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<THE TOPIC OF THIS MONTH> COVID-19 as at December 2020

Coronavirus disease 2019 (COVID-19), which first occurred in Wuhan, China in December 2019, spread worldwide in a short period of time and was declared to be in a pandemic state by the World Health Organization (WHO) on March 11, 2020. According to the Johns Hopkins University COVID-19 Dashboard dated January 4, 2021, a cumulative total of 85,136,586 cases and 1,843,342 deaths were reported from 191 countries and territories (see p.29 of this issue).

Causative virus

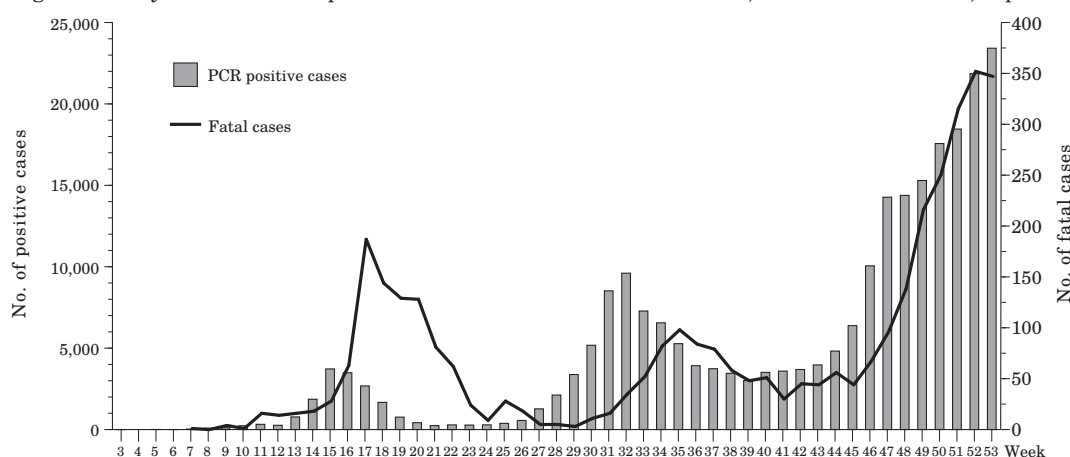
SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the causative virus of COVID-19, is classified into the family *Coronaviridae*, genus *Betacoronavirus*, and has a positive sense, single-stranded RNA genome consisting of approximately 30,000 bases. SARS-CoV-2 is closely related to the severe acute respiratory syndrome coronavirus (SARS-CoV) that emerged in China in 2002, but is considered to be more infectious (see p.30 of this issue). SARS-CoV-2 is an enveloped virus and is inactivated by alcohol or detergents. The virus also infects other animals such as cats, minks, and ferrets.

The genome sequences of part of the detected SARS-CoV-2 virus have been determined and used to analyze the relationships among cases and between clusters (see p.32 of this issue). Notably, mutated viruses may have altered transmissibility, pathogenicity, or antigenicity, and may not be detected by PCR methods used for diagnosis. The VOC-202012/01 strain detected in the United Kingdom has mutations in the spike (S) protein gene and is of concern because analysis of the epidemiological data suggested that the virus is more transmissible. Viruses with mutations in the S protein gene have also been detected in the Republic of South Africa and Brazil, and analysis of their properties is ongoing at a rapid pace.

Clinical presentation and transmission route

COVID-19 exhibits numerous clinical manifestations. Common symptoms observed in most patients are fever, dry cough, and malaise, which may be accompanied by sore throat, diarrhea, conjunctivitis, headache, or loss or disorder of taste/smell. Approximately 80% of patients who develop symptoms recover without hospitalization, but approximately 20% develop dyspnea and require oxygen inhalation, of whom approximately 5% require intensive care (Clinical Management of Patients with COVID-19, ver. 4.1: <https://www.mhlw.go.jp/content/000712473.pdf>). Patients may die from respiratory failure, acute respiratory distress syndrome (ARDS), thromboembolism, or multiple organ failure, including heart, liver, and kidney damage. Older persons aged 65 years and over and those with underlying disease, such as chronic obstructive pulmonary disease, chronic kidney disease, diabetes, hypertension, cardiovascular disease, or obesity, are at high risk for aggravation and death. The risk of death for patients aged 80 years or older with underlying disease can reach approximately 20%. In addition, there are reports of mildly ill patients suddenly deteriorating and dying

Figure. Weekly number of PCR-positive cases and fatal cases of COVID-19, weeks 3 to 53 of 2020, Japan



Based on the number of PCR-positive and fatal cases from the Ministry of Health, Labour and Welfare's open data web site (<https://www.mhlw.go.jp/stf/covid-19/open-data.html>; accessed 5 January 2021); data aggregation method is as described on the web site.

(THE TOPIC OF THIS MONTH-Continued)

(see p.34 of this issue), and of cases of fatigue, dyspnea, disorders of taste/smell, or hair loss that persist for 2-3 months (so-called long COVID), although the association with COVID-19 is not yet clear. On the other hand, approximately 20% of those infected are thought to be asymptomatic.

