

NATIONAL CENTRE FOR INFECTIOUS DISEASES

The National Centre for Infectious Diseases (NCID) is a purpose-built facility designed to strengthen Singapore's capabilities in infectious disease prevention and management. Alongside TTSH, it has been the epicentre of Singapore's battle against the COVID-19 pandemic – providing clinical care and outbreak management, and leading in diagnostic testing, surveillance, and infectious disease research.

AT THE FOREFRONT OF THE NATIONAL COVID-19 RESPONSE

SCREENING OPERATIONS

The NCID Screening Centre started operations in late January 2020 to screen suspect COVID-19 cases. Protocols, COVID-19 screening and infection controls, and safe distancing measures were implemented to ensure the safety of patients and healthcare workers.

When COVID-19 cases spiked in March 2020, the Screening Centre was expanded, with tentages set up to meet the increasing demand. When the COVID-19 cases eased in December 2020, COVID-19 screening was integrated with NCID's outpatient Clinic J.

INPATIENT MANAGEMENT

To accommodate the surge in COVID-19 patients, the Centre rapidly ramped up bed capacity from 330 to 586, which allowed NCID to care for more patients. NCID staff were well-prepared to manage the outbreak as they had been thoroughly trained during peacetime and were equipped with the necessary skills and knowledge. At the peak of the pandemic, NCID housed 500 suspect and confirmed COVID-19 cases in its wards.

To prevent healthcare institutions from being overwhelmed, patients who were recovering well were transferred to Community Care Facilities (CCFs) before being discharged. This process freed up bed resources for critical and high-risk patients admitted to NCID. The medical, nursing, pharmacy, infection control, security, and operations teams also worked closely with MOH to ensure the safe transfer of patients between sites.

To augment patient care, National Heart Centre Singapore (NHCS)/ Singapore General Hospital (SGH) and National University Hospital (NUH) provided support for Extracorporeal Membrane Oxygenation (ECMO) treatment for COVID-19 patients warded in NCID. To gear up for such scenarios, hybrid teams comprising staff from NCID, NHCS, and NUH participated in EMCO drills conducted in February and March 2020. There were three COVID-19 patients who received ECMO support in NCID's ICU in 2020.



OUTPATIENT SERVICES

Clinic J provides holistic, integrated, and multidisciplinary outpatient clinical services, including medical consultation, pharmacy, care and counselling, and diagnostic radiology.

During the course of the pandemic, Clinic J continued to sustain essential business-as-usual (BAU) services while supporting the Ministry of Health (MOH) in other public health functions, such as swab and serology procedures for COVID-19 patients. Clinic J also served as a site for convalescent plasma therapy screening.

As COVID-19 cases gradually declined, Clinic J progressively expanded its BAU services in August 2020, including resuming clinic sessions and patient consultations. To enhance efficiency, clinicians leveraged technology and teleconsultation to ensure patients continued to receive care. Specialty services such as Psychiatry, Dermatology, and Ophthalmology were gradually restored in September 2020.



Prof Leo Yee Sin in discussion about a patient with the clinical team at an isolation ward in NCID.



RESEARCHING THE VIRUS AND DEVELOPING TREATMENTS

COVID-19 RESEARCH WORKGROUP

In January 2020, NCID responded swiftly to the COVID-19 outbreak with the formation of the National COVID-19 Research Workgroup (RWG). The Workgroup is chaired by Professor Leo Yee Sin, Executive Director, NCID, and advised by Professor Tan Chorh Chuan, Chief Health Scientist, MOH, and includes members from NCID, Agency for Science, Technology and Research (A*STAR), National University of Singapore (NUS), Duke-NUS Medical School, MOH, National Research Foundation, NUH, Nanyang Technological University (NTU), National Medical Research Council (NMRC), DSO National Laboratories, Singapore Clinical Research Institute, and NHG. The Workgroup's research efforts to understand COVID-19 transmission in Singapore have since contributed immensely to the nation's success in managing and controlling the pandemic.

A critical component of the RWG's research was "PROTECT" – a multi-centre prospective study to detect novel pathogens and characterise emerging infections. This protocol, covering all public hospitals in Singapore, enabled the collection of information and biological samples for research. The first PROTECT subject was recruited on 24 January 2020, a day after Singapore reported its first confirmed COVID-19 case. As of December 2020, more than 600 COVID-19 patients were recruited for the study.

