



Leading the NCID's PANDEMIC RESPONSE

Interview with **Prof Leo Yee Sin**

Interview by Dr Tina Tan, Editor
Photos by National Centre for Infectious Diseases

The past one-and-a-half years of combating COVID-19 has been a long-drawn journey with many Ministry and healthcare leaders stepping up to lead the charge. *SMA News* editor, **Dr Tina Tan (TT)**, speaks with **Prof Leo Yee Sin (LYS)**, the executive director of the National Centre for Infectious Diseases (NCID) and infectious disease specialist to find out about her work and thoughts on the nation's battle against COVID-19.

TT: Thank you so much, Prof Leo, for agreeing to the interview, and I'm really honoured to e-meet you. Focusing on COVID-19 and leading the NCID in the whole national response, how has life been for you, especially having to deal with so many constant changes?

LYS: My life is possibly not much different from many of yours and my colleagues', with every day being a full day of work both during and after office hours. I spend my day working, trying to keep up with the pace of the virus. It is still a long journey to understand fully the long-term consequences of the virus, not only in human bodies, but in the entire healthcare system and the broader scope of things. This virus has basically impacted almost every facet, every aspect of human life and human interactions, and how the systems will work and cope with it.

Technology and connectivity has evolved a lot since 2003. In the past, I had to make phone calls and prior connections to link up with counterparts in other parts of the world to be able to exchange information. Today, we have so many Zoom conferences and

webinars for updates and discussions. It is convenient and useful, but it takes up a lot of time, especially in the evenings.

Early days of COVID-19

TT: If you look back at the early days of the pandemic, what was it like just trying to catch up with the constantly evolving nature of things, and dealing with the amount of information – both accurate and inaccurate?

LYS: There is still a lot of information going around and as you said, some of them are real while some are fake news. Sometimes, it is actually not that easy to differentiate the real from the fake, even for medical professionals. What you read in journals may not be what is reported. And sometimes, it is not because of intent, but about the science. When you address science from a different angle, you get a different result. And that different result may lead you to erroneous conclusions. I think SARS-CoV-2 really brings out a lot of things, including socio-economic issues in relation to health delivery. In my work with international partners, we face a different set of challenges.

In Singapore, we were able to engage international partners right from the beginning. We managed to link up with the National Institutes of Health in the US that has access to the latest medications. They brought in remdesivir at a very early stage, and we were fortunate to be able to partner with them and bring in the medicines on a clinical trial basis. We could then use it for our very ill patients.

There was a lot of information regarding some medication with clinical efficacy being published in high impact journals as well. That really confused the people on the ground with what would be the best for patients. But we were very fortunate in the sense that we have a good team of people who were able to understand the biology and the pharmacology, and guide us in terms of how we can best utilise or repurpose medications for treatment.

One medication that is still being debated in the international arena is ivermectin. The first ivermectin clinical trial came out very early, but it was a small and biased study that showed a beneficial effect in reducing mortality.

It was a profoundly significant survival benefit that, I would say from my own assessment, clouded the minds of many people and that sparked off a lot of debates as to whether these medications could be used to treat COVID-19. As you can imagine, it is not easy as a clinician on the ground who has to take extra effort to understand the information flooding the desk.

I am glad to say that Singapore is very fortunate and still maintains a very low mortality rate, owing to a few factors. One is our healthcare system that allows us to do early testing. We also learnt from the clinical trials about the best time to intervene with therapeutic agents. SARS-CoV-2 is a very tricky virus and you have to target its life cycle or different periods using different medication. We need to have that degree of understanding in terms of what would give the patient the best chance of survival with the use of therapeutic agents.

TT: Thank you so much for that very comprehensive response, Prof Leo. You've mentioned that you have a team of people analysing all this information. I would imagine you don't just have infectious disease physicians on this team. Who else do you have?

LYS: At the very early phase of the COVID-19 outbreak, I had asked Dr Shawn Vasoo, clinical director of NCID, to chair a therapeutic work group. We brought in ID clinicians from various public healthcare institutions, pharmacists, intensivists, immunologists, and also the drug regulators. The team has to date done up seven versions of the Therapeutic Guidelines, which are published as and when a new drug is released. The Guidelines are available on the Academy of Medicine, Singapore website (<https://bit.ly/3ljSAZR>) and NCID website (<https://bit.ly/3lIFECF>).

