not necessarily associated with disease.

And that's going to be an area is quite interesting research to see what that means. But of course, we do know that older women can develop cervical cancer. And so it's still worth continuing to have cervical screening tests even into what kind of an older age group.

[Dr Michael Dray] So you've mentioned COVID 19 is creating problems and challenges in a whole variety of space. What else has COVID 19? How has that affected cytology and cervical screening programs?

[Dr Annabelle Farnsworth] You need people to enter into the program. What we call recruitment. And of course, the critical thing in a public health program is public health messaging and getting women to realise that this is an important part of their general health.

And what a great thing it is now in Australia. And I'm sorry I don't have any data from New Zealand, but in Australia, the government actually commissioned a look at what would be the impact of the fact that because of COVID, as we know, the provision or the availability or the keenness or the ability to go and look after all the other aspects of

somebody's health have been left behind a little bit, both with the significant lockdowns that both New Zealand and Australia has had, the overwhelming in the medical system by looking after COVID patients and just the general focus on COVID, which is completely understandable.

But the messaging from the Australian government is that because of the lack of recruitment or the lack of participation in the program in Australia, there could be a measurable increase in the number of cancers. There could be a measurable increase in the number of young women with this disease that could actually be women presenting with later stage disease, which means it's slightly more at risk. And they could also be failure of women to do adequate follow up, because, again, the hesitancy to go into or entrance into the health system and it's a measurable risk, it's not clear.

But I guess one of those things that we really need to be very conscious of as the medical profession is to encourage women, encourage women to continue to have their cervical screening tests, irrespective of COVID if they can. And it's a really important health issues that we need to keep talking about.

[Dr Michael Dray] Coming back to vaccination, which we can sort of think of vaccines in two ways. One is that the New Zealand Australia system, and then the other one is the and the health jurisdictions that haven't got a proper screening program.

How are we faring in terms of reaching elimination in New Zealand, Australia and elsewhere in the world?

[Dr Annabelle Farnsworth] In Australia, we've been we've had a hugely successful screening program, commenced in 2007, and it's given in the first year of high school. It commenced with girls, but it was extended to vaccinate boys in 2013. And so our coverage rates up around seventy five per cent.

And with everybody's, you know, keen interest now in COVID vaccination, we all know that if we've got a vaccination rate of over 70 per cent, you're doing extremely well. And so Australia certainly has achieved that. And it's that it's a great it's a great, you know, again, a credit to the health programs that the government is putting in place. New Zealand was a little bit slower off the mark. Certainly they introduced it early on. But there were there was a little bit of vaccine hesitancy. We know all about that. So it reached about 50 per cent vaccination rate.

But I now know it's it's gone much higher than that. So in both countries, we are looking at really high coverage rates and we now can measure the voting rights of HPV related diseases. So that's a really good thing in our underdeveloped countries.

It's still a little bit of a worry. The country that's probably the most impressive, which does go to show it's not really a third world country, but our northern neighbour, Malaysia had a group that actually was a gynaecological oncologist, who was a very enthusiastic woman who was able to persuade the government.

And remember, it's a it's a Muslim state community. So it had issues, but they introduced a vaccination program, hugely successfully about 2010, 2011. And it's been again, it's a huge success. And it's really an example of if you get the government on board, if you get your public health messaging correct, you can make this huge difference.

And so their coverage rates have been excellent and it's being well accepted by families and young women. And so it's done really well. But there are other countries that I do have to just mention this, because it was knowing that a country like Japan, which is a highly developed, wealthy nation, developed a huge kind of issue with vaccine hesitancy and the right to vaccination are negligible. And their rates of cervical cancer are incredibly high. And, you know, women are still dying from cervical cancer in a country like Japan. So it really is worth just remembering, you know, if you look around the world and see, you want to see effects or effects or lack of effects, then there are several sort of examples. So let's just hope that once COVID is conquered and it becomes a, you know, the health emergency that we're living through eases, other health issues can you know, we can turn our attention to other significant health issues.

[Dr Michael Dray] so there's been this remarkable experiment almost with demonstrating the efficacy of vaccine worldwide. And it seems to be tragedy [Dr Annabel Farnsworth in some jurisdictions, as you've described. And it's wonderful saying that we are making a difference with vaccinations.

