Public Relations Magazine for NCGM

Feel the NCGM

Special Issue No. 2

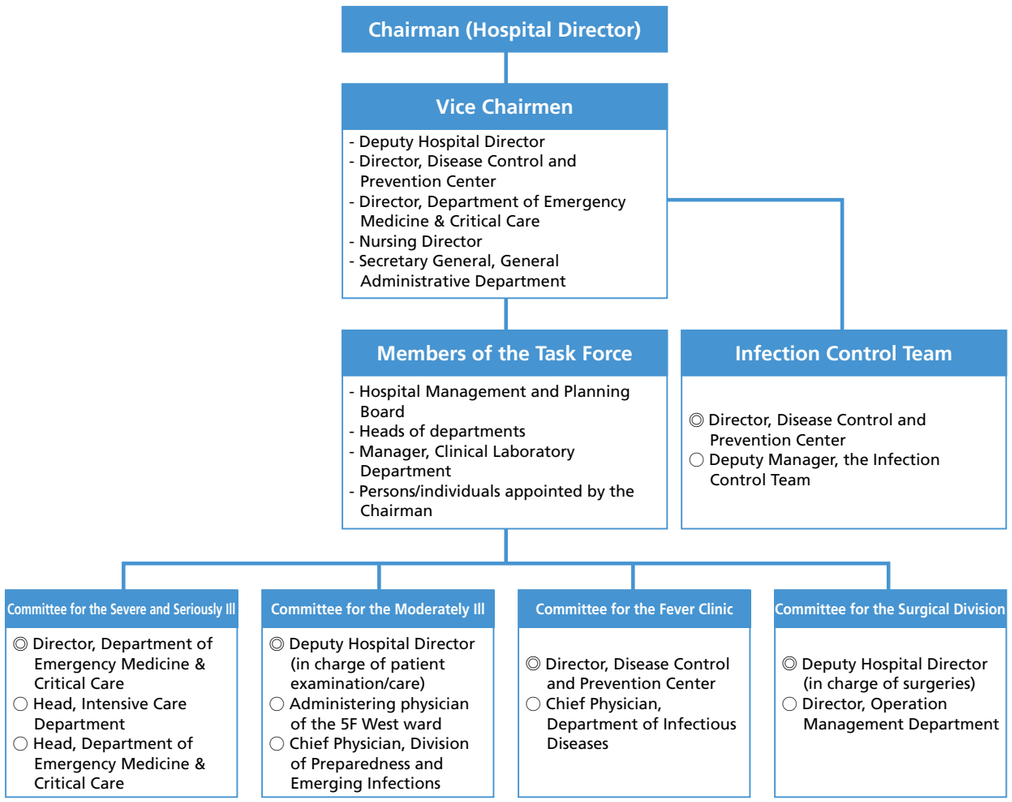
National Center for Global Health and Medicine
Office of Public Relations

July 2021
Special Issue
No. 2

NCGM Fights against COVID-19 – Lessons Learned (2nd Edition) –

Photos: NCGM COVID-19 on-line seminar for the press (top left), Vaccination for NCGM staff (top right), Nursing care in the High Care Unit (bottom)

The NCGM COVID-19 Task Force and Organization



Feel the NCGM Special Issue No. 2 July 2021

Foreword

Norihiro Kokudo, President
National Center for Global Health and Medicine

National Center for Global Health and Medicine (NCGM) is a National Center whose primary missions include infection control. Our staff members have strived as a team to tackle Coronavirus Disease 2019 (COVID-19). We carried out physical examinations and PCR testing of Wuhan returnees in late January 2020. In February, the following month, some staff members boarded the cruise ship anchored in Yokohama to cooperate in addressing the COVID-19 cluster among its passengers. Affected passengers included some severe cases. We started to provide them with intensive care while struggling to find effective ways to control this unknown virus. Examination data from 11 early cases, and their treatment methods and clinical courses, were promptly published on our website, and were actively used nationwide as a reference by institutions that were then treating COVID-19 patients.

Reflecting back on NCGM's long history of over 150 years, we have responded to numerous pandemics in the past, starting with the Spanish flu of 1919, SARS of 2003, swine flu of 2009, Dengue fever of 2014, the Ebola outbreaks of 2014, 2018, and 2019. We have always been fully trained and prepared for such crises as one of the four medical institutions in Japan designated for treatment of specific infectious diseases, having a total of four beds available for this treatment (which is the most out of all four institutions). Due to our efforts and preparedness, we were able to act swiftly in the midst of this pandemic, and we are thankful that no nosocomial clusters of COVID-19 cases have been reported in NCGM as of the writing of this message.

For our activities in responding to COVID-19, we addressed a wide range of needs regarding the treatment and research of COVID-19, including development of new therapeutic drugs, convalescent plasma therapy, and advanced medical care for the severely ill, establishment of COVID-19 Registry Japan (COVIREGI-JP), fever clinic, and the Shinjuku City COVID-19 Testing Center, support for the mildly ill accommodated in hotels, and vaccination to government VIPs. Since the beginning of the pandemic, we had felt an urgent need for organizational research and development to contain the spread of this unknown disease, and we launched a "Novel Coronavirus Infection Academic Advisory Board" in the beginning of February 2020. This Board covered a wide range of fields related to COVID-19, including treatment, testing, pathophysiology, and epidemiology. They also aided in the development of research protocols, coordinated with the IRB, managed and advised through the course of trials. More than 100 projects are currently underway, and as many as 124 papers have already been published in academic journals. The above NCGM activities to address the COVID-19 pandemic are recorded in this booklet.

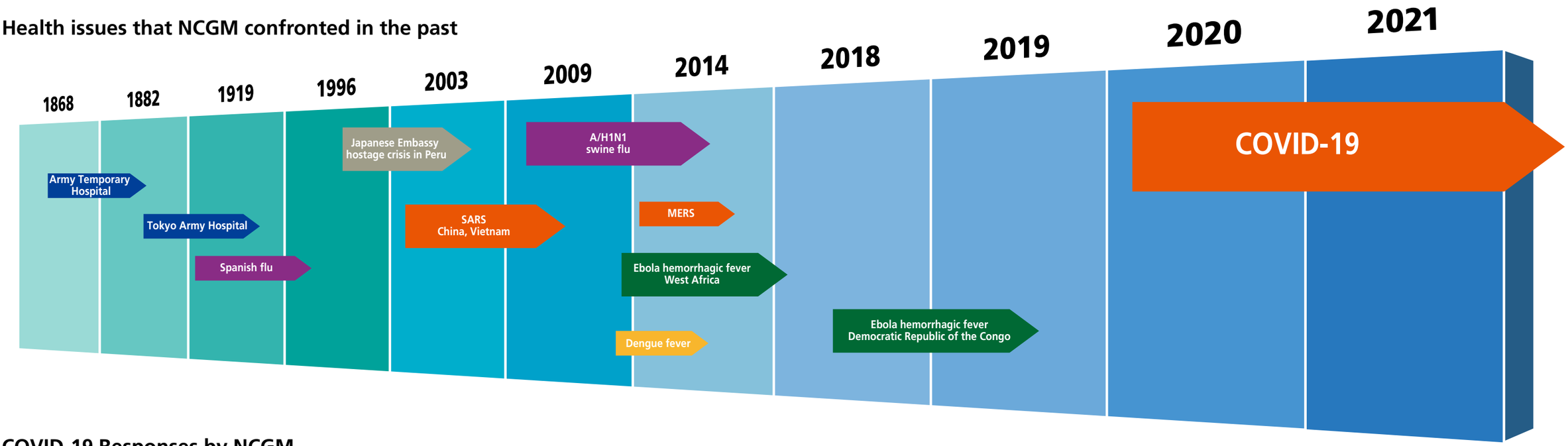
In Japan, vaccination began in February 2021 first for healthcare providers, followed by elderly people and high risk patients. Vaccination is rapidly progressing, and a workplace vaccination program has also begun. However, as of the writing of this message, the fourth wave of the pandemic and the spread of virus variants are matters of great concern. It is still unclear when this pandemic will end. We at NCGM will continue to strive as a team to confront this challenging disease. Through this booklet, I would like to express my respect and gratitude to all of the healthcare workers and NCGM staff who are fighting against COVID-19.

July 2021

1 Overview of NCGM History in Response to Various Health Issues and Our Multifaceted Role

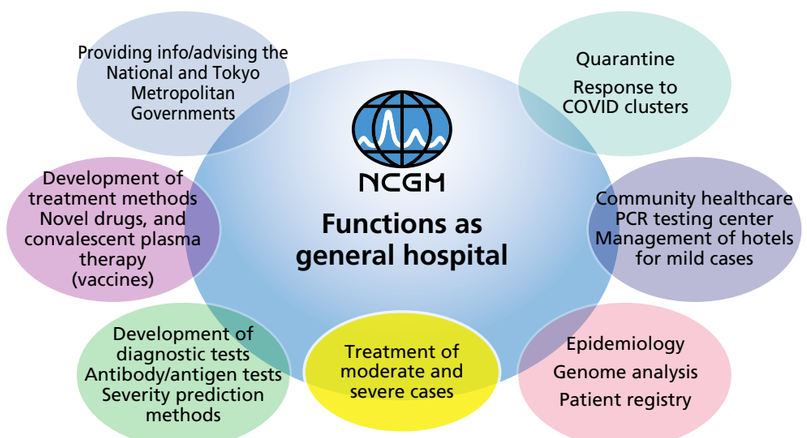
Akira Harita, Director General, Bureau of Strategic Planning, NCGM

Health issues that NCGM confronted in the past



COVID-19 Responses by NCGM

The one and only medical institution capable of undertaking a multifaceted role in public health and medical treatment



Ever since the establishment of the "Army Temporary Hospital" (currently NCGM) in 1868, we have always played a pivotal role in responding to health issues in Japan. We still have medical records preserved of numerous patients that were treated at Tokyo Daiichi Eiju Hospital during the Spanish flu pandemic in 1918-1920, over 100 years ago.

The accumulation of our experience within this century in confronting emerging/re-emerging infectious diseases such as SARS, H1N1 swine flu, MERS, Ebola hemorrhage fever, and Dengue fever outbreaks is being put to use in our current COVID-19 response. NCGM is not only a general hospital offering advanced medical care to patients with various diseases, including infections, but a medical institution capable of undertaking a multifaceted role in public health and medical treatment. This includes providing advice and information to government policy-makers, conducting quarantine/responding to COVID-19 clusters, studying and developing treatment methods, novel drugs, and vaccines, developing diagnostic tests and severity prediction methods, conducting epidemiological studies, performing genome analysis, creating a patient registry, and taking part in the local healthcare cooperation system as seen in the "Shinjuku Model."

2

Treatment and Nursing of COVID-19 Patients and Suspected Patients

Norio Ohmagari, Director, Disease Control and Prevention Center (DCC), Center Hospital, NCGM
Tatsuya Okamoto, Head, Intensive Care Department, Center Hospital, NCGM
Tomoko Sato, Nursing Director, Center Hospital, NCGM
Yuko Sugiki, Deputy Manager, 5th Floor West Ward, Center Hospital, NCGM
Miho Takahashi, Manager, HCU, Center Hospital, NCGM
Masayuki Hojo, Head, Department of Respiratory Medicine, Center Hospital, NCGM

Treatment of COVID-19 patients

At NCGM, the first COVID-19 patient was identified among the patients consulting with the Department of Infectious Disease in late January 2020. Since then, our Hospital has treated numerous patients. We also performed COVID-19 screening tests and provided medical care to the patients who arrived in Japan on the flights from Wuhan, China chartered by the Japanese government on January 29, 2020.

We initially had limited knowledge about the clinical features and natural course of this disease and its treatment as well. Thus, we treated patients with Lopinavir/Ritonavir, of which in vitro activity against SARS-CoV2 had been confirmed by applying our experience and expertise. In February, many critically-ill patients were frequently identified among the patients aboard the cruise ship Diamond Princess, which had been anchored in Yokohama Port. In order to treat these patients, we ordered Remdesivir which is an anti-viral drug from Gilead Science, Inc. in the USA, and started its compassionate use on the patients. In the same month, we started preparing for multiregional clinical trials in collaboration with the NIH (National Institutes of Health, USA) using Remdesivir, and the investigator-initiated clinical trials were launched on March 25, 2020. Four different trials were conducted over about one year, and the results demonstrated that the efficacy of remdesivir was significantly higher compared to a placebo, and that the efficacy of remdesivir in combination with baricitinib was significantly higher compared to remdesivir alone. Based mainly on these data, remdesivir and baricitinib were approved in Japan for the indication of COVID-19 and have become clinically available. As of May 2021, we are conducting a randomized comparative trial at NCGM to evaluate the efficacy of convalescent plasma. We also participated in a global study of hyperimmune intravenous immunoglobulin (IVIG), and conducted a multicenter randomized comparative trial to evaluate the efficacy of ciclesonide. While the expected efficacy was not demonstrated in either investigated drug, it is important to conduct clinical trials expeditiously to find effective drugs in order to cope with emergency situations. In this sense, we think we have played a prominent role in Japan.