Keeping at it

TT: Things have been dithering along for one-and-a-half years, what do you suppose will be the continuing challenges of managing the pandemic?

LYS: I think we still face many, many challenges.

First of all, we look at the virus. The virus, I must say, runs faster than humans; we are just barely trying to catch up with the fast-moving pace of the virus. It will continue to mutate and evade, and I do not know how the virus will behave next or how it would change in terms of its characteristics. And because we don't know, we have to really keep an eye on the virus.

Next, the healthcare system. After these ups and downs, many healthcare workers are showing signs of fatigue. It is a constant battle, the virus is still there, it is still evolving. So, I think the greatest challenge within the healthcare system is physically fatigued and mentally stressed healthcare providers. We have put aside regular care for some time to cope with COVID-19. We need to now have the mechanisms and ability to bring back management of these other illnesses.

The next layer I want to touch on is the national layer, and how the entire nation is going to have to pull together to be able to cope with the situation. This is what a lot of people are looking at – how do we get to a stage where we can start seeing less restriction, allowing more businesses to go on and activities in the past to be reinitiated without overwhelming the healthcare system. That would really be a challenge in terms of how we would balance all these needs in a way to enable us to cope.

And then beyond the national layer, it's regional. If you look at our region, it has not shown signs of stability. Our immediate northern neighbour is seeing 17,000 cases a day and they have reached over one million cases nationally. Similarly, Indonesia is reporting big numbers, and Thailand and Vietnam are seeing a huge wave. These regions, in terms of COVID-19, are still quite volatile.

Coronavirus insights

TT: It is a very difficult balancing act for those in leadership positions, with many different sectors calling for different things based on their needs. So much seems at stake now, though in a different way than it was back during the time of SARS, where the disease lasted for a much shorter period of

time but the mortality rate was also significantly higher. What do you feel is the difference between our battles with COVID-19 and SARS?

LYS: As you mentioned, the most distinctive difference and impact on our healthcare system is the duration. SARS in 2003 lasted about three months, so it was very intensive and it was fortunately, at that point, short-lasting. In contrast, COVID-19 is very intensive and it hits you real hard, but refuses to go away. It just lingers on, and intermittently, it would return and cause another surge of cases. It is quite a different ball game. In fact, these two viruses, although they both belong to the coronavirus family, behave differently.

TT: Do you have any other insights about COVID-19 that you wish to share with our readers?

LYS: I would just want to bring out this very distinct observation about COVID-19 and influenza. It is being observed across the whole world, that in areas where COVID-19 is surging, the number of influenza cases is being suppressed to very low levels. Because of that, we have had very low levels of influenza cases in the past year. Why is that so? What are the plausible reasons, scientifically? This is something that we have to continue to research on.

I recently also read a very interesting article looking at excess mortality – how much the impact of COVID-19 has led to an increase in the number of deaths in different parts of the world. Some of the countries that are being affected very badly have a significant excess mortality. Whereas in certain countries, like Singapore, it's a negative excess mortality. One of the reasons for this that I, and many epidemiologists, thought of is that it could be because of the reduced influenza cases. In other words, we reduce the number of influenza cases and therefore we ironically reduce the overall mortality during the COVID-19 outbreak. And yet the COVID-19 mortality in Singapore is relatively low – it's one of the lowest in the world – and therefore you have this negative excess mortality.

TT: That's very interesting because I didn't know about that negative excess

mortality. It's really great to know, because as a psychiatrist, what I do know is that we had a slight excess of suicide cases last year and I do wonder how things will be like this year. Speaking of 2020, I read a *BBC* report of you being in the BBC 100 Women 2020 list and you also received the Public Administration Medal (Silver). What are your thoughts on these recognitions for the work that you have done?

LYS: Of course, I am pleased and very honoured to receive all these recognitions, but I think the first thing I'd like to say is that it's not one person's work. I'm not the only one working on managing COVID-19. I have seen many colleagues who have worked so much harder, putting in effort around the clock to make sure that they can get the pandemic under control. I must say that I am very fortunate to receive these recognitions, but I also hope that my work is not restricted to just outbreaks. There are other areas of infectious disease work that I am also focusing on as well, so I certainly hope my work and what I've done can contribute to not just outbreaks, but the entire infectious disease field.

