Outbreak of Health Care-associated Novel Coronavirus (SARS-coV-2) COVID-19 infections in the Spring of 2020

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As the Director General of Keio University Hospital, I hereby document the recent outbreak of health care-associated novel coronavirus (SARS-CoV-2) COVID-19 infections at our hospital in the spring of 2020. (DOI: 10.2302/kjm.kjm-covid19-01; Keio J Med 70 (1): 1–6, March 2021)

First COVID-19 Patient Hospitalized at Keio University Hospital

The Diamond Princess cruise, on which a mass COVID-19 infection occurred, was docked at the Port of Yokohama on 3rd February 2020.1 As the Keio University Hospital was not a part of nationally designated infectious disease system, mild cases from the cruise were admitted to our hospital as a cooperative facility for treating infectious diseases on 13th February and treated in the hospital’s negative pressure rooms that were previously used for tuberculosis patients. A team of specialists led by the Department of Pulmonary Medicine proactively took initiative to treat the COVID-19 patients with professionalism and commitment.

On 17th February, The COVID-19 Countermeasure Taskforce was established. This taskforce centralized the collection of information, proposals of countermeasures and communication with the faculty members. A working group was also established on the same day and preparations were started to develop an on-call system involving multiple clinical departments. A previously closed-off area of the hospital was refurbished to be used as a triage site where attending physicians could report, if any of their patients developed a fever. A dedicated COVID-19 zone was also prepared for the predicted pandemic phase of the disease. A protective system was prepared while carefully monitoring the information from the Health Center on faculty members with fever as well as the number of outpatients with fever who consulted the Division of Infectious Diseases and Infection Control.

From 13th February, all emergency outpatients with pneumonia were hospitalized in private rooms. On 27th February, a polymerase chain reaction (PCR) testing system for COVID-19 was quickly established as a result of prompt preparations by Professor Mitsuru Murata of the Department of Laboratory Medicine. A strict quarantine policy was implemented including PCR testing as well as ensuring that all emergency hospitalisations of patients with community-acquired pneumonia were placed in private rooms. Upon PCR testing, all 21 patients showed negative results. The dedicated COVID-19 zone was safely managed and treatment of the mild cases from the cruise resulted in these patients subsequently testing negative on PCR tests and being discharged from the hospital. The virus was not detected by PCR testing performed on samples taken from the environment surfaces within the dedicated COVID-19 zone while the patients were hospitalized.

Maintenance of Hospital Functions and Preparations for the Pandemic Phase

As the situation in Europe and America continued to worsen through March, tragic collapses in medical systems occurred in countries and regions that were considered to be developed nations in terms of medical care. There were also news reports of medical workers being overwhelmed by the stress of treating COVID-19 patients. At this time, our greatest risk was a sudden increase in infections due to people returning from Europe and America, rather than China and other Asian countries. Overseas travel of medical students upon graduation presented a major risk. Since April, preparations were started to strictly manage the health and check the travel histories of new graduates and new faculty members in all departments of our medical school. We introduced thorough body temperature checks before starting work for Shinanomachi faculty members, daily online input of body temperature by medical students engag-
ing in practical training within the hospital, and a system for confirming these results by the responsible parties. The system for managing symptomatic individuals at the Health Management Center was also enhanced. Since 9th March, all overseas travel was forbidden. Since 18th March, all individuals returning from overseas were forbidden entry into the Shinanomachi campus for 14 days, regardless of which country they had visited. There were no subsequent requests to admit COVID-19 patients, and on 23rd March, there were no faculty members or patients infected with COVID-19 according to our data.