Aside from the patients who disembarked from the Diamond Princess, from February to March 2020, many patients who had a travel history to Wuhan visited our outpatient department, and were diagnosed with COVID-19 infection. However, in March, we began to observe a pronounced rise in the number of COVID-19 patients who had not apparently traveled to Wuhan. Critical cases, mainly of elderly patients began to be identified. Correspondingly, the number of COVID-19 inpatients increased. In spite of the nationwide state of emergency declared by the Japanese government on April 7, 2020, as many as 48 patients including eight patients on ventilators were admitted to our Hospital at the same time in the following week.

After late April, the number of new inpatients gradually decreased, consequently, the total number of the patients in our Hospital gradually decreased. However, the number of patients began to increase again after the lifting of the state of emergency, leading to the so-called “second wave” of the pandemic. In this outbreak, as opposed to the outbreak from March to May, fewer patients were in a critically ill condition - probably because there were fewer elderly patients - and most of the affected people were young adults in their 20s-30s who acquired the infection mainly in downtown areas. Therefore, the Japanese government did not declare a state of emergency during the second wave.

The Japanese government made an effort to enhance economic activity while trying to prevent COVID-19 transmission. However, this was not an easy task. The number of new COVID-19-positive cases remained high in Fall, and began to increase with the decrease in temperature in Tokyo in December 2020. With a rapid increase in the number of new cases, the so-called third wave set in at the end of December.

Under these circumstances, we also began to accept many moderately or severely affected patients around this time. The Japanese government declared its second state of emergency in January 2021. During the third wave of the pandemic, in which most patients were elderly and most moderate or severe cases were reported in Tokyo, many medical institutions in Tokyo struggled to accept these patients. Even after February, clusters of COVID-19 cases were identified one after another in elderly facilities and medical institutions, preventing a decrease in the numbers of new positive cases and severe cases. The situation finally settled in March, when long-awaited vaccinations began for the NCGM staff members. With the cooperation of many staff members from various departments, vaccination was conducted smoothly and swiftly. Prime Minister Suga also came to NCGM to receive his vaccination.

As of the writing of this section (May 1, 2021), the fourth wave of the pandemic has reached Japan, and the government has declared its third state of emergency. In Tokyo, there are currently about 2000 inpatients with COVID-19, and the number of moderate cases admitted is increasing. The situation in the Kansai region is becoming of more concern. The number of severe cases has already exceeded the hospital bed capacity for COVID-19 patients, leaving about 15 thousand patients staying at home or waiting at home for a hospital bed. The condition of some of these patients at home has taken a sudden turn for the worse. We at NCGM have renovated the High Care Unit (HCU) to prepare to accept COVID-19 patients with severe symptoms.

(Norio Ohmagari)

Medical cases were quickly reported to deliver information to healthcare providers nationwide.

症 例

当院における新型コロナウイルス(2019-nCoV)感染症患者3例の報告

国立国際医療研究センター

中村 啓二　忽那 賢志　鈴木 哲也　井手 聡　太田 雅之　守山 祐樹
中本 貴人　野本 英俊　秋山裕太郎　宮里 悠佑　脇本 優司　奥濱 絢子
神田 宏平　氏家 無限　木下 典子　山元 佳　石金 正裕　森岡慎一郎
斎藤 翔　早川佳代子　大曲 貴夫

Key word:2019-nCoV 感染症

序 文

新型コロナウイルス(2019-nCoV)感染症は中国武漢市で2019年12月以降報告されている．2020年2月3日現在，世界では17,267人の患者が報告されている．内訳として武漢市で5,142人（死亡者 265人：致命率 5.15%），武漢市以外の湖北省で6,035人（死亡者 85人：致命率 1.4%），湖北省以外の中国全土で6,090人（12人：0.19%），中国以外の国183人（死亡者1人：致命率 0.5%）となっており，中国での症例が大半を占めており，本邦での臨床像の詳細な報告はまだない．臨床像の把握は今後の2019-nCoV感染症の診療および感染防止対策に寄与すると考えられるため当院で経験した3症例をここに報告する．

重腎炎として加療開始した．その後も38℃台の発熱，咳嗽，喀痰が続き，1月30日に受診．胸部レントゲン検査を施行したところ左下肺野に新たな浸潤影の出現がみられた．胸部単純CTでは両側下葉にスリガラス影と浸潤影の出現があり，2019-nCoV肺炎の可能性が強く疑われ同日入院となった．

初診時現症：意識清明.血圧 148/90mmHg，脈 106回/分，体温 37.8℃，呼吸数 16回/分，SpO_2 97%(室内気)．

初診時の Review of system にて主要な陽性所見（以下 ROS(+)）：頭重感・倦怠感・咽頭痛．

初診時の Review of system にて主要な陰性所見（以下 ROS(-)）：悪寒・頭痛・咳嗽・喀痰・筋肉痛．咽頭発赤なし，扁桃腫大なし，呼吸音正常で左右差なし，肋骨脊柱角に叩打痛なし．

http://www.kansensho.or.jp/uploads/files/topics/2019ncov/2019ncov_casereport_200205.pdf

Installing positive pressure ventilation system in Nurses' station (Designation of Green Zone)

Treatment of critically ill COVID-19 patients in the ICU

On February 15, 2020, the first patient in critical condition (a Diamond Princess passenger) was admitted to room 10 (negative pressure isolation room with an anteroom) in the ICU, and underwent intensive care including bronchial intubation and ECMO therapy, which was conducted without interrupting our normal intensive care operations (Phase 1).

As the first wave surged in late March, we came to experience difficulties in treating patients using the only bed provided for COVID-19 patients during Phase 1. Correspondingly, five isolation rooms were renovated in a week, installing ventilation systems to achieve negative pressure environments and using vinyl sheets to achieve positive pressure ventilation in the nurses' station (designation of Green Zone). From April 2, these six beds were converted to exclusive use as an ICU ward for COVID-19 patients (Phase 2).

The healthcare providers of the ICU and the Departments of Emergency Medicine and Critical Care, Respiratory Medicine, DCC, ACC, Nephrology, Physical Medicine and Rehabilitation, Thoracic Surgery and many others collaborated in providing medical care. We also, held cross-sectional clinical conferences with healthcare providers including nurses, ICT, PT, MT, twice a day including Saturdays and Sundays to disseminate information about the condition of the patients and treatment courses.

In comparison with typical acute respiratory distress syndrome (ARDS), COVID-19 patients are mechanically ventilated for a longer period (longer than three weeks), and have a higher incidence of complications such as pneumothorax, mediastinal emphysema, oxygen toxicity, and ventilator-associated pneumonia (VAP). Many patients required tracheostomy due to difficulties extubating. Also, patients were required to engage in long-term rehabilitation during the ICU admission and after leaving the ICU because of severe muscle weakness. We were able to provide the most advanced medical care possible by conducting clinical trials of antiviral drugs such as Remdesivir, Chloroquine, and AVIGAN®, combining with treatments such as steroid therapy and blood purification therapy using PMX to treat cases of cytokine storm. We were able to enlist the help of young doctors from the Emergency Medicine and Critical Care Department and the Surgery Department to supplement the shortage of healthcare providers. Since December, Dr. Sekihara from the Thoracic Surgery Department has also joined the dedicated staff to further enhance our medical care.

We treated a total of 37 intubation patients (including three cases in the New Infectious Diseases ward) in about one year up to the end of March 2021. Among the ICU inpatients, 11 patients died (30%), seven patients were on ECMO (19%) and 25 patients were eventually discharged (68%).

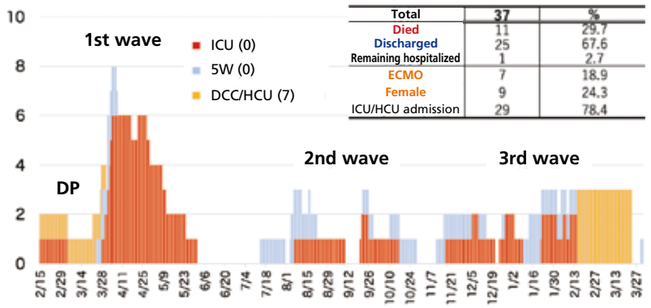
(Tatsuya Okamoto)

Daily clinical conferences

Performing tracheostomy wearing PPE/PAPR

Yasutoshi Nishimura, the Minister in charge of the COVID-19 response, visited NCGM on March 29, 2020.

Changes in numbers of intubated patients (up to March 31, 2021)



Total	37	%
Died	11	29.7
Discharged	25	67.6
Remaining hospitalized	1	2.7
ECMO	7	18.9
Female	9	24.3
ICU/HCU admission	29	78.4

Nursing of COVID-19 patients and suspected patients

New Infectious Disease ward
Admission of three patients (two on ECMO) between February 19 and March 29, 2020
Nurses: eight-hour shift (three or four nurses on day shift, two nurses on night shift)
Nursing care was provided to critically ill patients including those on ECMO by nurses who were concurrently assigned to the New Infectious Disease ward and were reinforcement staff from the ICU.

ICU: Six beds (critically ill patients)
The first patient was admitted to the ICU from February 14 to March 5, 2020, and six beds were allocated for COVID-19 patients from April 1.

As infection prevention measures, the use of personal protective equipment (PPE) was strictly implemented, and we also allocated staff to engage in ward environment preparation. Since alarms became muffled due to the partitions, a nurse was stationed inside of the partitions to communicate with the outside using a tablet device, etc.

Since family members were not able to visit the patients, we encouraged on-line visits using tablet devices and tried to help the family to understand and accept the medical condition of the patient.

West ward on 5th floor: 40 beds (patients in mild to moderate condition, suspected patients)
Passengers on the chartered flights from Wuhan who were confirmed as being infected with COVID-19 or suspected of being infected were admitted to this ward. When the number of critically ill patients increased, four patients on ventilators were accepted in this ward. Since it was a tuberculosis ward originally, nurses were trained to administer nursing care using protective gear (PPE), however, when there was a surge in the number of critically ill patients, the reinforcement of personnel became necessary. Normally, three nurses work the night shift, however, five to six nurses were deployed on the night shift to address the situation.

14th floor (partial use), 13th floor (partial use), east ward of 7th floor (one bed)
Due to an increase of the number of patients and critically ill patients, a shortage of beds had occurred in the west ward 5th floor, so, that suspected patients with low clinical probabilities were admitted to those floors. We installed partitions and implemented infection prevention measures since those wards were concurrently allocated to non-COVID-19 patients. Also, we strived to ease the increasing anxieties experienced by both the patient in isolation and their families by listening carefully to their concerns and providing detailed explanations.

(Tomoko Sato, Yuko Sugiki)

Nursing in New Infectious Disease ward

Partitions in ICU nurses' station

Anterooms were created in ICU rooms

Designated area for PPE donning with posters instructing their use.

PAPRs (powered air-purifying respirators) were worn during ECMO treatment.

Areas for PPE donning were designated with posted manual. Instructions for doffing were posted inside ward rooms.

Negative pressure beds in HCU

HCU photographed from the station

Care and treatment at the High Care Unit (HCU)

At the beginning of 2021, there was a sharp rise in the number of COVID-19 patients. We hurriedly decided to open the HCU as a ward for severe COVID-19 cases so that we would be able to accept more patients with severe symptoms.

Necessity for remodeling
Air conditioning duct work was needed to make the HCU available as a care unit for COVID-19 patients. Acrylic walls and doors were installed to divide the ward into the infection-free area and the potentially contaminated area. Before starting the remodeling, we had a number of meetings with the parties concerned to discuss the location of the anteroom and zoning. Three negative pressure booths were installed to minimize the risk of transmission during treatment or care provision.

Arrangement for necessary materials/devices
Arrangement for medical materials/devices was more difficult than expected due to limited preparation time. Under the effects of the pandemic, infection prevention goods were thinly distributed and the shipping took longer. We had to acquire various types of goods after opening the ward.

Staff training
Training related to infection prevention, such as the donning and doffing of PPE, zoning and the cleaning operation, was repeatedly implemented under the instruction of certified infection control nurses, and training related to ECMO and CHDF was also performed with the aid of doctors and clinical engineers. We produced an educational video for nurses working in shifts, creating an environment that allowed all the staff to be sufficiently trained.