So you mentioned the phrase HPV related disease. What are you what are you incorporating in that group of diseases?

[Dr Annabelle Farnsworth] Well, let's that's a great question, because, of course, human papillomavirus is a very ubiquitous it's the same virus that causes common warts on fingers and toes or plantar warts if you've been to the swimming pool, but it is associated with other cancers.

And in fact, one of the main reasons why Australia extended the vaccination program to include boys was because men who have sex with men can get cancers of the lower general tract as well. And it can be quite a scourge.

And you can get oropharyngeal, so cancer of the head and neck can also be associated with HPV. And so it's a terrific vaccine for for those kind of cancers as well. So it's a virus that wherever it is able to infect cells that are turning over rapidly, it can become cancer producing and try to get it.

So so men can get affected as well as girls and boys. And so so it's it's a great vaccine in those instances as well.

[Dr Michael Dray] So so vaccinating against HPV had some unexpected result?

[Dr Annabelle Farnsworth] Absolutely. Absolutely. And we've all heard of genital warts, but the first vaccine came out, Gardasil, and it's a brand name, but it went 4 viral subtypes. And they included the two most common cancers forming viral subtypes. They also included the two viral subtypes that cause genital warts.

And so it's been a fantastic marker because the incidence of genital warts is just literally disappeared in vaccinated populations. So so, yes, unexpected consequences. But, you know, again, good markers of the vaccine working really well.

[Dr Michael Dray] What is the vaccine done to sort of the the are we getting weirder subtypes of HPV or is it sort of the evolutionary driving, the rise of other HPV subtypes? Is that something that is looking at people thought that might happen?

[Dr Annabelle Farnsworth] And again, that's a great question. But insurance, all the data. And by the way, people are monitoring this all the time. So the big fall in HPV related disease has been in the bar in the vaccine subtype.

So that's type 16 and 18. But the non-vaccine subtypes are still the ones that are causing a reasonable amount of disease in even in vaccinated women. Which, of course, comes to the point of if there's one message from even, you know, this conversation is to get people to participate in the screening program.

[Dr Michael Dray] And so even if people have been vaccinated, they need to continue to have their cervical screening test. And that is a message that is is not has not been well spread. And it is probably one of the biggest issues certainly we have in Australia at this low level of participation.

[Dr Annabelle Farnsworth] Yes, we had low level of participation during COVID lockdowns, but the level of participation was already very low and even among well-educated, knowledgeable people the number of times I've heard people say, well, I'm vaccinated and I don't need to have a survival screening test is it's really a common belief and it's actually not correct.

[Dr Michael Dray] So just to summarise what you're saying, the vaccine only protects you against nine out of quite a few subtypes of HPV. But the HPV test can detect a far wider range of subtypes that people haven't necessarily been vaccinated for.

[Dr Annabelle Farnsworth] Exactly. Very important message. And more importantly, the nine subtypes, it's only was available here recently. So the great majority of women who have been vaccinated at school are really only vaccinated against two subtypes. And there are many, many subtypes can cause cervical cancer. So, yes, you need to continue to have cervical screening.

[Dr Michael Dray] Well, Annabel, it's been wonderful talking to you about cytology, cervical cytology, HPV. Is there anything that we haven't covered that you think would be important for our listeners to know?

[Dr Annabelle Farnsworth] No, I think it's just I think it's again don't be frightened, go and have the test. It could save your life. And I think that it's really being take home message.

[Dr Michael Dray] Thank you. And finally, you've been a pathologist and you've been a wonderful pathologist and you've done so much. What advice would you consider to someone looking at pathology as a career?

[Dr Annabelle Farnsworth] I would highly recommend it. I think pathology has always been one of the unsung areas of medicine. Of course, the many, many things that I've seen through my working life. But one of the one of the many good things is that the pathology has become really central to patient management.

The inclusion of pathology and pathologists in clinical decision-making is becoming greater and greater. It's a wonderful scientific discipline that I've particularly enjoyed the science behind it. It's varied. There are many different areas that you can do. But it's a really it's a wonderful career that I couldn't recommend more highly.

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.