**Outbreak of In-Hospital Infections**

On the night of 23rd March, a physician who was working at an affiliated hospital informed the Division of Infectious Diseases and Infection Control that an unofficial report was circulating about a serious in-hospital infection outbreak of SARS-CoV-2 at that hospital. In light of this report, a meeting was held early in the morning on 24th March and directions were provided to immediately investigate whether any patient had been transferred from that hospital to Keio University Hospital. We found that one patient had been transferred from that hospital to Keio University Hospital on 19th March to undergo surgery. PCR testing was performed on this patient on the evening of 24th March, and the result was positive for SARS-CoV-2. The physician in charge of the transferred patient decided to admit the patient to Keio University Hospital after consulting with the Division of Infectious Diseases and Infection Control and also confirming with an internist at the other hospital that the patient had no active pneumonia and no symptoms of COVID-19. At the time, PCR testing was not being performed on all patients before hospitalisation; therefore, it was difficult to detect asymptomatic patients. Subsequent investigation revealed that the patient was transferred to Keio University Hospital on 19th March, and another patient in the same room developed fever and COVID-19 infection was suspected. All individuals suspected of being in contact with the patient, including both patients and medical workers in the same ward, immediately underwent PCR testing. Results confirmed COVID-19 infection in four patients, one physician, two nurses and one radiological technologist in the ward.

The inviolable rule in infection control is to first isolate the at-risk population and then conduct thorough testing. The spread of infection must be prevented, even if it would temporarily reduce ability to offer medical treatment services. The in-hospital infection outbreak was reported to the Kanto-Shin’etsu Regional Bureau of Health and Welfare, the Tokyo Metropolitan Government and the Shinjuku City Public Health Center. On 26th March, the in-hospital infection outbreak was made public on the hospital’s website after confirmation with the Tokyo Metropolitan Government. Patients and medical workers who were confirmed to be infected were hospitalized and isolated. All medical workers confirmed to be negative upon PCR testing were requested to remain on standby for 14 days. These workers were hospitalized if found to be positive during this period. On 28th March, another ward was closed and all staffs were reassigned to this ward. A new team was then required to treat all non-infected patients who were hospitalized in this ward. When any patient was transferred or discharged from this ward, PCR testing was again performed to confirm they were negative for COVID-19. With the outbreak of the in-hospital infection, no new first visit outpatients or emergency outpatients were accepted. Medical functions were drastically reduced while we continued to offer treatment only to patients requiring continued outpatient treatment and highly urgent surgeries.

The hospital at which the first infected patient had been hospitalized is closely affiliated with Keio University Hospital and many physicians from Keio University Hospital had been visiting that hospital. Therefore, PCR testing was performed in all 99 physicians who had been visiting that hospital from 1st February. The results of this testing revealed that five physicians were positive for COVID-19. Secondary infection in one to two other physicians was also confirmed. We thus became aware that, at a time when we had implemented flawless quarantine control and believed there was not a single infected individual within our hospital, several completely asymptomatic physicians were positive for COVID-19.

**Mass Outbreak among Junior Clinical Residents**

On 31st March, a report was received from the Health Center that several junior clinical residents had developed fevers and that one of these junior clinical residents had a positive result on PCR testing performed that evening. We feared that when these residents were assigned to their new work site the following day, i.e., on 1st April, they would pose a risk to other medical workers who would be in close contact with them. It was decided that it would be impossible to determine the extent of the situation and take action for all persons in contact with the residents with the limited time remaining before their new appointment. Therefore, a decision was made to return to the rule of infection control and temporarily isolate all risk populations. Staff from the Postgraduate Medical Education Center joined the staff at the Division of Infectious Diseases and Infection Control, who had been working at night as well, to engage in contact and tracing operations. Specialised infection committee members from all departments engaged in rapid response. As a result, all 99 junior clinical residents, including those from the Department of Dentistry and Oral Surgery, were requested to self-isolate at home. All faculty members were asked to temporarily suspend all work outside the hospital, including appointments at new work sites and work at other hos-
pitals. All affected individuals were contacted by dawn on 1st April. This resulted in a sudden stop of duties, causing a significant amount of trouble for planned new work sites and dispatch sites, including some at affiliated hospitals.