The RWG made significant research contributions to the battle against COVID-19, including: rapid development and validation of diagnostic tools, a greater understanding of virus pathogenesis and transmission patterns, elucidation of biomarkers of infection, pathogenesis and disease severity, investigation of COVID-19 clusters in Singapore, characterisation of environmental contamination with the SARS-CoV-2 virus, development and evaluation of potential therapeutic agents, and greater understanding of the socio-behavioural aspects of the pandemic on healthcare workers and other segments of the community.

To-date, the RWG has contributed to numerous local and international research publications, including top-tier scientific journals such as the *New England Journal of Medicine*, *The Lancet*, and *JAMA*.

CLINICAL THERAPEUTICS FOR COVID-19 PATIENTS

The COVID-19 Therapeutic Workgroup led by NCID was formed to evaluate and recommend the use of existing (repurposed drugs) and novel therapeutics to treat patients with COVID-19, including antivirals, immunomodulators, and humoral therapies such as convalescent plasma and biologics, and vaccines. From February 2020, the multidisciplinary workgroup, comprising clinicians from different hospitals, reviewed available evidence as it emerged from trials conducted both locally and globally, and made recommendations for COVID-19 therapy.

NCID participated in various multi-centre randomised controlled trials to investigate potential treatments. This included conducting clinical trials to determine the efficacy of remdesivir as a treatment for the disease, and participating in the United States National Institutes of Health's (NIH) *Adaptive COVID-19 Treatment Trial* (ACTT) that tested the efficacy of a combination of remdesivir with existing drugs – such as baricitinib, interferon-beta-1a, and dexamethasone which are used to treat other diseases – as a treatment for COVID-19. In October 2020, NCID took part in another NIH-led clinical trial, *Accelerating COVID-19 Therapeutic Interventions and Vaccines* (ACTIV-3), which investigated multiple monoclonal antibodies as therapeutic agents for COVID-19 treatment.

NCID, together with TTSH's Department of Haematology, Health Sciences Authority (HSA), and Duke-NUS Medical School, started a national convalescent plasma programme for the treatment of patients with COVID-19 in March 2020. Under the programme, patients who recovered from COVID-19 were invited to be plasma donors, and underwent stringent checks to ensure that the donated plasma was safe and carried sufficient quantities of COVID-19 antibodies. Blood plasma treatment is based on the principle that recovered patients have protective antibodies that may help to fight against infection. Preliminary reports indicated that convalescent plasma therapy may have a role in the treatment of patients with severe COVID-19, and could be considered when these patients were not eligible for other treatments.

IDENTIFICATION OF CRITICAL ANTIBODY TARGET SITES IN SARS-COV-2 VIRUS

In July 2020, NCID and A*STAR's SigN disclosed research findings that antibodies found in recovered COVID-19 patients in Singapore were able to limit the spread of SARS-CoV-2 in the body by counteracting (neutralising) four specific sites (epitopes) of the virus. Epitopes are specific parts located on the surface spike proteins of the virus, which are recognised and bound by antibodies produced by human immune systems.

Key findings of the two studies:

- Tests on more than 100 recovering COVID-19 patients showed evidence that these four epitopes were recognised in COVID-19 patients, indicating that they were good detection markers to identify patients who had been exposed to the virus.
- Antibodies in these COVID-19 patients demonstrated the ability to neutralise more than 50 per cent of the virus, and were able to prevent the virus from entering the human body by counteracting two epitopes.
- Usage of the epitopes to measure antibody responses could serve as useful indicators for the degree of infection in COVID-19 patients, and function as highly specific and sensitive sero-immunosurveillance tools for recent or past COVID-19 infections. The flexibility of these epitopes to be used alone or in combination will allow for the development of improved point-of-care-tests (POCTs).

These epitopes will be used by A*STAR in a multi-centre collaborative study for the development of the World Health Organization (WHO) International Standard and Reference Panel for COVID-19 antibody. Further studies will be conducted to enable the design of diagnostic tools and the development of vaccines and therapeutics.

DISCOVERY OF NEW SARS-COV-2 VARIANT THAT CAUSES LESS SEVERE INFECTIONS

In August 2020, NCID, A*STAR's Singapore Immunology Network (SigN) and Duke-NUS Medical School announced research findings that COVID-19 patients infected with a new variant of SARS-CoV-2 had better clinical outcomes, including a lower proportion of patients developing low blood oxygen (hypoxia) or who required intensive care. This variant ($\Delta 382$) has a large deletion in its genome that removed the ORF8 gene. It was first detected in travellers who arrived in Singapore and Taiwan from Wuhan, China; and was transmitted across several clusters in Singapore from January to March 2020, before being contained.

