

Coronavirus outbreak



A couple of hundred people in Singapore were infected with Sars in 2003 and this "shadow of Sars", says Professor Wang Linfa of Duke-NUS Medical School, gives the Republic a problem in testing for Covid-19 as the two coronaviruses are 80 per cent similar. Targeting the remaining 20 per cent that is different was key in the tests. ST PHOTO: KEVIN LIM

Test for Covid-19 antibodies a world first for Singapore

Duke-NUS professor behind test to successfully trace infected person who has recovered

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Nothing is as important as speed and accuracy when it comes to testing for Covid-19.

It was a test developed locally that helped Singapore trace the source of infection of two Covid-19 clusters here – to one where infection was known to have been transmitted by visitors from Wuhan.

The link was a woman who had become infected at the Life Church and Missions Singapore, gone to a Chinese New Year gathering when feeling unwell, and later to the Grace Assembly of God church.

By the time she was traced, she no longer had any of the virus and it was only by proving she had Covid-19 antibodies that the link was made.

That test was a world first. When it comes to testing someone for Covid-19, Singapore has a problem that many countries do not. Call it the shadow of Sars.

This is because more than a couple of hundred people here had been infected by the severe acute respiratory syndrome (Sars) in 2003, said Professor Wang Linfa of Duke-NUS Medical School.

And the two coronaviruses are 80 per cent similar.

So a test to flag Covid-19 will have to specifically target the 20 per cent that is different between the coronaviruses.

When news of the novel coronavirus broke out, Prof Wang, who is the director of the programme in emerging infectious diseases at the school, immediately decided not to work on a test for the virus.

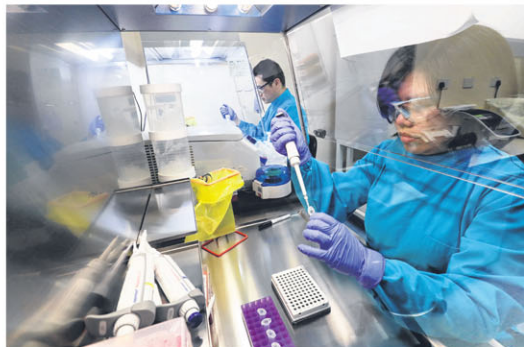
Many were doing that. Instead, he decided to develop a test for antibodies.

The virology test indicates if a person has the virus. But once the person has recovered, there will no longer be the virus in the body.

However, in fighting the virus, the body would have developed antibodies, which would remain in the blood serum, ready to mount an immune response should the person be exposed to the virus again.

If someone has this antibody, it is certain that the person had been infected in the past.

Singapore got its first confirmed Covid-19 patient on Jan 23.



Instead of working on a test for the virus, Prof Wang and his team worked to develop a test for antibodies. The virology test indicates if a person has the virus. But once the person has recovered, the virus will not be in the body and he would have developed antibodies. ST PHOTO: KELVIN CHING

Prof Wang, 59, and his team of about 20 researchers received samples of the live virus, in the form of swabs from patients here, on Jan 26, becoming only the third place outside of mainland China to get live coronavirus samples. The other two are Hong Kong and Australia.

By Jan 30, his team had isolated the virus.

"We're battle-ready. We grow the virus in vitro (in the laboratory), so now we have an unlimited supply," he said. The virus is needed for various tests.

While his team was working in the laboratory, Prof Wang was under quarantine, having been in Wuhan to visit scientists there from Jan 18 to 20.

"I have been working on this since I returned from Wuhan. I was quarantined but I didn't stop working," he told *The Sunday Times*.

He said: "The test has to be specific. We know it is a coronavirus that's 80 per cent identical to the Sars coronavirus."

"Unfortunately, Singapore was hit heavily by both viruses. So we put a lot of effort into developing a test that is able to differentiate it from the Sars coronavirus."

The team actually came up with two tests – a quick and dirty one with about 90 per cent accuracy, and a recognised gold standard test that requires four to five days in a high level 3 biosafety laboratory.

There are four levels of biosafety labs, with level 4 as the highest.

Level 3 has the safety features to protect workers when dealing with microbes that can cause serious and potentially lethal illness if breathed in.

The first test – "because the Min-

ANTIBODIES' LONGEVITY

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PROFESSOR WANG LINFA on how long someone who has been infected could have the antibody.

DON'T JUMP TO CONCLUSIONS

There are so many things about this outbreak that are difficult to explain. The public half understands and jumps to conclusions.



PROF WANG on the many misconceptions swirling around.

istry of Health (MOH) wanted to know as soon as possible" – uses man-made proteins – "so it's very safe", from a part of the virus that would bind the antibody to it, said Prof Wang.