However, the gravity of the situation was later discovered during our contact investigation of junior clinical residents. At this time, requests were made by the national and Tokyo governments to refrain from large gatherings such as banquets. Despite the fact that Keio University Hospital also requested that faculty members refrain from large gathering, some junior clinical residents had attended an unofficial banquet on 26th March. As a result, a mass infection occurred amongst these residents. It is extremely unfortunate that this banquet was held despite the fact that it had been decided one month ago to cancel the junior clinical resident completion ceremony and social gathering that are held each year by the medical departments and hospital. A detailed epidemiological study conducted later revealed that a resident with community-acquired COVID-19 had passed it to a small number of residents, leading to the mass infection that occurred at the banquet held on 26th March. This was promptly reported to the Shinjuku City Public Health Center and the Tokyo Metropolitan Government.

Finally, the situation was made public on our website on 6th April, when the results of PCR testing of all the junior clinical residents were available. The matter was also conveyed in writing to all inpatients and outpatients, and an apology was offered. All residents who attended the banquet were requested to self-isolate for 14 days, even if their initial PCR test was negative. PCR testing was again performed on a later date to confirm that they were negative. Contact tracing of 99 people in close contact with the residents revealed that the infection had not spread from this cluster to other medical workers or any patient.

In order to control two clusters (i.e., health care-associated infections from another hospital and a mass infection of residents) and to stop the further spread of infections, we prepared our response system and further reduced medical treatment functions. Personnel from each treatment department were organised into multiple teams as much as possible. Medical workers other than those on the teams were required to maintain necessary treatment functions and were requested to remain on standby. Such staff would then be rotated to replace the aforementioned staff for fixed periods of time. At this time, in order to maximise our strengths as an advanced treatment hospital and a university hospital in the event of a large number of severe COVID-19 cases occurring in the metropolitan region, a system for accepting a fixed number of patients divided amongst several hospitals was prepared under the guidance of the Tokyo Metropolitan Government. Multiple wards were closed in a stepwise manner to secure manpower and space to proactively accept severe and moderate cases. Thus, despite the challenges, Keio University Hospital was miraculously able to establish an emergency treatment system ahead of other university hospitals.

Thorough Information Disclosure and Sharing

Since the in-hospital infection outbreak, each stage of the situation was reported on the hospital’s website. Detailed data was also reported each day to the Shinjuku City Public Health Center and the Tokyo Metropolitan Government. We considered it to be of utmost importance to continue to convey accurate information to all faculty members and staff at the affiliated hospitals. On 10th April, meetings of an ad hoc Professor Committee, the assembly of directors of all the clinical departments, Manager/Director Physician Committee (all management-level faculty members) and the Specialised Infection Committee were simultaneously held to directly respond to those with questions. We reaffirmed the extreme importance of such bilateral information sharing in removing anxiety and building trust. Sharing the situation in real-time contributed to building unity among our faculty members as well as building trust.

Initiatives for COVID-19 Treatment and Research

Since 13th February, all regular patients requiring hospitalisation due to complaints of a poor physical state were assigned to private rooms because the possibility of COVID-19 infection could not be denied. PCR testing was performed on these patients since late February. Successive cases were found to be positive since the last week of March, indicating that community-acquired infections were rapidly spreading. In Tokyo, a system was initiated to enable doctors at a general headquarters to confirm the status of empty beds at each facility and then organise the transfer of severe and moderate patients to such facilities. A large number of severe and moderate patients had already been transferred to Keio University Hospital.

A COVID-19 critical care team was created comprising individuals from multiple treatment departments in order to save the lives of severe cases and prevent moderate cases from becoming severe while sharing relevant information (Fig. 1). Professor of the Department of Pulmonary Medicine was appointed as the Team Leader. Under his leadership, severe cases were overseen by internal medicine and surgery departments, including the Department of Emergency and Critical Care Medicine led by Professor of the Department of Anaesthesiology/Intensive Care Team. Moderate cases were overseen by an internal medicine team focusing on pulmonary medicine to treat the underlying disease. Mild cases were treated by teams comprising physicians from several other treatment departments including experts in immune response and inflammation.

Mental healthcare is also an important issue for COV-
ID-19 patients, their families and frontline medical workers. A mental healthcare team offering diversified stress management was established by Professor of the Department of Neuropsychiatry. This team proactively engaged in mental healthcare support activities.