Opening of the ward
We started gradually reducing the number of patients admitted into the HCU at the beginning of February. All patients were removed from the HCU by the morning of February 15. In the afternoon of the same day, COVID-19 patients with severe symptoms were admitted and the newly-opened ward started its operation with seven beds. Working in PPE in the potentially contaminated area, healthcare workers were exposed to heat stress and had trouble breathing. N-95 masks made it hard to communicate. Work in this area was far more inefficient than that in the infection-free area, and the staff looked exhausted. Being in an unfamiliar environment and feeling nervous about caring for severely-ill patients, some of the staff members said they were scared or they wanted the HCU to be remodeled back into its original state. Meanwhile, some other staff members actively discussed what to do to improve efficiency and to reduce the work burden. They eventually began recommending each other to take breaks when working long hours, and the strained communication between the infection-free area and the potentially contaminated area became much milder.

At the HCU, care and treatment were also provided to patients on ECMO. Because caring for these patients requires advanced knowledge and skills, some mid- to high-level nurses who had received relevant training, and who were nominated by certified ICU nurses and the Manager, were assigned to this task. Less experienced nurses wished to help these experienced nurses when they saw them looking nervous and caring for patients on ECMO with strained looks on their faces, despite having dealt with any situation calmly and perfectly so far. The Manager of the ICU promptly proposed to conduct a training program about care for severely-ill patients. The training started in the ICU for young nurses, mainly those with less than one year work experience. These nurses, who had had difficulty performing many of their tasks, began to actively study in advance for the next training session. I still clearly remember them, eyes lit up, telling me the details of their ICU training.

Closing of the ward
Up until March 7, only COVID-19 patients with severe symptoms were admitted to the ward. In response to requests to accept post-surgery patients as well, we divided the ward into the area for COVID-19 patients with severe symptoms and the area for post-surgery patients, and started the operation the following day. With a higher possibility of persons or materials crossing the infection-free area and the possibly contaminated area, the relevant staff members were required to be even more cautious. Later, COVID-19 patients tested negative for PCR, and the ward returned to the ordinary HCU from March 22 onward.

Unfortunately, the COVID-19 pandemic has not yet ended. We are ready to open the ward for COVID-19 patients with severe symptoms at any time when there is a rapid rise in the number of severe cases.

(Miho Takahashi)

Healthcare system at COVID-HCU

Three departments (Intensive Care Department, Respiratory Medicine Department, and DCC) collaborated in taking care of patients admitted into the HCU. Treatment started under the following two preconditions: 1) Up to seven patients (up to two patients in each department) would be admitted into the HCU; and 2) The Intensive Care Department would be in charge of patients on ECMO with the aid of the Department of Emergency Medicine and Critical Care. In order to have support from on-call doctors from the Internal Medicine and the ICU during the nighttime and holidays, a joint conference was held from 17:30 every weekday to share detailed information. With the cooperation of the nursing staff, doctors from their respective departments, infection control team (ICT) specialists, and medical engineers (MEs), we were capable of safely treating severe cases during the third wave of the pandemic.

(Masayuki Hojo)

3 Policy Recommendations

Norio Ohmagari, Director, Disease Control and Prevention Center (DCC), Center Hospital, NCGM

Medical institutions and the administration must work in unison to handle the COVID-19 pandemic. We at NCGM have contributed to various cases from administrative issues to policy recommendations.

From January 29, 2020, we started performing screening tests for Japanese returnees from Wuhan, China followed by hospital admissions of symptomatic patients. Our staff members were dispatched to support the Ministry of Health, Labour and Welfare (MHLW) in their mission to address the issues on the Diamond Princess which had anchored in Yokohama Port in February. Also, we supported the members of the United States Public Health Service Commissioned Corps, a subordinate body of the Department of Health and Human Service (HHS) that visited Japan to help American citizens on the cruise ship return to their home country. Their mission was to assess the situation of American COVID-19 patients who were critically ill and support them and their family. NCGM helped the team collaborate with Japanese medical institutions in helping the patients and their families (Photo 1).

Due to these circumstances, Remdesivir which was an unapproved drug was decided to be subject to compassionate use not only to critically ill American patients but also Japanese and other international COVID-19 patients. It was administered to nine patients in Japan. In order to develop necessary drugs for COVID-19 treatment speedily, we started preparing for multiregional clinical trials using Remdesivir collaborating with the NIH in USA, which was commissioned by MHLW, and began investigator-initiated clinical trial on March 25 (Photo 2). The result of this investigator-initiated clinical trial became the evidence for special approval of Remdesivir for COVID-19 treatment on May 7. A multicenter, randomized comparative trial using Ciclesonide which was another candidate therapeutic drug for COVID-19 was conducted principally at NCGM, which was also commissioned by MHLW. Additionally, we created COVIREGI-JP, which is a registry study, and as of June 21, 2021, clinical information on more than 42,000 patients has been accumulated.*

*Registration status as of June 21, 2021: 909 collaborating institutions, 42,932 registered cases including 627 cases from NCGM (including cases in the registration process).

Our staff members have been dispatched to the "Expert Meeting on Novel Coronavirus Disease Control" convened by MHLW in response to the request for participation from the chairperson from February 2020, where we provide advice and make proposals to the government from the standpoint of medical experts engaged in treating COVID-19. In addition, our staff participates in the Weekly Novel Coronavirus Infection Monitoring Meeting established by the Tokyo Metropolitan Government to assess the spread of COVID-19 and the status of medical institutions and provide advice on policies as well (Photo 3). We also dispatch staff specialists to other medical institutions in Tokyo experiencing incidents of nosocomial infections.

In addition, we dispatched staff specialists as members of the Development Committee for "Coronavirus Disease 2019 (COVID-19) Treatment Guidelines" and "Coronavirus Disease 2019 (COVID-19) Pathogen Testing Guidelines," and contributed to the establishment of national treatment guidelines.

Photo 1 Commemorative photo taken on the day before departure of United States Public Health Service Commissioned Corps

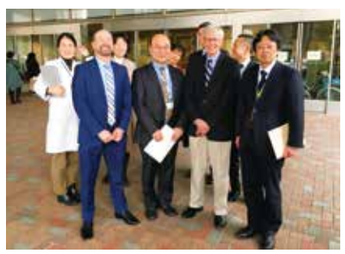


Photo 2 Taken with two doctors who visited us from the NIH in USA for the meeting of multiregional clinical trials

Photo 3 Press conference with Tokyo Governor Yuriko Koike

4 Countermeasures against COVID-19 at Our Emergency Department

Akio Kimura, Director, Department of Emergency Medicine and Critical Care, Center Hospital, NCGM
Ryo Sasaki, Head, Department of Emergency Medicine and Critical Care, Center Hospital, NCGM
Kentaro Kobayashi, Chief Physician, Department of Emergency Medicine and Critical Care, Center Hospital, NCGM

One of the crucial issues regarding COVID-19 measures at our Emergency Department (ED) has been to identify and isolate suspected patients to prevent them from becoming a source of nosocomial infection and protecting the safety of healthcare providers at the same time, while providing initial management for all kinds of emergency patients. As community transmission was on the spread, all patients with fever and respiratory symptoms brought by ambulances were treated as suspected patients, so, we are required to respond as through we are confronting a considerable number of COVID-19 patients. All suspected patients have been triaged by using a checklist for screening indicated in Figure 1, which enquires into the history of overseas travels, close contacts, symptoms of fever and respiratory system, etc.

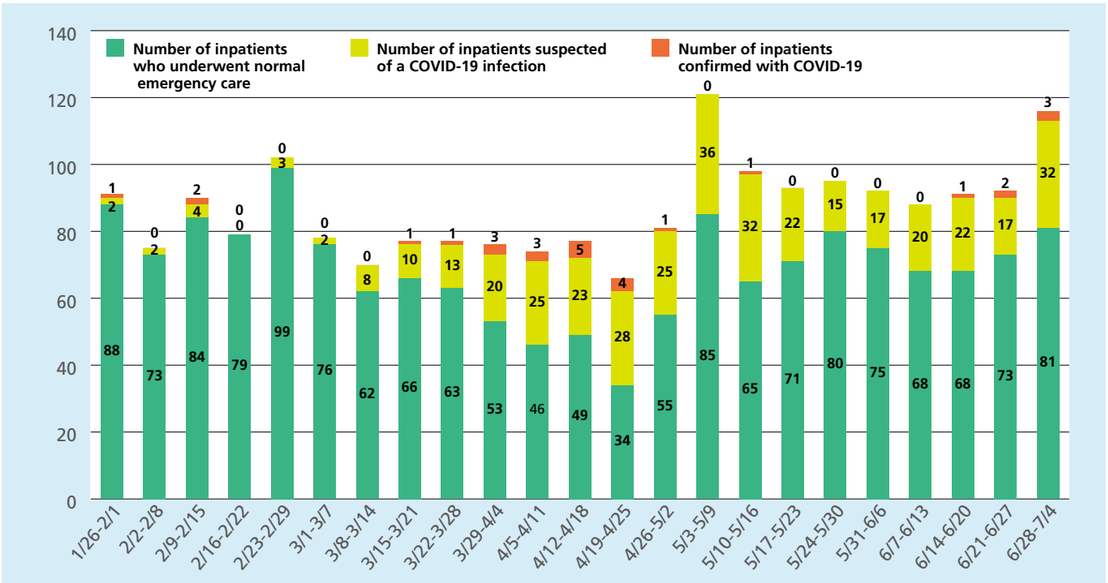
Figure 2 shows flow of inpatients who underwent normal emergency care, suspected COVID-19 patients and confirmed COVID-19 cases. From late March 2020, when community transmission was prevalent, the number of inpatients suspected with a COVID-19 infection increased rapidly, and in the week from April 19 to 25, almost half of the inpatients were suspected or confirmed with COVID-19 infections during a social alert for COVID-19. Later, it became possible to admit patients after confirming their COVID-19 infection status using more rapid result of PCR testing. However, due to the limitations of test kits number, we have to keep basic precautions for all emergency patients during stay at the ED because we cannot test them all.

Figure 1

Checklist for COVID-19
Surgical masks must be provided to all patients!!

[Social history in suspected COVID-19 infections]
☐ Fever over 37.5°C (99.5°F)
☐ Respiratory symptoms, cold symptoms
☐ Loss of sense of taste and/or smell
☐ Close contact with a COVID-19 patient
☐ Fever and respiratory symptoms of individuals in the same household
☐ Overseas travel history in past 2 weeks
☐ Contact with returnees from oversea countries
☐ Attendance of mass gathering events in past 2 weeks
☐ Visit to city center/nightlife district

Figure 2



From mid-June in 2020, when the second wave presumably began, new items were added to the screening questionnaire to visiting occasions to nightlife districts, due to an increase in the number of COVID-19 clusters among night-time workers in the relevant districts.

Regarding infection prevention in the ED, we began mandatory protective mask wearing for all patients against droplet transmission. Also, strict requirements were placed on healthcare providers to use standard precautions against droplet and contact transmissions as well as to wear N95 masks and goggles at all times to prevent aerosol transmission (Photo 1). However, in treating many patients, donning and doffing such equipment was a time-consuming task.

In addition to these precautions, we have used transparent plastic boxes as shown in Photo 2 and used video laryngoscopes during intubation, a procedure in which substantial droplet exposure might be anticipated.

Photo 1 All healthcare providers at the ED wore N95 masks and goggles at all times.

Photo 2 A transparent plastic box usage in addition to PPE during intubation.

Photo 3 Entrance to the ED. The negative pressure room is located to the right of the entrance.

Photo 4 Negative pressure room. Patients suspected with COVID-19 have been basically treated in the negative pressure room installed in the ED. If the room is occupied, other two rooms are available for isolation purposes.

5

Health Checkups and Tests Conducted on Returnees on Chartered Flights from Wuhan

Satoshi Kutsuna, Former Chief Physician, Division of Preparedness and Emerging Infections, Disease Control and Prevention Center (DCC), Center Hospital, NCGM
Takeo Kawamata, Special Advisor to the President, NCGM

On January 23, 2020, the Chinese government imposed a lockdown in Wuhan and its nearby cities, trapping many Japanese and their families who were unable to travel back to Japan. The Japanese government evacuated a total of 829 nationals on chartered flights from January 29 (the first flight) to February 17 (the fifth flight).

NCGM responded to the government's urgent request to conduct health checkups and PCR tests on returnees. It was a mission carried out under a critical situation, in which the WHO declared a Public Health Emergency of International Concern (PHEIC) on January 30.

Individuals detected with fever at the Haneda Airport quarantine were directly taken to a hospital, and other returnees were transported to NCGM on five to seven buses. First, temperatures were taken and questionnaires were filled out on the bus. After disembarking, returnees were checked in at the entrance of the conference room (auditorium) and received medical consultation by a physician. Those with symptoms were taken to the Department of Infectious Diseases, and those suspected of infection were hospitalized. Those who were asymptomatic underwent blood tests and PCR nasopharyngeal swab tests. Rice balls, bread, and tea were distributed, and they were taken on the bus to accommodations provided by the government.