The second, which is the accepted gold standard called a virus neutralisation test, takes blood from the person to be tested, and infects it with live virus. If the blood is able to knock the virus out, it has the antibody, he explained. "It's a highly sophisticated test and needs a controlled environment."

Because live virus is used, the test can be done only in a laboratory that is at least level 3, so the virus cannot be accidentally released into the community.

So how long will someone who has been infected still have the antibody? "For Covid-19, we don't know. We're just two months into it. But our Sars survivors in Singapore still have antibodies 17 years later," said Prof Wang. "I think it will last for years to come."

So he does not quite buy reports that patients who have recovered have been reinfected, since their antibodies would have fought back.

He said: "As a scientist, I would believe it if they publish it in a scientific journal."

That a person can be reinfected is just one, but the least likely, of several possible scenarios for the cases highlighted in Japan and China, he said.

Another is that the polymerase chain reaction (PCR) test used to diagnose if someone is infected does not show if the virus is "live", just that it is there.

Said Prof Wang: "The PCR test is super effective but a positive result does not equate to live virus. The genetic material is not infectious but is still in your body, so PCR will spot it even when it is not viable."

Another possible scenario is there is "persistent infection". Some people, when they recover, completely clear their bodies of the virus. Others may have residual virus in them. He said this happens to the herpes virus. When people who have residual herpes virus are stressed, they get cold sores.

So these people may still be infected, but are not sick, said Prof Wang. Because they are not sick, they would not be spreading the virus to others.

Prof Wang said: "There are so many things about this outbreak that are difficult to explain. The public half understands and jumps to conclusions."

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Q&A

Who should be given the vaccine first?

Professor Wang Linfa, director of the programme in emerging infectious diseases at the Duke-NUS Medical School, answers some pressing questions on Covid-19.

Q When will we likely have a vaccine?

A By the end of this year. It is possible because everybody's moving so fast. It used to take many months to crack the genome code of a new virus. Now, they can do it in two days. The Chinese made it available on Jan 9.

Q Why does it take so long to develop a vaccine? Can the vaccine developed for the 2003 Sars (severe acute respiratory syndrome) outbreak be used since the two coronaviruses are 80 per cent similar?

A No. Genetically, Sars and Covid-19 have 20 per cent difference. That difference is enough for the body to recognise only Sars but not Covid-19. It is much better to start developing a vaccine from scratch.

Q When a vaccine is available, will there be enough for everyone? If not, who should we give it to first?

A Most of the time when you have emerging infectious disease vaccines, you give to those at high risk first.

You also do what we call ring vaccination. For example, in a nation like South Korea, you do not vaccinate everybody. You vaccinate the churchgoers and those associated with the church, and maybe Daegu city and the health-care workers in that city first.

We want to vaccinate the population preemptively. Of course, we want to prevent people from getting sick and dying. But equally important is to stop the transmission.

It is really about identifying the key transmission events and who are at most risk to transmit. If we vaccinate these populations first, we not only save them, but more importantly, prevent further transmission.

Q If I get a vaccine for Covid-19, will it last me for a lifetime or is it like the flu vaccine where you have to get one jab every year?

A There are two different scenarios. One is lifelong immunity. Some viruses can produce that, like the measles virus. If you are infected with measles, then you get lifelong protection.

Other viruses, when you get infected, you will get protected for a few years, maybe.

With the flu, every year you get a jab because the flu virus is changing. So, one year, you get a vaccine against one type; the next year, if it is a different type, you need a different vaccine. It does not mean the immunity has waned, it is immunity against that particular seasonal flu, so you need to have another injection.

Q Which is likely for Covid-19? Will it change much and will different vaccines be needed over the years?

A If there is any kind of silver lining, it is that this virus looks like it does not change as rapidly as Sars and Mers (Middle East respiratory syndrome). It is genetically relatively stable. And that is good in terms of developing tests and vaccines.

If the virus changes rapidly, even if you have a vaccine, you may not be able to predict the next variant. In 40 days, over 100 genome sequences – the whole genetic code of the virus – has been deposited in the public gene bank.

These are not only different generations of the virus, but also those from different geographic locations. It looks like it is stable so far.

Q Can Covid-19 be contained?

A This is difficult to answer. Developed nations may be able to contain it, but developing nations may not be able to do so. It is worse if there is a super-spreader, who may infect 30 people when most patients infect just three.

Q Did the virus come from an animal and, if so, which animal?

A It is very clear that it is a zoonotic transmission. It is not a human virus, it is an animal virus that got into the human population.

Originally from bats, but most likely, there is another animal in between... This is a hot area (of research) and so far, we do not have enough data.

Salma Khalik

VACCINATE MOST-AT-RISK FIRST

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PROF WANG LINFA on who to vaccinate.



SCAN TO WATCH
Prof Wang on why antibody testing is important.



http://str.sg/serology