The infectious disease field

TT: I've also noted the significant contributions you've made in the research of dengue and HIV. You had set up an infectious disease programme for

HIV in Singapore in 1995. Could you share more about the progress of HIV treatment since then, and what things are going to be like going forward?

LYS: It is a vast difference now from the time I picked up HIV medicine as my primary subspecialty in infectious disease. HIV medicine was almost like a doomsday medicine in the past, but the condition has become a chronic illness today. The disease itself is currently well under control and very treatable, with treatment of HIV universally accessible. What is actually lacking is in the public's mindset, the discrimination against HIV-positive people.

TT: Let's go back to your younger days. You were initially interested in immunology as a medical student, so what drew you towards infectious disease at the end of the day?

LYS: The infectious disease specialty was unheard of when I obtained my Master of Medicine and also my Membership of the Royal College of Physicians. It was not a specialty by itself at that point. I had wanted to do Rheumatology Immunology when I graduated, but unfortunately, there wasn't any available position.

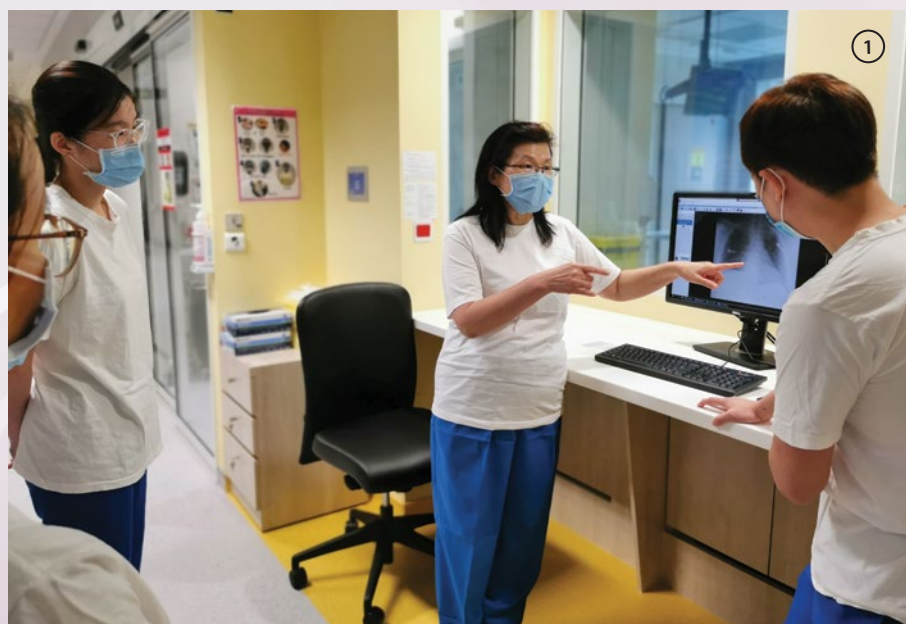
However, I was very fortunate because almost immediately after I obtained my higher degrees, Prof David Allen came to Singapore and introduced the concept of infectious diseases. I then became one of his trainees – in

fact, I was in the pioneer training group. Three of us, myself, Dr Wong Sin Yew and his wife, Dr Lam Mun San, graduated around the same time and decided to take up infectious disease. Before us, we had two other colleagues who had started work in infectious diseases – Prof Helen Oh went over to Canada to be trained as an infectious disease physician and Dr Brenda Ang trained under Prof Ti Teow Yee, who is a clinical pharmacologist. Because there were no infectious disease pioneer or specialty at that point in time, we had to find the closest specialty to train under. There were basically the five of us in the initial period.

The field has progressed and advanced so much. I had to go to the US to do my one-year Health Manpower Development Plan to study general infectious diseases. Today, I would not have to send my trainees for that, because they can pick up these skills in Singapore. They go overseas for skills that are not available locally.

TT: How different things are! Let's talk about your work at NCID. How has it been like and where do you see NCID moving forward in the future?