Many of the returnees included small children under age six and Chinese speakers, requiring attentive care, such as help from pediatric specialists, provision of nursing rooms and rest areas, and medical interpreters. The number of NCGM staff involved in this mission topped 356 within an approximate span of five days (107 physicians, 115 nurses, 24 clinical technicians, and 110 clerical staff).

Buses carrying returnees on the first chartered flight from Wuhan arrives at NCGM

Of the 793 returnees who received PCR tests at NCGM, eight tested positive (Refer to the table below). Here, a striking new fact was discovered in our country, that positive cases were seen in asymptomatic individuals. This had a huge impact on the public. It was the beginning of our challenge against the novel COVID-19.

Flight	Date of arrival	Nnumber of returnees	Tested cases at NCGM	PCR testing results (Positive/Negative)	
1	Thursday, January 29	206	199	(Positive)	3
				(Negative)	196
2	Thursday, January 30	210	197	(Positive)	2
				(Negative)	195
3	Friday, January 31	150	140	(Positive)	2
				(Negative)	138
4	Friday, February 7	198	194	(Positive)	1
				(Negative)	193
5	Monday, February 17	65	63	(Positive)	0
				(Negative)	63


NCGM staff awaiting the arrival of Wuhan returnees at the site of health checkup and PCR testing


NCGM staff in protective clothing, awaiting the arrival of Wuhan returnees


Returnees receiving health checkups


Returnees undergoing PCR nasopharyngeal swab tests


A staff meeting held on the initial day after caring for returnees on the first chartered flight from Wuhan

6 Cruise Ships: Diamond Princess and Costa Atlantica

Hajime Inoue, Former Director General, Bureau of Strategic Planning, NCGM

A major spread of COVID-19 was seen on board the Diamond Princess cruise ship, which docked in Yokohama on February 3, 2020. We were faced with an unprecedented challenge of isolating, quarantining, and providing medical care to approximately 3,700 passengers and crews, with limited clinical knowledge of this disease.

NCGM dispatched a team of medical providers including physicians and nurses to the Diamond Princess, and accepted many severely-ill patients for treatment. This was done in response to a request made by MHLW taking command of the situation. From early March until late April, an on-land quarantine of the captain and crew members totaling near 240 took place at the dormitory of the National Tax College in Wako City, Saitama Prefecture. This mission was commanded by NCGM specialists who supervised a diverse team of professionals gathered from around the world for support.

The Diamond Princess docked in Yokohama Port

Inside the captain's cabin. Meeting held every evening at 9:00 PM with the captain.
Captain Gennaro Arma (seated second from the left)
Gaku Hashimoto, former State Minister of Health, Labour and Welfare (seated third from the right)
Hanako Jimi, former Parliamentary Vice-Minister of Health, Labour and Welfare (seated second from the right)

Furthermore, a crew boarded on the Costa Atlantica cruise ship docked in Nagasaki Port was confirmed with COVID-19 on April 20. Making use of the Diamond Princess experience, NCGM dispatched staff to Nagasaki in an effort to contain the virus.

An NCGM staff boarding the Costa Atlantica docked in Nagasaki Port, in response to a request for quarantine (Hajime Inoue)

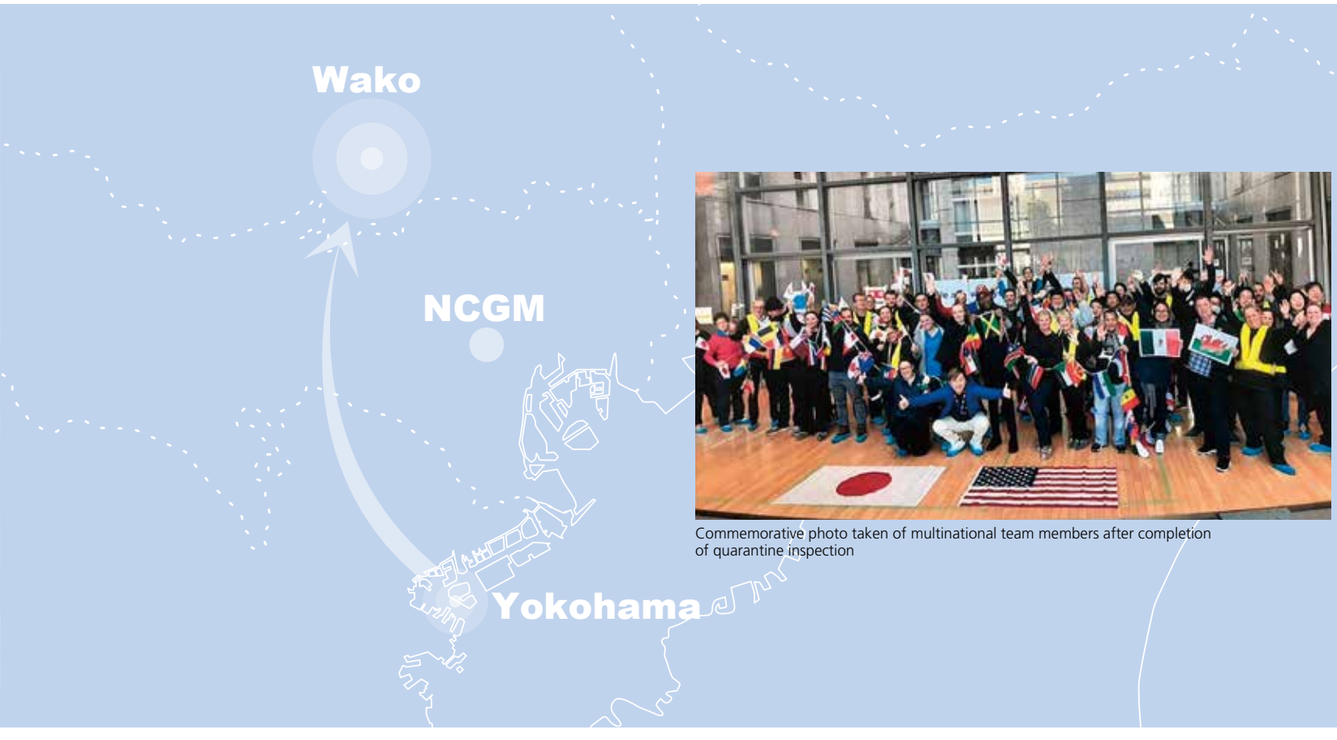
On-Land Quarantine of Diamond Princess Crew Members Conducted by a Multinational Team

On-land quarantine check-in

Taken in front of a message board filled with words of gratitude from the captain and crew members who underwent quarantine

Quarantine team members of the Diamond Princess crew

Meeting held every day by quarantine team members



Commemorative photo taken of multinational team members after completion of quarantine inspection

7 Accomplishment and Future Outlook of Develop ment Research of COVID-19 Therapeutics Led by NCGM

Hiroaki Mitsuya, Director-General, Research Institute, NCGM
Wataru Sugiura, Director, Center for Clinical Sciences, NCGM

On February 15, 2020, H. Clifford Lane MD, who leads Clinical Research and Special Projects of the U.S. National Institutes of Health (NIH), and Robert Walker MD of the U.S. Department of Health and Human Services visited Japan and conveyed the proposal to NCGM of involvement in the NIH initiated Adaptive COVID-19 Treatment Trial 1 (ACTT-1) of Remdesivir (RDV). NCGM deemed the trial top priority and agreed to conduct a domestic investigator-initiated trial in Japan (Representative institution: PMDA) on February 17. Starting with this, NCGM has been leading and participating in numerous clinical studies inside and outside of Japan (Figure 1).

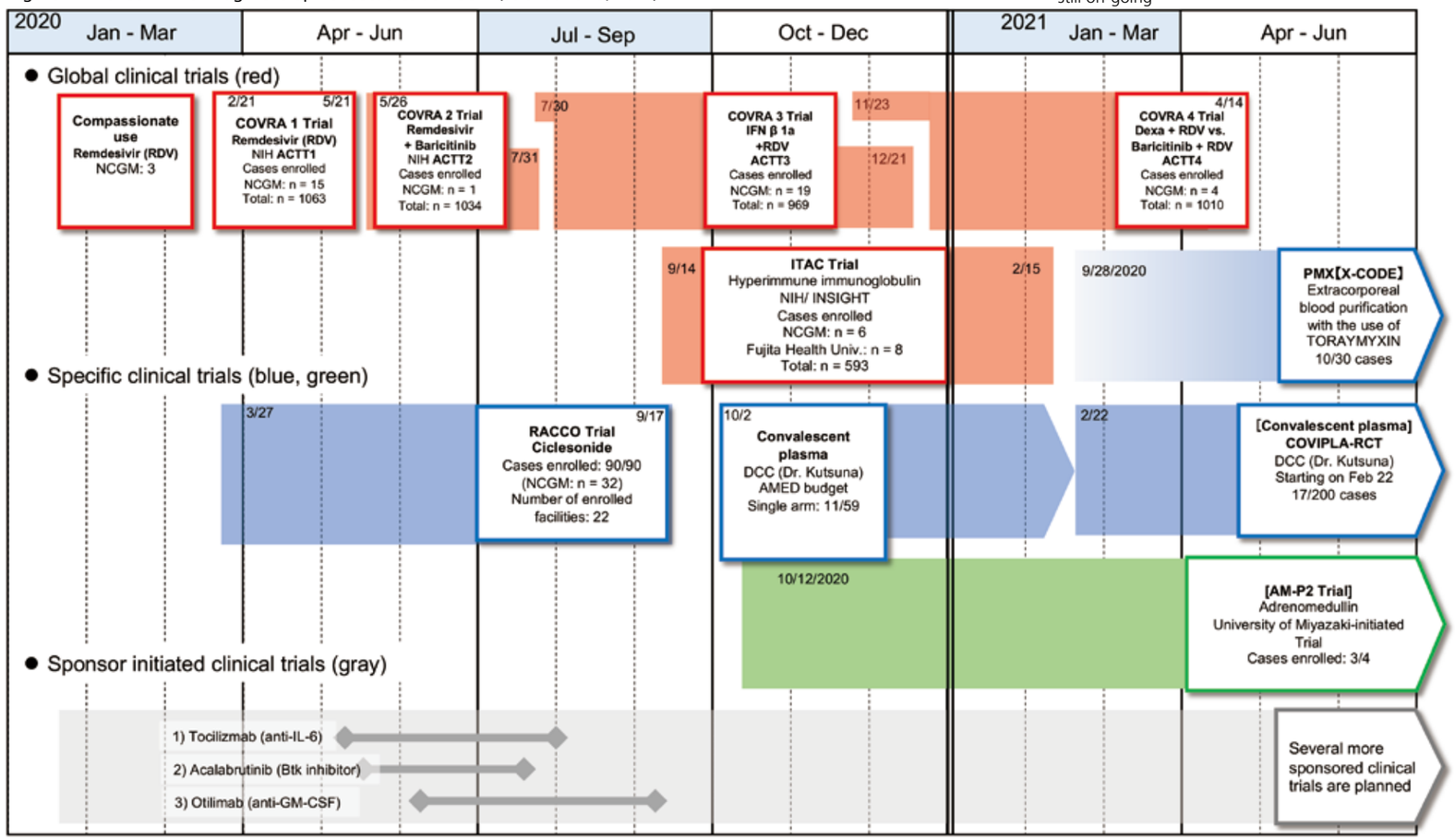
Specified clinical trials led by NCGM currently in progress

1. **Convalescent plasma therapy RCT**
   (Investigator: Satoshi Kutsuna)
   February 22, 2021 – in progress
   A specified clinical trial to evaluate the efficacy of convalescent plasma transfusion therapy on COVID-19 patients. It is in progress, supported by Health and Labour Sciences Research Grants and a grant from the Japan Agency for Medical Research and Development (AMED). As a single-arm study conducted on 11 cases confirmed its safety, a two-armed, open-label, randomized, controlled trial (target sample size: 100 for each arm) is in progress from February 22. It is for COVID-19 patients with mild to moderate stratum because it aims for potent antiviral activity of neutralizing antibodies contained in convalescent plasma collected from patients recovered from COVID-19.

2. **PMX specified clinical trial [X-code trial]**
   (Investigator: Shinyu Izumi)
   September 28, 2020 – in progress
   A trial to evaluate the efficacy and safety of a blood purification therapy (PMX-DHP) for moderate to severe COVID-19 patients. Removal of endotoxin in blood by TORAYMYXIN™ (PMX™), polymyxin B-immobilized polystyrene column-direct hemoperfusion (PMX-DHP) is expected to prevent disease exacerbation.