Dean of the Keio University School of Medicine, and Director of the Clinical and Translational Research Center, established a Keio Donner Project to promote diverse COVID-19 research for clinical application by basic researchers. This project, created by a veteran team of doctors from basic research departments, was named after the nickname of Doctor Shibasaburo Kitasato, first Hospital Director and Dean of the Department of Medicine (‘Donner’ means ‘thunder’ in German).

A COVID-19 Clinical Trial/Clinical Research Task Force comprising mainly members from the Clinical and Translational Research Center was established to support the safety and rapid implementation of large numbers of observational studies, specific clinical studies and clinical trials related to COVID-19.2–7

A Keio COVID-19 Registry was also established to unify multiple studies to develop a database that could provide large amounts of research data in the future. A large-scale nationwide team was established to study genomic susceptibility of the host genome focusing on the low number of serious and fatal cases among Japanese patients. An epidemiological research team led by Professor of Department of Preventive Medicine and Public Health offered expert advice on health care-associated infection control activities.8 The viral genetic analysis team was established by Professors of molecular biology, medical genetics, and public health to study effect of conduct molecular epidemiologic studies.9

Research progressed at a very fast rate. Professor of the Division of Infectious Diseases and Infection Control, and Professor of the Clinical Testing Department verified a new method of serum diagnosis.10 Meanwhile, Professor of the Center for Transfusion Medicine and Cell Therapy and others developed plasma therapy and implemented clinical trials and research for various drugs. All Keio members worked in unity, resulting in a tremendous display of the Kitasato spirit of working like a family for basic and clinical medical science in the 100th year since the hospital was established. I was truly thankful for the trustworthy efforts of everyone involved.

**Starting Pre-Hospitalisation PCR Testing**

With the cooperation of Professor of the Department of Laboratory Medicine and Professor of the Department of Diagnostic Radiology, our hospital became the first in Japan to introduce PCR testing for all inpatients as well as PCR and chest computed tomography scans for all surgery cases since 6th April. During the first week, there were no COVID-19 patients identified among those hospitalized for other diseases (0/97). However, in the week of 13th April, when the number of infections in Tokyo increased, five positive cases (5/67) were confirmed. Each
case appeared to be a subclinical community-acquired infection. This data was published on our homepage. One positive patient transferred from another hospital had no symptoms at the time of transfer, and this appeared to be a health care-associated infection that occurred within the several days leading up to onset. It has been reported that the possibility of transmission is the highest between the period from 2 days before onset to immediately after onset. If procedures that potentially produce aerosols such as laparoscopic surgery or endoscopy are performed in infected but completely asymptomatic patients, there is a major risk of transmission and also the possibility that the patient will develop severe symptoms. This testing was considered necessary in light of the current situation in the Tokyo metropolitan area as a measure to protect both patients and medical workers before hospitalisation as well as high-risk testing and treatment.

Resolution of Health care-associated Infections and Further Enhancement of Monitoring System