The main transmission route of COVID-19 is considered to be droplet and contact infection. The possibility of aerosol transmission has also been suggested. The incubation period is 1 to 14 days (5 to 6 days on average), and the period in which the virus can be transmitted to others is considered to range from 2 days before illness onset to 7 to 10 days after the onset. Asymptomatic cases are also infectious, although they are less infectious than symptomatic cases (see p.35 of this issue).

Diagnostic testing

Tests for COVID-19 diagnosis include viral gene detection tests (e.g., PCR method and LAMP method), quantitative antigen tests, and qualitative antigen tests. In order to obtain more accurate results, it is necessary to collect appropriate samples at the right timing, considering the characteristics, sensitivity, and specificity of each test. Diagnosis should be made carefully taking into account the fact that no test is perfect. In addition, elevated D-dimer, elevated CRP, elevated LDH, elevated ferritin, decreased lymphocytes, elevated creatinine, and elevated interferon λ 3 are used for clinical decision-making as laboratory markers of severe COVID-19.

Domestic epidemiological surveillance of COVID-19 and epidemiology

Since February 1, 2020, COVID-19 has been classified as a “Designated Infectious Disease” under the “Act on the prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases” (referred to as the Infectious Diseases Control Law). Physicians who have diagnosed COVID-19 must make a notification immediately (notification criteria; <https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-shitei-01.html>).

According to the open data (<https://www.mhlw.go.jp/stf/covid-19/open-data.html>) provided by the Ministry of Health, Labour and Welfare (MHLW) in Japan, since the first patient was confirmed on January 16, 2020, 243,063 test-positive cases and 3,598 deaths have been reported through January 3, 2021 (week 53 of 2020) (Figure). Following the first wave in April 2020 and the second wave in July - August 2020, the number of test-positive cases began to increase around November (the third wave), overwhelming the medical care provision system. As a result, the government declared a “state of emergency” for the second time since April 2020—first to Tokyo and to three other prefectures in the Kanto region on January 7, 2021, followed by seven other prefectures, including Osaka, Aichi, and Fukuoka, on January 13, 2021.

According to the domestic epidemiological surveillance data of COVID-19 (preliminary figures as at 18:00 on January 13, 2021) (<https://www.mhlw.go.jp/content/10906000/000719997.pdf>) released by the MHLW, the male/female ratio of the test-positive cases was 1.2 and the proportionate distribution of the test-positive cases by age group was, in the order of highest to lowest, those in their 20s (24.0%), followed by those in their 30s (16.1%), 40s (14.9%), 50s (13.5%), 60s (8.6%), 70s (7.3%), 80s and over (6.9%), 10s (6.3%), and under 10s (2.4%). The case-fatality rates of the reported test-positive cases by age group were as follows: 80 years or older (12.0%), 70s (4.5%), 60s (1.3%), 50s (0.3%), 40s (0.1%), and those in their 30s or younger (0.0%). For fatal cases, those aged 80 years or above accounted for 62.5% of all deaths (rounded to the first decimal place).

Vaccine and treatments

Vaccines using new technologies are being developed overseas, and at least two types of mRNA vaccines and one type of viral vector vaccine have been approved for manufacturing and marketing or received emergency use authorization in multiple countries. More than 40 countries, including the United States and the United Kingdom, have started vaccination. In Japan, with the aim of starting vaccination in the first half of 2021, revisions to the vaccination law, vaccination system, and vaccination prioritization are being considered (see p.36, 37 of this issue).

No drug has been developed that is highly effective against COVID-19, but the uses of remdesivir, dexamethasone, and heparin were approved depending on the symptoms. In addition, know-how on treatment methods for patients with severe pneumonia, such as ARDS, has been accumulating, with a decreasing trend for the case-fatality rate.

Challenges for the future

As at mid-January 2021, under the state of emergency, the MHLW is working to ensure the provision of medical care while strengthening quarantine measures as a border control strategy to prevent the entry of variant viruses from overseas. Regarding vaccination, the MHLW is also planning to ensure the requisite amount of vaccines by the first half of this fiscal year and proceed with vaccination while confirming its efficacy and safety. Even if the vaccine is effective as expected, until the epidemic subsides, the following measures are necessary to reduce the number of infected persons while maintaining societal functions.

Individuals are requested to exercise infection prevention measures such as maintaining physical distance, wearing a mask (cough etiquette), practicing hand hygiene, and carrying out actions that reduce contact with others, such as avoiding the so-called 3 “Cs” (closed spaces, crowded places, and close-contact settings) and refraining from going out when it is not necessary or urgent.

In addition, the national and local governments need to prevent an increase in infections and expansion of clusters through situational awareness of the epidemiological situation of COVID-19 and appropriate active epidemiological investigations (see p.39, 40, 42 of this issue). To this end, an effective surveillance system that allows information to be shared among the national government, local governments, and medical institutions, and reduces the burden on medical institutions and public health centers, is required (see p.43 of this issue). HER-SYS (Health Center Real-time information-sharing System on COVID-19), introduced by the MHLW, requires improvement (see p.45 of this issue). There is also an urgent need to train specialists at the local level, strengthen the local public health center system, and shift to a medical care provision system that focuses on severe cases.

In addition, the national and local governments need to maintain close communication with medical experts, relevant businesses, and local residents, and maintain working relationships to enable cooperation with requests, such as movement restrictions, that accompany state of emergency declarations.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.