Figure 1: Anti-COVID-19 Drug Development Studies at NCGM (as of June 23, 2021)

Many clinical studies were executed. Some are still on-going



Specified clinical trials that NCGM is currently participating in

1. **AMP-2 trial (Led by University of Miyazaki: NCGM Investigator: Norio Ohmagari)**
   October 12, 2020 – in progress
   Adrenomedullin is a circulatory adjusting peptide which exhibits anti-inflammatory effect. It is expected to prevent further exacerbation of severe COVID-19 patients on ventilator.

2. **Ephedra Herb extract (Led by Kitasato University: NCGM Investigator: Norio Ohmagari)**
   April 30, 2021 – in progress
   An exploratory Phase I / II trial of Ephedrine alkaloids-free Ephedra Herb extract (EFE).

Specified clinical trials and investigator-initiated trials which have completed or have completed enrollment

1. **Ciclesonide specified clinical trial [RACCO trial]**
   (Investigator: Haruhito Sugiyama)
   March 27, 2020 – September 17, 2020
   Ciclesonide, an inhaled corticosteroid was reported to be efficacious for the treatment of COVID-19 by doctors and researchers in Japan.

   NCGM started an exploratory phase 2 trial on March 27, 2020. Twenty-two facilities in Japan participated in the trial, and the number of enrollments reached 90, its targeted sample size, on September 17, 2020. Analysis of the pneumonia exacerbation rate, which was the primary endpoint of the study, indicated that exacerbation was significantly higher (p=0.057) in the ciclesonide treatment group, 39% (16/41), than in the control group, 18% (9/48). On the basis of this result, NCGM released a statement not recommending its use on December 23, 2020.

2. **Compassionate use of Remdesivir (RDV): (Investigator: Norio Ohmagari)**
   In February 2020, the U.S. Embassy in Japan conveyed a proposal to the Chief Medical and Global Health Officer at MHLW of compassionate use of RDV in patients who got infected on board the Diamond Princess. On February 23, critically ill patients admitted to NCGM received RDV for the first time in Japan. Three patients received RDV at NCGM and all of them recovered and were discharged from the Hospital [1].

3. Adaptive COVID-19 Treatment Trial-1 (ACTT-1)
[NCT04280705: Domestic COVRA-1 trial in Japan]
(Investigator: Norio Ohmagari)
February 21, 2020 – May 21, 2020
ACTT-1 was a double-blind, two-arm trial to evaluate the efficacy and safety of RDV on moderate to severe hospitalized adult patients. Enrollment for ACTT-1 began on February 21, 2020, and ended on April 20, 2020 (n=1063). Fifteen cases were enrolled from NCGM in total.

On April 27, an interim report which showed the efficacy of RDV was made public. On receiving the results, the Second Committee on New Drugs of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) evaluated RDV and granted special approval on May 7. The result of ACTT-1 was published in the May 22 issue of the NEJM [(2)].

4. Adaptive COVID-19 Treatment Trial-2 (ACTT-2)
[NCT04401579: Domestic COVRA-2 trial in Japan]
(Investigator: Norio Ohmagari)
May 26, 2020 – July 31, 2020
Following ACTT-1, ACTT-2 was conducted to evaluate the combination of baricitinib, an inhibitor of janus kinase (JAK), and RDV compared to RDV alone. ACTT-2 was a double-blind, two-arm trial to evaluate the combination of RDV and baricitinib compared to the combination of RDV and placebo in moderate to severe hospitalized adult patients. The first case from NCGM was enrolled on June 23, 2020, and enrollment of 1,034 cases was completed in the entire trial by July 1, 2020. Recovery time for the group receiving the combination of RDV and baricitinib was significantly shorter (p=0.03) by about a day, compared to that of the control group receiving RDV and placebo, and efficacy of the combination use has been confirmed. These results led to the approval of baricitinib by the pharmaceutical affairs on April 23, 2021 as the third therapeutic agent for COVID-19, following remdesivir and dexamethasone [(3)].

5. Adaptive COVID-19 Treatment Trial-3 (ACTT-3)
[NCT04492475: Domestic COVRA-3 trial in Japan]
(Investigator: Norio Ohmagari)
July 30, 2020 – December 21, 2020
Following ACTT-1 and ACTT-2, the NIH/NIAID team started ACTT-3 to evaluate the efficacy of the combination of RDV and interferon beta-1a on July 30, 2020. ACTT-3 was a double-blind two-arm trial to evaluate the combination of subcutaneous injection of RDV and interferon beta-1a compared to the combination of subcutaneous injection of RDV and placebo. There were 969 enrollments worldwide and 19 enrollments from NCGM. The analysis results of the trial have not been published yet. (As of June 23, 2021)

6. Adaptive COVID-19 Treatment Trial-4 (ACTT-4)
[NCT04640168: Domestic COVRA-4 trial in Japan]
(Investigator: Norio Ohmagari)
November 23, 2020 – April 14, 2021
ACTT-4 is a double-blind two-arm trial with the combination of subcutaneous injection of RDV and dexamethasone and the combination of subcutaneous injection of RDV and baricitinib to evaluate the efficacy.

It started on November 23, 2020 and the enrollment was completed on April 14, 2021. A total of 1,010 cases were enrolled worldwide and four cases were enrolled from NCGM. The analysis results of the trial have not been published yet. (As of June 23, 2021)

7. Inpatient Treatment with Anti-Coronavirus Immunoglobulin（ITAC）clinical trial (NCT04546581: Investigator: Norio Ohmagari)
September 14, 2020 – February 15, 2021
ITAC trial is a randomized, double-blind, placebo-controlled two-arm trial with hyper immune intravenous immunoglobulin, hIVIG and placebo groups led by NIH and INSIGHT. Total enrollments of 593 worldwide. From Japan, Fujita Health University and NCGM participate in the trial, and enrolled eight cases and six cases respectively. The official results of the ITAC trial have not been published yet. (As of June 23, 2021)

Sponsor initiated clinical trials

For development of treatments, NCGM is proactively involved in sponsor initiated clinical trials. To date, NCGM has participated in trials studying tocilizumab (an anti-IL-6 receptor antibody), acalabrutinib (a selective Bruton's tyrosine kinase inhibitor) and otilimab (an anti-GM-CSF antibody) and completed enrollment of contracted number of cases for each of them. Multiple trials are in progress at present. (As of June 23, 2021)

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Basic Research

Development of therapeutic agent for COVID-19
Approximately 20% of COVID-19 patients develop moderate to severe respiratory symptoms requiring ventilator or ECMO support and the mortality is high in older patients and those with complications such as diabetes, chronic kidney/pulmonary diseases, and obesity. On the other hand, 70 to 80% of SARS-CoV-2-infected individuals either remain asymptomatic or develop only mild symptoms. The fact that many infected people do not have symptoms and recuperate without treatment makes is complicated to conduct clinical trials of potential anti-COVID-19 therapeutics. Those with no or only minor symptoms when they receive "hopeful anti-COVID-19 drug(s)" are, if not tested with formal randomized blinded clinical trials with sufficient numbers of enrollees, erroneously judged to have benefited from such hopeful drug(s), leading to a false conclusion that "that therapeutic candidate" was efficacious. On top of that, many observational clinical studies of "therapeutic candidate drugs" was started without sufficient basic in-vitro data or animal testing [4, 5]. It is argued that groundless expectations such as "repurposed drugs (identifying new therapeutic activity in existing unrelated drugs)" may have worsened such inclination. Indeed, the development of antiviral drugs against SARS-CoV-2 $_{2019}$ has been much delayed in such chaotic circumstances. In fact, only a few compounds examined to have antiviral activity against SARS-CoV-2 $_{2019}$ are currently under clinical trials, such as PF-07304814, molnupiravir, and T-527.

Development of SARS-CoV-2 M^{pro} inhibitor guided by the structure of M^{pro}
The main proteases (M^{pro}) of coronaviruses take a dimeric structure and function as a proteolytic enzyme, which processes polyproteins of the virus (Figure 2). Based on the notion that M^{pro} of SARS-CoV-2$_{2019}$ and that of SARS-CoV$_{2002}$, which also originated in China in 2002 and produced casualties in multiple countries, maintain very high amino acid sequence identity of about 96% [4], we postulated that SARS-CoV$_{2002}$ protease inhibitors that were generated in 2003 and later may have potential activity against SARS-CoV-2$_{2019}$. We, therefore, synthesized the existing SARS-CoV$_{2002}$ protease inhibitors and their derivatives, and identified GRL-0920 [4], GRL-1720[5], and GRL-2420(5h) [5]. These three small molecule compounds specifically block M^{pro}'s enzymatic activity by forming covalent and hydrogen bonding with the enzyme active site of M^{pro} of SARS-CoV-2$_{2019}$ (Figure 2) and potently inhibit the infectivity and replication of SARS-CoV-2$_{2019}$ at concentrations that do not exert cytotoxicity in cell-based assays [4, 5]. Even though these three M^{pro} inhibitors are not applied to clinical use as therapeutic agents for COVID-19, they offer suggestions as prototypes for future therapeutic agents for treating COVID-19.
(Hiroaki Mitsuya)

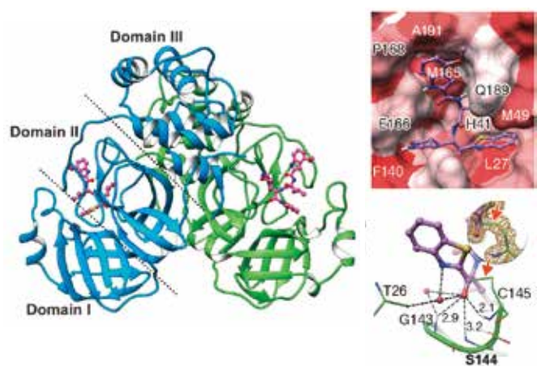

Figure 2 Legends
While GRL-2420(5h) (compound on the upper right inset) forms a covalent bond with Cys-145 (shown in a red arrow on the lower right inset) of M^{pro}, it also forms hydrogen bonds (shown in black dashed lines on the lower right inset) with amino acids forming the enzyme active site and specifically blocks enzymatic activity of M^{pro}. Thereby, it inhibits the infectivity and replication of SARS-CoV-2. The left inset shows M^{pro} in the dimeric form to which two GRL-2420(5h) molecules (in magenta) bind. (Cited from reference 5)

8 Responses to COVID-19 Outbreak in Hospitals/Facilities

Yoshiaki Gu, Former Chief, Information and Education Division, AMR Clinical Reference Center, Center Hospital, NCGM
Yumiko Fujitomo, Chief, Information and Education Division, AMR Clinical Reference Center, Center Hospital, NCGM

The Disease Control and Prevention Center (DCC) and the AMR Clinical Reference Center form part of MHLW's National COVID-19 Cluster Taskforce and the Infection Control Team of Tokyo Center for Infectious Disease Control and Prevention (iCDC). As such, we help hospitals and elderly facilities in Tokyo and many other prefectures deal with the COVID-19 outbreak. We as infection control specialists assist in the specialized tasks involved in epidemiological studies and nosocomial infection control in the respective hospitals/facilities in response to requests from municipalities. As of March 2021, we have helped 20 hospitals/facilities deal with outbreaks.

We have made various efforts by collaborating with relevant organizations. Specifically, we conducted epidemiological investigations to take countermeasures by assessing the spread of infection and the cause of outbreaks, and gave advice after infection control rounding to assess the current status of prevention measures at each division of hospitals.

These efforts were aimed to promote successful COVID-19 responses, with the ultimate goal of ending outbreaks as soon as possible. Furthermore, in several hospitals, we provided support in resuming healthcare services that closed down due to the outbreak and helped establish a foundation for voluntary/continuous quality improvement of infection prevention and control.

Insights gained from our mission were reported to MHLW and the Tokyo Metropolitan Government, which are being utilized in establishing a new system and preparing for outbreaks expected in healthcare facilities.

Rounding was conducted in wards.

Infection control rounding being conducted to assess current prevention measures

Problems were addressed on the spot and changes were implemented.

Infection control education is vital for healthcare providers to work safely. Implementing basic measures in a constant and continuous manner is the key.

9 From COVID-19 Registry JAPAN (COVIREGI-JP) to REBIND

Nobuaki Matstunaga, Chief, Division of Clinical Surveillance, AMR Clinical Reference Center, Center Hospital, NCGM
Wataru Sugiura, Director, Center for Clinical Sciences, NCGM

Introduction

Starting with the identification of pneumonia clusters due to novel coronavirus in Wuhan, China in December 2019, novel coronavirus cases are still on spread worldwide. COVID-19 keeps changing in clinical manifestations, clinical course, severity rate, case fatality rate, etc. over time under the influence of the spread of variants.

To comprehend these information in real time as much as possible and to directly return the achievements to public health and clinical settings, we have implemented a registry of COVID-19 hospitalization cases, "COVIREGI-JP" (https://covid-registry.ncgm.go.jp/). (Figure 1)

Figure 1

Official COVIREGI-JP website

Summary of registry study

This is an observational study which is being conducted under approval of the ethical committee of NCGM with financial support from MHLW grant-in-aid for Scientific Research (Titled: COVID-19 Development of treatments for critically ill patients, Principal investigator: Norio Ohmagari, NCGM).