On 21st April, we explained on our website that the cases of health care-associated infections had been resolved. As of 11th May, at least 40 days have passed since the final response day (end of isolation for the final high-risk contact individuals) for the major clusters of infection that began with a patient being transferred from another hospital, infections of physicians visiting other hospitals and the mass infection of junior clinical residents. Data from other isolated cases also suggests that the infection has not spread. Analyses performed by the Keio Donner Project epidemiological and viral genetic analysis teams jointly formed by Department of Molecular Biology and Center for Medical Genetics also found that the cluster arising from another hospital and the cluster noted among the residents had different specific gene sequences, suggesting that they were not related to the other suspected cases of isolated occurrences and community-acquired infections.8,9 As a result of the great efforts taken by the Division of Infectious Diseases and Infection Control, Department of Clinical Laboratory, epidemiological research team and viral genetic analysis team, along with an investigation of high-risk individuals, requests for individuals who were close contacts to self-isolate, repeated PCR testing and detailed epidemiological analysis, we were able to confirm cessation of health care-associated infections. PCR testing was performed in all 72 patients found to have fever of 37.5 °C or higher between 16th and 22nd April. All results were found to be negative. After the final week of March, PCR testing was conducted for all inpatients with fever of 37.5 °C or higher that was unrelated to the underlying disease. Any faculty member who had mild symptoms was required to visit the Health Center, went on standby for 3 to 4 days and then undergo PCR testing. They were allowed to resume duties after the disappearance of symptoms and confirmation of a negative PCR result. Normally, even if medical workers were asymptomatic or sub-clinically infected with COVID-19, the risk of transmission to patients was considered to be low if standard preventive measures were thoroughly followed for all medical procedures. However, PCR testing was performed and negative results were confirmed for all 132 medical workers involved in the treatment of immune-compromised patients at the Cancer Center, Immunotherapy Center, Apheresis and Dialysis Center, and Organ Transplant Center. Even after health care-associated infections were controlled, we implemented the strictest system in Japan at that time: mandatory PCR testing in all new inpatients, patients who developed fever at the hospital and faculty members who exhibited symptoms. A single negative PCR result would not guarantee safety. We continued to request that all faculty members would carefully avoid any close contact while engaging in treatment procedures and at all other times.

Recovery of Hospital Functions and Steps for the Future

The situation in Tokyo remained extremely tense. A decision was taken to extend the declaration of a state of emergency until 31st May, and a second wave of community-acquired infections could occur at any time. Keio University Hospital experienced unforeseen health care-associated infections and was greatly compromised by a mass infection of residents. However, staff in the clinical departments and basic science departments as well as other faculty members combined their strength to persevere through an extremely difficult month and finally embark on the road toward recovery. We would also like to express our deepest gratitude for the efforts and support of all those at Sanshikai, the Alumni Association and our affiliated hospitals.

Since 7th May, we started accepting appointments for new patients while continuing to limit cases to malignant tumours, refractory immune diseases, complex surgery and treatment cases and pregnancies. Upon resuming outpatient services, outpatient treatment for cases that had previously been postponed owing to the infection situation was implemented in a stepwise manner considering the degree of urgency. The number of surgical procedures gradually increased while confirming adequate supplies of personal protective equipment and focusing on performing the procedures that had been postponed as a result of the spread of infection. During May, about 20 surgical operations could be performed per day.

This experience taught us that the novel COVID-19 virus could drastically reduce the treatment services. As we started to regain functionality, it was difficult to offer the same routine treatment that we previously offered. It was not a small task to control infections while safely treating 3500–4000 outpatients per day. The situation pushed us to accelerate the introduction and popularisa-
tion of online treatment consultations including initial consultations and to construct a system that would avoid very high crowding for medical treatment. As an artificial intelligence hospital model, Keio University Hospital attempted to automate operations and increase efficiency to secure time for medical workers to interact with patients. The unprecedented novel infectious disease made ‘medical treatment involving direct contact with patients’ difficult. Various sensing technologies as well as elaborate imaging and communication technologies need to be leveraged to develop methods of medical treatment involving new ways of interacting with patients. Moreover, new concepts of preventive medicine and public hygiene need to be investigated in order to fight infectious diseases.

After learning through this ordeal, we, at Keio University, have a mission as ‘leaders’ to create a new society in this rapidly-changing age. ‘Education’ and ‘research’, which were minimized in the state of emergency, will be the motivating force for this mission.

Acknowledgements

In this period of just more than 1 month, we dealt with an extremely difficult situation. Despite this, we were able to keep moving forward because of the dedication of our medical workers who continued to provide treatment despite being in a tense situation on the frontline as well as the diligent efforts of all the faculty members supporting them and the great physical and mental support received from all Keio members, Sanshikai members, many patients and other supporters. The battle against COVID-19 will continue for a long time as we continue to search for the ideal means of fighting this infection through Keio’s medical science and treatment. We will take efforts to use this difficult experience as fuel to recover our functionality as a leading global hospital.

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