Similar deletions were also detected with SARS in 2003, but the exact function of this protein was obscure. Laboratory studies with the $\Delta 382$ -variant of SARS-CoV-2 indicated that despite the deletion, the virus was not defective and replicated similarly to the wildtype virus.

131 individuals, who participated in NCID's PROTECT study and had been infected with either the $\Delta 382$ -variant or the wild-type virus, were studied. Among them, 92 patients were infected with the wild-type virus while 39 patients were infected with the $\Delta 382$ -variant.

Key findings of the study revealed that:

- Clinical outcomes were considerably better in patients infected with the $\Delta 382$ -variant than with the wild-type virus. None of the patients infected with the variant required supplemental oxygen or ICU care.
- Patients infected with the variant had less systemic release of pro-inflammatory cytokines and lower levels of growth factors associated with lung injury.
- Patients infected with the variant had more effective T-cell responses and platelet regulation during the early phase of the infection. T-cell responses correlate with disease severity in COVID-19.

Further studies to understand the function of the ORF8 protein, and the impact of its removal at the cellular level and on the immune response to infection are on-going.



SUMITOMO MITSUI BANKING CORPORATION DONATES TO NHG FUND

In October 2020, the NHG Fund received a donation from the Sumitomo Mitsui Banking Corporation (SMBC), for COVID-19 research projects conducted by NCID. The donation was from SMBC Asia Pacific Division's "SMBC Together with You Fund". It was launched as an immediate response to support people and businesses in the region during the COVID-19 pandemic.

"As we continue the battle against the virus and progress towards a state of endemic COVID-19, the road ahead may be long and winding but NCID's mission remains unchanged – to protect the people of Singapore from infectious diseases. NCID will continue working with our partners in the healthcare sector, academic and research institutions, and the community to safeguard Singapore's public health."

Professor Leo Yee Sin
Executive Director, National Centre for Infectious Diseases

PARTNERING THE COMMUNITY

PROVIDING INFECTION CONTROL TRAINING

NCID provided training to public and private organisations in adopting best practices for managing COVID-19. NCID collaborated with CCFs, Swab Isolation Facilities (SIFs), and private and community hospitals to train staff on PPE, N95 mask fitting, infection control measures, hand hygiene, and nasopharyngeal, nasal, and throat swabbing. In addition, NCID advised on facility design and process flows to enhance infection control and reduce infection risk at CCFs, SIFs, and cruise ships.

PUBLIC EDUCATION PROGRAMMES ON DISEASE OUTBREAKS

NCID's Training and Education Office (T&E) worked with community partners on public education programmes aimed at enhancing community preparedness against disease outbreaks. Also covered were the benefits of influenza and pneumococcal vaccination. In 2020, T&E engaged close to 2,700 members of the public through its outreach efforts.

“The majority of the COVID-19 patients I cared for recovered from the infection. For those who required deeper emotional and psychological support, I helped them acknowledge their grief, make sense of their loss of health or loved one, and journeyed with them to find new meaning in their lives. I am glad I was able to comfort them during their times of anxiety and loneliness.”

Mr Daniel Chee Medical Social Worker, National Centre for Infectious Diseases



BRINGING CHEER TO PATIENTS

EXERCISING WITH MIGRANT WORKERS

NCID nurses organised exercise sessions for migrant workers admitted for COVID-19 infection in April and May 2020. All patients, except those on oxygen support or who were breathless, were encouraged to get out of bed for some light physical activity. This helped uplift their mood and spirits.

DISTRIBUTING SNACK PACKS

To bring comfort to migrant worker patients, NCID staff prepared food familiar to the patients. Initiated by doctors, medical social workers, and nurses, the care team distributed snacks to patients admitted to the wards between April and July 2020.

“EVERY OUTBREAK BEHAVES DIFFERENTLY. IT’S IMPORTANT FOR US TO CREATE EFFECTIVE PROTOCOLS DURING PEACETIME THAT CAN BE EASILY SCALED AND ADAPTED TO MEET DIFFERENT INFECTIOUS DISEASE OUTBREAKS. NCID HAS BROUGHT CLINICIANS AND RESEARCHERS WITH DIFFERENT EXPERTISE, AS WELL AS STATE-OF-THE-ART FACILITIES, UNDER ONE ROOF – THUS ENABLING THE CRUCIAL COMMUNICATION AND FLEXIBILITY NEEDED TO FUNCTION DURING THIS COVID-19 CRISIS.”

Professor Leo Yee Sin Executive Director,
National Centre For Infectious Diseases