We have created a CRF (case report form) to collect epidemiological information in clinical settings and treatment-related information within Japan by referring data originally collected by the ISARIC (International Severe Acute Respiratory and emerging Infection Consortium) with some alterations (https://isaric.tghn.org/covid-19-clinical-research-resources/). Its design is centered on basic patient information, demographic data, epidemiological data, clinical data regarding hospitalization or treatment, and infectiological data.

In parallel with issuing revisions of the report depending on the situation, an on-line registration system along with preparing case reports has been set up. They have been available on our website since April 2020. As of May of the same year, the number of registry enrollments surpassed 1,000 and recorded 10,000 in October of the same year. As of May 2021, data of over 40,000 cases have been collected.

Achievement of registry study

Aside from obtaining academic results, we promptly analyze collected data and provide outcomes to the administrations and municipalities. We also return the outcomes to participating institutions with a view to advance the study in a multi-faceted manner. Our current achievements are as follows.

Academic publications

We conducted an epidemiological investigation on 2,638 cases that had been registered by 227 medical institutions as of July 2020. Median age of inpatients was 56 (interquartile range [IQR] : ages 40-71). More than half of the cases were male (58.9%, 1542/2619) and nearly 60% of inpatients had history of close contact with suspected or confirmed COVID-19 cases. Median length of symptoms in inpatients until their hospital admission was seven days (IQR: 4-10 days). The most frequently reported comorbidities were hypertension (15%, 396/2638) and diabetes mellites without complications (14.2%, 374/2638). Non-severe cases (68.2%, n=1798) were twice as many as severe cases on admission (31.8%, n=840). As regards to respiratory support, patients without respiratory support (61.6%, 1623/2636) were followed by patients on supplemental oxygen (29.9%, 788/2636) and patients on IMV/ECMO (invasive mechanical ventilation or extracorporeal membrane oxygenation), (8.5%, 225/2636). On the whole, 66.9% of the patients (1762/2634) were discharged home, whereas, 7.5% (197/2634) of the patients died. In comparison with studies on inpatients conducted in other countries, less patients have comorbidities and mortality rate tends to be low [(1)] .

We conducted a comparative analysis on the first and second waves in Japan. The result showed that the percentage of severe cases on admission during the second wave was lower than in the first wave (12.0% and 33.1% respectively). Also, the period from onset of COVID-19 to admission was shorter than during the first wave (median of each were four days and seven days). Patients during the second wave were younger than in the first wave (median age of each was 37 and 56), and was less frequently transferred from other hospitals (3.8% and 15.0% respectively), tending to have fewer comorbidities such as cardiovascular (1.9% and 5.9% respectively) and cerebrovascular diseases (1.8% and 6.1% respectively). It also showed that mortality rate during the second wave was lower than in the first wave (1.2% and 7.3% respectively). Data from the second wave indicated that patients were demographically younger, had fewer comorbidities, had a lower percentage of severe cases on admission and had lower rate of mortality. Even though the data on age and severity were stratified, mortality rate was still lower during the second wave. It is considered that this was due to shorter period of time from onset until admission, differences in backgrounds and comorbidities, advances in treatment, etc.[(2)]

Furthermore, we reported the case fatality rate of each age group based on the COVID-19 registry data to IASR[(3)]. We included 12,599 patients who had been admitted to hospitals by September 30, 2020 in the report and 37.6% of them were 60 years of age or older. The case fatality rate was 4.2% for the entire case (the rate was 0.3% for patients under age 60, and 10.7% for patients over 60), that is, fatal cases among patients under 60 years of age were rarely seen. We also investigated whether the patients

We are striving to provide information and promote relevant studies via a dedicated website (https://rebind.ncgm.go.jp/).

had underlying health conditions or not. The case fatality rate of patients who had no underlying health conditions was only 0.1% for patients under 60 years of age, which was extremely low. Whereas, the case fatality rate increased with age (the rate was 3.7% for patients aged 70-74, and 12.8 % for patients over 80. The case fatality rate of patients with underlying health conditions was 1.0% even in patients under age 60. Case fatality rates were shown to be 4.4% for patients aged 60-64, 7.2% for patients aged 65-69, 7.5% for patients aged 70-74, 12.8% for patients aged 75-79, and 20.5% for patients over 80, indicating that the percentages for patients with underlying health conditions was higher than those without health conditions and it increased with age. We strived to gain public understanding for the situation where case fatality rate is high among COVID-19 patients with underlying health conditions and even among the elderly with no such conditions. Besides, our advices regarding information dissemination to individuals at high risk of fatality from COVID-19 is being reflected in the national policy (Figure 2).

Providing information to the administration and municipalities

In parallel with preparing academic papers, we provide information to the administration and municipalities in a timely manner to reflect our study in the national policy. Here, we will introduce a part of our achievements.

In the COIVD-19 Advisory Board of MHLW held on August 24, 2020, we reported a study comparing the first and second waves as previously mentioned. This report was used as a valuable resource in obtaining an objective view of the clinical course of COVID-19 and the features of each wave. In the 41st Health Science Council of MHLW held on November 9, 2020, we provided supplemental data to the committee of basic immunization and vaccination policy discussing “COVID-19 Vaccine Prioritization”. We reported that those aged 60 or older tended to have higher risk of mortality than those under 60. Furthermore, those with pre-existing conditions had higher risk of mortality than those without conditions in each age group. These data have helped the committee develop a criterion on how to prioritize COVID-19 vaccine distribution.

So far we have disclosed three conference materials and provided essential information as needed to the Tokyo Novel Coronavirus Response Headquarters. We have also reported various features of COVID-19 and made a comparison between the first, second, and third waves. These features include epidemiological characteristics of COVID-19 patients, clinical rates of medication use and respiratory support care, severity of patients, and correlation between the infected and the so-called “three Cs” (closed spaces, crowded places, close-contact settings).
We hope to obtain further findings from epidemiological studies by sharing data with participating facilities and further analyzing factors associated with exacerbation and death from various aspects. We also plan to do cross-sectional and longitudinal studies concerning efficacy of medication and association with lifestyle, as well as evaluation of long-term prognosis. It is our vital role to analyze data periodically and contribute to both the academic field and government policy-making.

Figure 2 Case fatality rate by age group setting 60 year-old as threshold.

Age group	Under 60		60-64		65-69		70-74		75-79		80 and over	
Term	- May 31	June 1 -	- May 31	June 1 -	- May 31	June 1 -	- May 31	June 1 -	- May 31	June 1 -	- May 31	June 1 -
Without pre-existing condition												
Number of patients	1988	3891	156	148	138	166	108	107	83	88	66	75
Number of death	3	0	5	0	4	1	6	2	8	1	14	4
(case fatality rate %)	(0.2%)	(0%)	(3.2%)	(0%)	(2.9%)	(0.6%)	(5.6%)	(1.9%)	(9.6%)	(1.1%)	(21.2%)	(5.3%)
With pre-existing condition												
Number of patients	756	1232	211	261	249	305	287	367	243	310	602	762
Number of death	14	6	13	8	30	10	41	8	38	33	170	110
(case fatality rate %)	(1.9%)	(0.5%)	(6.2%)	(3.1%)	(12%)	(3.3%)	(14.3%)	(2.2%)	(15.7%)	(10.6%)	(28.2%)	(14.4%)

From COVIREGI to REBIND

REBIND
新興・再興感染症データバンク事業ナショナル・リポジトリ
Repository of data and biospecimen of infectious disease

The developments in inspection method, therapeutic agent and prophylactic vaccine are indispensable to fight against emerging/re-emerging infectious diseases such as SARS-CoV-2, the biggest threat at present. This development requires biospecimens such as blood and saliva samples, and viral/human genomic data along with medical records of infected patients aggregated through COVIREGI. Nevertheless, researchers are often confronted by difficulties in the access to such information and in obtaining biospecimens, where the lack of cooperation can be seen between research & development and medical practice, namely researchers and practitioners who provide medical care to patients.

Thus, the implementation of organization, biobank or repository in particular, is waited to eliminate the obstacles of this kind, and to promote the development. Such organization will liaise researchers with healthcare providers, consequently, researchers can easily access to sufficient biospecimens as well as genomic data and medical records. In fact, biobanks have already been established and even functioning in many countries including Europe and North America. Some of them succeeded by applying the resource in the control of the spread of COVID-19 infection in the relatively early stage.

Entrusted by the government, NCGM launched the project named REpository of data and Biospecimen of INfectious Diseases (REBIND) in 2021. The nationwide project is driven by four key organizations: National Institute of Infectious Diseases (NIID); The University of Tokyo (the affiliate hospital and the Institute of Medical Science); Tohoku Medical Megabank Organization; NCGM. Based on the experiences and expertise accumulated through COVIREGI, we have started the operation of REBIND in July 2021 along with researchers throughout the country.

Last but not least, we would like to express our sincere gratitude for the cooperation provided by patients and the healthcare providers, who have been taking care of COVID-19 patients and who supported our registry. Your further cooperation and guidance for REBIND would be greatly appreciated.

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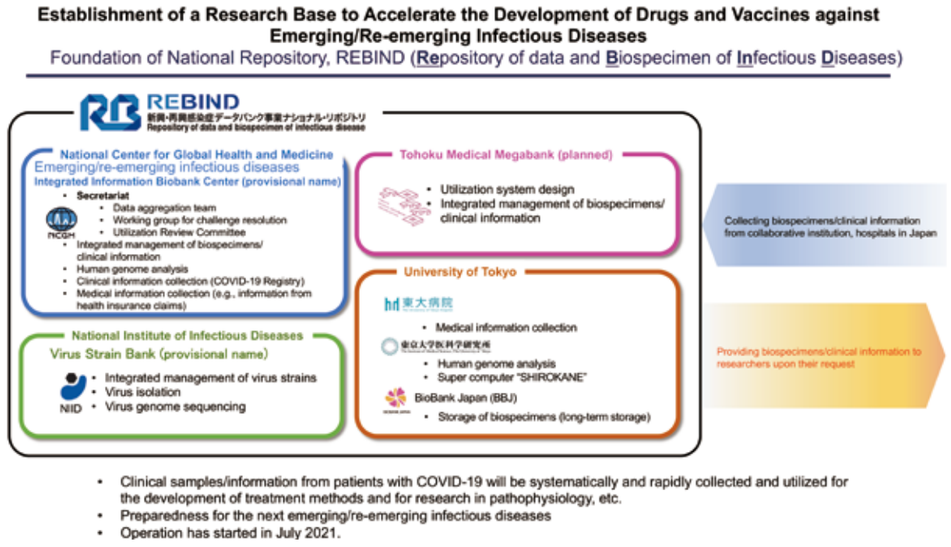


10 International Cooperation and Joint International Research

Hidechika Akashi, Director, Department of Health Planning and Management, Bureau of International Health Cooperation, NCGM
Tatsuo Iiyama, Director, Department of International Trial (DIT), Center for Clinical Sciences, NCGM
Masato Ichikawa, Manager, Public Relations Section, Department of International Trial (DIT), Center for Clinical Sciences, NCGM

COVID-19 and International Cooperation

The Bureau of International Health Cooperation (BIHC) is engaged in the following international cooperation activities.

1.Contribution of experts dispatched from the BIHC through World Health Organization (WHO): Philippines and Laos

The BIHC also sends an expert to WHO Western Pacific Regional Office (WHO-WPRO) in the Philippines. The Japanese expert has joined the WPRO infection control department to engage in COVID-19 response measures in the region and have provided support to the Ministry of Health in the Philippines (Photo 1 and 2). In response to a request from the said department, the BIHC collaborated with DCC to hold an on-line conference with the WHO and the Ministry of Health in the Laos to share our experiences in accommodation facilities for COVID-19 mild or asymptomatic cases in Japan.

2. Re-dispatch of experts from the BIHC to foreign countries through Japan International Cooperation Agency (JICA)

The BIHC sends experts to provide technical assistance for JICA projects. Although the COVID-19 pandemic forced many experts to evacuate to Japan temporarily, the BIHC had re-dispatched these experts by the Fall of 2020. They worked to provide the BIHC with the information on the status of the respective countries and to share the information related to Japan with local people as needed. In Myanmar, public safety has been deteriorating since the coup. Under such circumstances, experts dispatched to the country had to temporarily return to Japan again (Figure 1).