LYS: The SARS outbreak in 2003 gave us many learning points which we have implemented in the healthcare system. This included the need for a world class infectious diseases hospital with a purpose-built facility for handling infectious disease outbreaks. NCID was officially opened on 7 September 2019 with state-of-the-art medical facilities and features. So, in terms of the organisation, it is a very new organisation. In terms of the concept, why we need NCID and how it was put together, it's a very unique one as well. In comparison to many other parts of the world, Singapore was able to put the clinical components and outbreak response together with public health, and add to it the professional component, which is the research, training education and community engagement, all under one roof. There is a lot of interest in terms of studying the local policies and strategies, so we receive a lot of requests from different parts of the world trying to understand the Singapore system. I'm actually very



proud of it, because it is a Singapore brand that is being recognised by many other parts of the world.

Moving forward

TT: Do you have any words of encouragement for healthcare workers?

LYS: I think the most important thing is the system support, how we are able to support each other in our own respective team, and possibly beyond, within the institution as well as nationally. Community recognition and encouragement is very important, in my opinion. In other words, appreciation from the community for the hard work of the healthcare workers is one of the very important motivators. In contrast, if the community is discriminating against healthcare workers, that kind of negative effect can be very significant as well. We do need the encouragement and also support from all levels – within our teams, our institutions and community, as well as the public.

I just want to say, healthcare workers are not the only ones fatigued. In fact, you need to support everybody, regardless of their professions. It is not easy to sustain a livelihood in the pandemic. I also empathise with Singaporeans who have to bear with this very difficult period of their life. It's livelihoods we're talking about.

TT: One final question – I'm a little curious as to your thoughts on routine rostered testing (RRT). Healthcare workers started having bi-weekly RRTs, and migrant workers and those in other industries have been undergoing RRT for so much longer. What are your thoughts on continuing this?

LYS: I'm going to say something that our medical colleagues may not like to hear, but it is important to understand why we need to do RRTs, and why healthcare workers.

First of all, we need to understand the virus and how it manifests the disease in humans. For the current Delta strain, the vaccine effectiveness in preventing infection is just barely 60%. As such, any one of us, even though vaccinated, can still come down with the infection.



Photo: Pearl Gan

Secondly, we also learn that many of the cases of infections post-vaccination are in fact asymptomatic or mild, which is good in preventing serious illness but the signal of infection is lost without testing. Thirdly, regardless of your vaccination status, the viral replication is in high quantity in the respiratory system. So now you're caught in the situation where you are asymptomatic, you've lost the signal, could still be infected, and could also excrete a large number of viruses. On top of that, you are working in a healthcare setting where you are seeing patients who could be vulnerable populations. You add up all these things, and you arrive at a question: should I be tested regularly to make sure that I'm safe to work in my working environment? If the answer is, "Yes, I will go for my test regularly", the next question you want to ask is, "How regular? What is the interval?"

Then I will come back to the virus dynamic again. There is a lot of evidence pointing toward high virus secretions during the pre-symptomatic period. In other words, again, no signal but you have high viral load. And the high quantity viral load will last for the first seven days, before slowly reducing subsequently. Now, returning to the question on interval, what do you think would be the appropriate interval if we want to test regularly?

TT: Actually, if you put it that way, it should be weekly. *[laughs]* Your arguments are convincing. I suppose, the follow-up question would be whether it necessarily has to be by an intranasal swab, because there are so many other means.

LYS: Yes, that can be explored. That is the technological advancement in terms of our diagnostic capability. And I agree that we need to continue to research and explore different modalities of testing. They may not be as sensitive as nasopharyngeal swabs for PCR tests, but it may be a reasonable substitute, and also because we truly need to have a relatively high viral quantity to transmit. So, I would agree that once you understand why you need to go for the test, the next thing would be to determine the appropriate diagnostic test that we can rely on.

TT: Thank you so much, Prof Leo. It has been fantastic talking to you. The amount of work that you and so many people have put in over the past year is really amazing, and we at *SMA News* hope that we can showcase some of that through this interview. ♦

For more pearls of wisdom, visit <https://bit.ly/2WmFaC3> for the full interview with Prof Leo Yee Sin.



Legend

1. Prof Leo in discussion with the clinical team about a patient at an isolation ward in NCID
2. Prof Leo leading a discussion on managing the COVID-19 virus