(Hidechika Akashi)

Photo 1

A BIHC doctor engaging in surveillance and assistance provision at a local medical institution

Figure 1

Photo 2

The BIHC doctor at a press conference for the Vice Minister of Health in the Philippines

Joint International Research Projects

"Cooperating with other countries in the research and development of medical products to combat COVID-19"

Researchers and industrial companies around the world are currently committed to develop diagnostic tools, treatments, and vaccines to tackle the COVID-19 pandemic. Humanity has never witnessed in history such an unprecedented number of research and development projects for a single infectious disease being carried out simultaneously throughout the world. In the course of its involvement in international cooperation, NCGM has participated in numerous research and development projects with various countries, and has mounted a global response to this current pandemic by carrying out research and development activities.

The Department of International Trials of the NCGM Center for Clinical Sciences, which conducts overseas trials and clinical research, participates in international actions, such as the WHO R&D Blueprint, to acquire information about the global situation. They also respond to requests from other countries for pharmaceutical and technological assistance, providing assistance in the areas of clinical research and regulatory affairs. They are providing academic and technical assistance in order to conduct local clinical trials, gain local regulatory approval, and make clinical devices developed in Japan usable in the respective countries, as well as conduct clinical trials in each country (Photo 2 Clinical trial in Thailand).

Although the leading nations in the development of vaccines that are anticipated to contribute to end the pandemic are the United States and Europe, a number of other countries, including Japan, are also working on the development of new vaccines in order to respond to increasing global demand and the emergence of variant strains. Through clinical research and evaluations carried out in cooperation with research groups in and outside Japan, we will investigate and develop medical products to fight against the COVID-19 pandemic through international cooperation (Photo 1 WHO R&D Blueprint on-line conference).

As long as globalization and international travel continue to accelerate, there will always be a risk of infection by viruses and other pathogens. Therefore, a global response is required to counter the threat of a pandemic. As a research institution whose mission is to promote international cooperation, we will continue to work in collaboration with institutions both inside and outside of Japan in order to conduct tests, diagnoses, treatments, and vaccine development to overcome the COVID-19 pandemic.

(Tatsuo Iiyama, Masato Ichikawa)

Photo 1

Photo 2

Local staff participating in a Japan-Thailand international joint research project at Mahidol University, Bangkok

11

Releasing of Academic Achievements

Tatsuhiro Iida, Director, Division of Medical Research Management, NCGM
Takehiro Sugiyama, Chief, Division of Health Services Research, Diabetes and Metabolism Information Center, Research Institute, NCGM
Pei Pei Song, Chief, Division of Global Health & Medicine, Center for Clinical Sciences, NCGM

The "NCGM Novel Coronavirus Infection Academic Advisory Board" was established on February 7, 2020 to discuss the effective use of limited resources within NCGM and cross-functional support based on aggregated information on COVID-19 research and development, and has so far held 37 meetings (as of May 2021). The Advisory Board consists of executive members from NCGM including the President and doctors from Center Hospital and Research Institute. In April, Wataru Sugiura, Director of Center for Clinical Sciences, became the Chairperson, replacing Tamami Umeda, the former Director General of the Bureau of International Health Cooperation.

The Advisory Board engages in discussions, consultation and support to achieve the strategic promotion of research and development concerning COVID-19 (Photo). The Board requests researchers who are planning or preparing research and development projects on COVID-19 to register their projects with the Board in advance and to explain their research projects to the Board. The Board also tries to perceive the ever-changing state of COVID-19 research and development by updating the progress of ongoing projects regularly, with 121 projects have been registered so far.

Aside from the Academic Advisory Board, the "NCGM COVID-19 Publication Committee" (Chairperson: Haruhito Sugiyama, Hospital Director of NCGM Center Hospital [for fiscal 2020], Wataru Sugiura, Director of the Center for Clinical Sciences [for fiscal 2021]) was established in March 2020 to support the strategic and prompt paper publications of NCGM researchers. With the attendance of executive members from NCGM including the President and doctors involved, the Committee has held 26 meetings as of the end of April 2021. The Board has been discussing strategies for the timely publication of academic papers related to COVID-19, sharing the progress charts uploaded by the researchers on Teams of Office 365.

As far as the Publication Committee understands, 124 papers, which include the NCGM researchers as the authors, have been published (as of the end of June 2021, including on-line releases). We appreciate the great efforts of the researchers (Figure 1). Abstracts in Japanese and the literature information of published papers whose first or corresponding authors are NCGM researchers are available on the NCGM website (Figure 2).

Figure 1 Number of papers which include NCGM researchers as authors (124 articles)

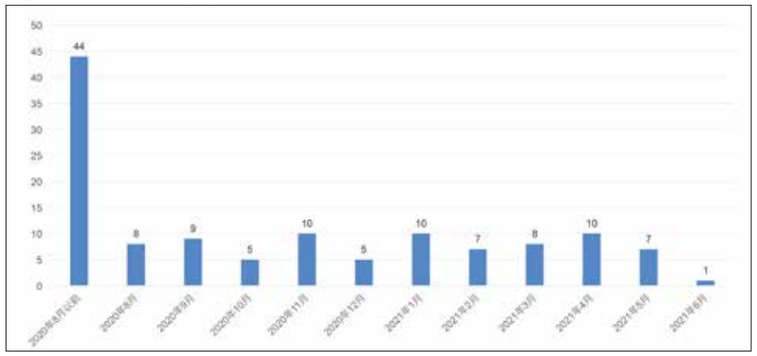
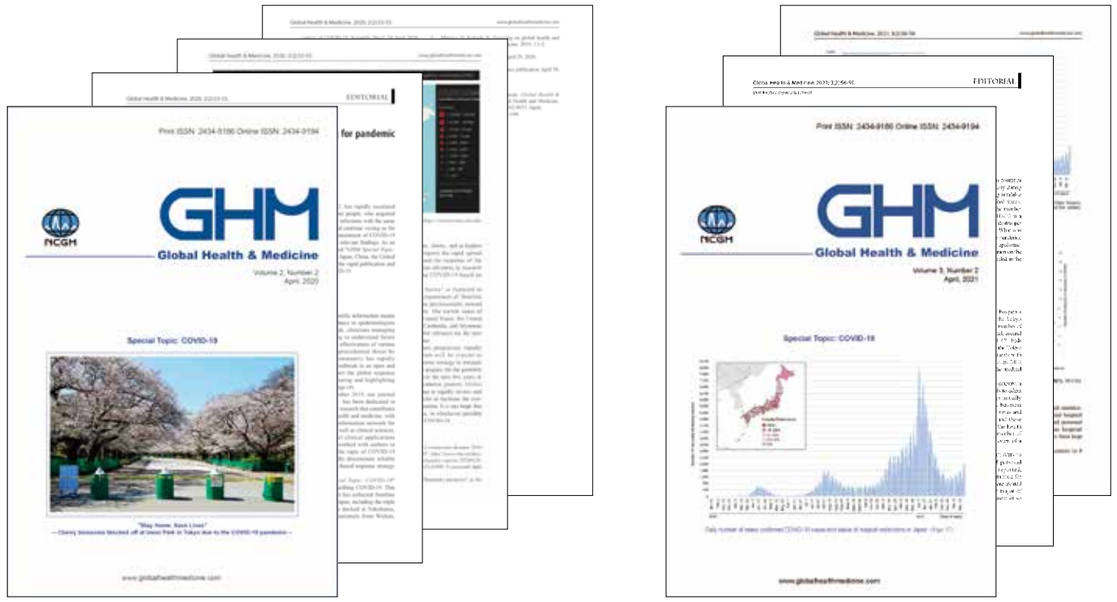


Figure 2

COVID-19-related papers are available on the NCGM website.
https://www.ncgm.go.jp/en/covid19/academic_articles.html

Since the outbreak of COVID-19, many articles containing the latest research findings have been published on *Global Health & Medicine* (https://www.globalhealthmedicine.com) – an international, open-access, peer-reviewed journal, published by NCGM. In particular, the two issues of "GHM Special Topic: COVID-19" (April 2020, Vol.2, No.2; April 2021, Vol.3, No.2) collected a range of articles describing COVID-19 based on frontline data from Japan, China, the United States, Italy, the United Kingdom, and other counties and areas worldwide. As of the end of June, 53 articles including 31 from NCGM have been published. In addition, as the journal was included in PMC (PubMed Central, a free full-text archive of biomedical and life sciences journal literature at the U.S. National Institutes of Health's National Library of Medicine) in December 2020, all published articles can be accessed on PubMed/PMC, with the goal of creating a global information network for the publication of high-quality original research.

NCGM will continue to strive to accumulate its experiences through COVID-19 responses and research results as the common heritage of mankind and pass them down through academic papers, etc.



Global Health & Medicine (GHM), an international academic journal published by NCGM. The two issues of "GHM Special Topic: COVID-19" (April 2020, Vol.2, No.2; April 2021, Vol.3, No.2) collected a range of articles containing the latest research findings.

12 The Fever Clinic and the Community-Based "Shinjuku Model" System

Makoto Tokuhara, Director, Division of Regional Medical Liaison and Public Relations, Center Hospital, NCGM

Photo 1 Katsunobu Kato, then Minister of Health, Labour and Welfare (front row, 3rd from the right) inspects the "Shinjuku Model" (April 23, 2020)

Photo 2 "Shinjuku City COVID-19 PCR Testing Center" launched in the NCGM Center Hospital grounds by commission from Shinjuku City

The spread of COVID-19 infections gave rise to serious problems concerning the need for widespread PCR testing and securing a sufficient number of hospital beds. NCGM started an outpatient fever clinic on March 9, 2020, establishing a system of PCR testing for patients with referrals from other medical institutions or who were residents of Shinjuku City. However, by April the number of patients visiting the outpatient fever clinic grew to more than 100 per day, overwhelming its capacity, since doctors were required to conduct medical consultations, perform various medical tests, and prescribe medications in addition to PCR testing. Furthermore, the increased workload strained the staff of the Hospital's Department of Infectious Diseases which managed the outpatient fever clinic, leading to concerns that the care of severely ill patients would suffer (Graph 1).

During a meeting between the President, the Hospital Director and other top-level NCGM officials, the creation of a COVID-19 response network was proposed, connecting the Shinjuku municipality office, Shinjuku Medical Association, and core hospitals in Shinjuku City. We were able to garner support from the Shinjuku City Medical Association President Seiichi Hirasawa and the directors of seven core hospitals in Shinjuku City (Yuko Kitagawa of Keio University Hospital, Tamotsu Miki of Tokyo Medical University Hospital, Kazunari Tanabe of Tokyo Women's Medical University Hospital, Nobuo Sekine of JCHO Tokyo Shinjuku Medical Center, Tetsu Yano of JCHO Tokyo Yamate Medical Center, Toshihiko Tujii of Ohkubo Hospital, and Tatsu Nakazawa of Seibo Hospital).
On April 11, we met with Shinjuku Mayor Kenichi Yoshizumi to present our proposal of the "Shinjuku Model" COVID-19 Medical Care System (Chart 1).

The "Shinjuku Model" is based on two major strategies of setting up a PCR Testing Center and of assisting in the management of hospital beds for COVID-19 patients. The purpose of the system is to enable smooth and efficient PCR testing by establishing a PCR Testing Center to which patients could be referred by local clinics and medical offices if so required. Another function of the system was to assist in securing a sufficient number of hospital beds required by the City's Public Health Office, by coordinating efforts between the seven core hospitals in the municipality.
Mayor Yoshizumi made the bold decision to go forward with our "Shinjuku Model" proposal, and the plan was announced at a press conference on April 15 held by the Shinjuku City Mayor, the President of the Shinjuku City Medical Association, and the President of NCGM.

Shinjuku City commissioned NCGM to establish the "Shinjuku City COVID-19 PCR Testing Center" within the Hospital (Photo 1, 2). This was an unprecedented undertaking for NCGM, and were faced with many obstacles, but with the cooperation of the various departments, the Testing Center was able to commence operations on April 27. The launch of the Testing Center was only made possible by the knowledge and experience we gained through our involvement in the medical crises of the charter plane returnees from Wuhan, the passengers of the Diamond Princess cruise ship, and our outpatient fever clinic. The Testing Center is staffed solely by those working within Shinjuku municipality, with doctors, nurses, clinical laboratory technicians, and clerical workers from Shinjuku's seven core hospitals as well as doctors of the Shinjuku City Medical Association. The Testing Center was set up to enable the testing of 200 people on weekdays between 9:00 and 11:00 AM, but in actuality we conducted testing for almost 300 patients on some days (Graph 2). The operation of the "Shinjuku City COVID-19 PCR Testing Center" was started by Shinjuku City in August 2020 and was relocated onto the compound of Shinjuku Public Health Office. Core hospitals are cooperating in its operation, and NCGM is also continuing to perform testing.

It has been about one year since the initiation of the "Shinjuku Model" system. During the third wave of the pandemic, the daily number of COVID-19-positive cases exceeded 2,000 in Tokyo, causing difficulty in the control of hospital beds. Under such circumstances, the "Shinjuku Model" system greatly contributed to the facilitation of functional bed control, enabling hospital admission of new patients soon after the discharge of recovered patients, and admission of patients depending on the severity of their symptoms, through close communication between the personnel in charge in each core hospital and those in the Public Health Office.

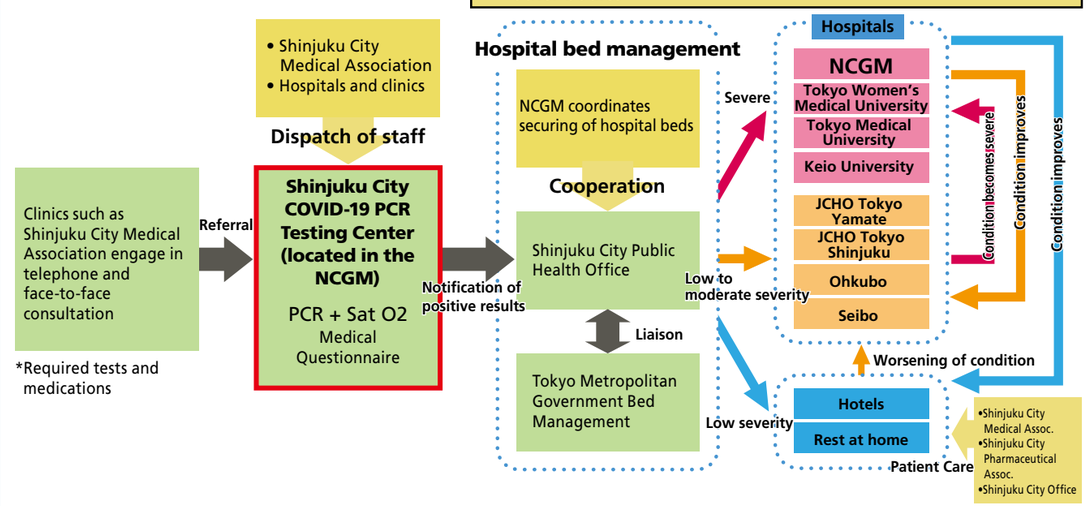
Chart 1

COVID-19 Shinjuku Model Medical Care System

- PCR Testing Center established at NCGM by commission from Shinjuku City
- Clinics such as Shinjuku City Medical Association refer patients to the PCR Testing Center
- Hospitals in the City coordinate efforts to secure hospital beds
- Shinjuku City Medical Association cooperates in the care of patients recuperating at home

A medical system for speedy testing and appropriate care for patients' symptoms in addition to the outpatient clinic for returnees and close contact persons

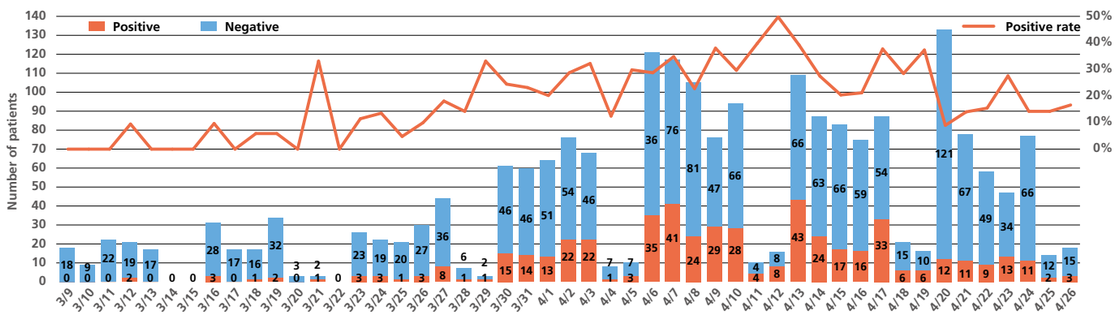
Shinjuku Model Medical Care System flowchart



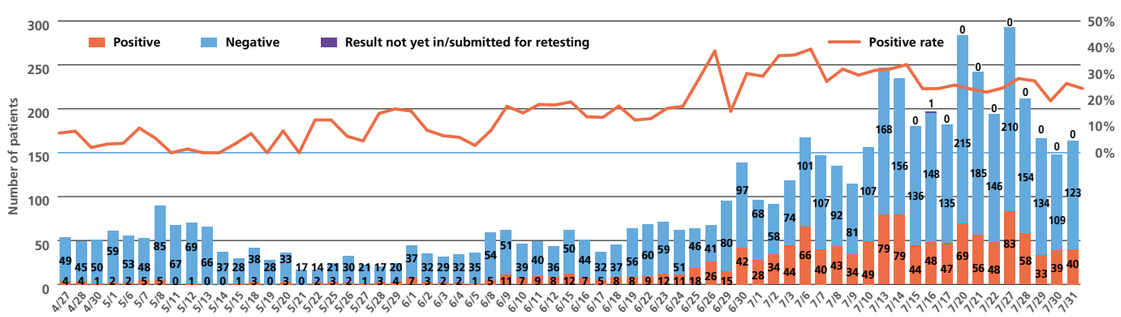
Source: The Shinjuku City press conference on April 15, 2020

Graph 1: Transition of outpatient fever clinic consultations

*Numbers between March 9 and April 26, 2020 include PCR testing of emergency medical care patients, outpatients and inpatients



Graph 2: Transition patient numbers at Shinjuku City COVID-19 Testing Center (2020)



13

Creation of a New Model for Recovery in Accommodation Facilities for COVID-19 Mild or Asymptomatic Cases

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Support for the setting up and management of accommodation facilities for COVID-19 patients identified during quarantine

Contribution to the enhancement of Japan's sustainable border control by helping on-site coordination with the expertise of the Bureau of International Health Cooperation

The Japanese government issued and enacted "Cabinet Order for Designating Novel Coronavirus Infection as a Type of Infectious Disease Under Article 34 of the Quarantine Act" in February 2020. Based on this cabinet order, the Japanese government has been trying to strengthen border control by conducting interviews, physical examinations, and testing of those who arrive in Japan from specified countries, and by making novel coronavirus carriers isolate, or detaining them for treatment accordingly. Furthermore, based on "Handling of People with Positive Result for COVID-19 PCR Test Conducted during Quarantine" issued as an MHLW ministerial notice in April 2020, new arrivals who are confirmed to be novel coronavirus carriers are required to be treated for a specified time period at accommodation facilities for COVID-19 mild or asymptomatic cases.

Under these circumstances, MHLW requested the BIHC to support the setting up and management of accommodation facilities for PCR test-positive people. In response to this request, the BIHC provided support for setting up and managing COVID-19 patient accommodation facilities using two hotels in the Tokyo metropolitan area.

(Toyomitsu Tamura)

Case 1

Further improvement of the first COVID-19 patient accommodation facility used as a model

To support the setting up and management of the first patient accommodation facility, the BIHC dispatched a total of 302 doctors, nurses, technicians, and administrative staff during the period from April 9 to September 28, 2020. Utilizing their knowledge and experience from years of international health cooperation, they helped to set up the facility, and provided empathetic assistance to the foreign residents by understanding their diverse cultural and religious backgrounds, thereby resolving various problems occurring among them.

In the globally persisting COVID-19 pandemic, border control has continued to be strengthened. Under such circumstances, the BIHC also helped to establish sustainable, safe facility management using private sectors instead of officers of MHLW and the quarantine station. For example, facility residents used to be interviewed by telephone twice a day in Japanese or English. The BIHC staff prepared a healthcare check form using FORMS and introduced FUJITSU applications, which had been used for quarantine support activities for the cruise ship, Costa Atlantica, to reduce the burden of both facility residents and healthcare workers and thereby increase efficiency in facility management. They continued to work on zoning, infection prevention, and instruction provision to private workers to promote safe facility management.

The staff also provided PPE-related training to private non-healthcare workers to facilitate sustainable facility management. Doctors of the BIHC with nurses from the quarantine station created a poster showing PPE donning and doffing procedures. Using this poster, the staff provided specific advice on the safe donning and doffing of PPE.

The staff of the BIHC going to collect samples from facility residents. Although it was not easy to conduct clinical research in a non-hospital environment, they accomplished their mission using their knowledge and experience from working in developing countries.

As members of a research and development agency, the BIHC staff also engaged in research activities within the patient accommodation facility. They performed various different tests simultaneously on facility residents, compared the results, and proposed optimal quarantine tests. Data from their research were published in Global Health & Medicine, an academic journal in English issued by NCGM.

(Masataro Norizuki)

Case 2

Support on the establishment of a new patient accommodation facility for scale expansion

To support the setting up and management of the second patient accommodation facility, the BIHC dispatched a total of 27 doctors, nurses, and administrative staff during the period from September 14 to October 4, 2020. Based on the experience from the above-mentioned support program for the setting up and management of the first patient accommodation facility, they worked on the setting up and management of the second one while providing advice on coordination among the hotel personnel, quarantine officers dispatched from various quarantine stations nationwide, public officers, medical institution personnel, private contractors, security companies, patient transporters, police officers, fire authorities, and people from various other organizations. For example, the staff members engaged in zoning within and outside the facility, management of materials and equipment, and preparation of various manuals. This patient accommodation facility was to be operated by a private company with little knowledge in healthcare. Therefore, it was one of our important missions to teach infection prevention measures to all of the people concerned, including the staff of the private company. In addition to providing training on the donning and doffing of PPE, the BIHC staff prepared a manual of sample handling, and instructed the facility staff about this issue with the help of quarantine officers.

Checking flow lines of the accommodation facility with quarantine officers

Training for correct donning and doffing of PPE was provided.

For the support for management of this accommodation facility, the patient information management system developed for the first accommodation facility has been used to enhance system unification. As shown above, the BIHC has provided support while paying attention to the sustainability of facility management, even after the support had ended. This reflects our basic operation policy for various projects in low- and middle-income countries. The support on the setting up of patient accommodation facilities can be seen as a good example of the on-site coordination capabilities.

(Toyomitsu Tamura)

Case 3

Response to COVID-19 in Okayama Prefecture: Support for the management of a patient accommodation facility and cluster intervention

The BIHC dispatches its staff members not only for overseas projects, but also to Okayama Prefectural Office. In Okayama, besides providing advice regarding the management of accommodation facilities for COVID-19 mild or asymptomatic cases, the staff members helped prefectural officers to create a framework for securing a system for COVID-19-related healthcare provision and taking anti-COVID-19 measures, and to establish the Okayama COVID-19 Cluster Intervention Team (OCIT), and provided lectures and instructions regarding infection prevention in many places throughout the prefecture. A series of COVID-19-related activities made in Okayama were presented in a document issued by MHLW. In addition, due to the contribution to the establishment of relevant systems in Okayama, the staff member received an SDGs Award from Okayama University.

At the award ceremony in Okayama Pref.

(Hidechika Akashi)

14

In Closing: Preparing for the Post- COVID-19 Era

Akira Harita, Director General, Bureau of Strategic Planning, NCGM

Despite the fact that all the countries in the world have been making a great effort to end the COVID-19 pandemic for more than one year, future prospects still remain uncertain. Even if this pandemic comes to an end, there is no end to the ongoing battle between humans and emerging/re-emerging infectious diseases. Just in the past two decades of this century, we have witnessed numerous emerging/re-emerging diseases around the globe; SARS, H5N1 highly infectious avian influenza, the pandemic H1N1 swine flu, MERS, Ebola hemorrhagic fever, Zika fever, and now COVID-19. These diseases have not only threatened our lives, but have also caused social and economic turmoil.

Therefore, we must build back on healthcare and social systems effective enough to fight against the threats of future emerging/re-emerging diseases in the post-COVID-19 era. NCGM is committed to playing a pivotal role in protecting human lives and society from emerging/re-emerging infectious diseases, based on an academic foundation in fields broadly ranging from basic medical science to clinical and social medicine.

Tsuyoshi Nagabuchi on "NCGM Encouragement Live Concert" held on the heliport of Center Hospital of NCGM on October 3, 2020
Photo by courtesy of Office Ren Inc.

Acknowledgements

We are going into the second year since NCGM has engaged in treatment and research of COVID-19. During the course, our nation has declared a state of emergency four times and we have seen repeated surge of infections. Yet we see a ray of hope with the start of vaccinations.

We would like to express our deepest gratitude to all who have made contributions and supported us to this point.

Due to surge in COVID-19 cases, Center Hospital of NCGM is partially limiting healthcare services, and either prohibiting or restricting visitors. Kohnodai Hospital of NCGM is also implementing visiting restrictions. We thank all our patients and families for understanding and cooperating with us.

In addition, we would also like to thank all our patients who have participated in the clinical trial of convalescent plasma therapy for COVID-19.

NCGM will continue to work in unity to confront COVID-19 in order to save lives of affected patients and help them recover as soon as possible. We greatly appreciate your continued support.

All Staff at NCGM

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