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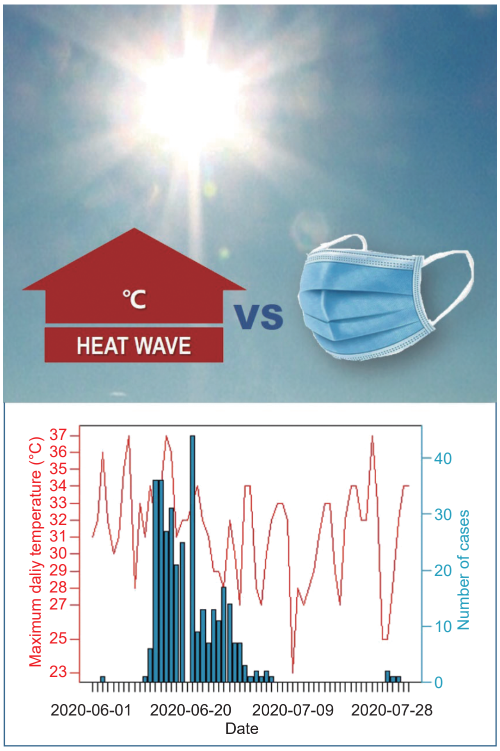

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Preplanned Studies

Changes in Public Perception and Behaviors under Compound Heatwave in COVID-19 Epidemic — Beijing, China, 2020

Jie Ban[1]; Yue Sun[1]; Yi Zhang[1]; Mike Z. He[2]; Qinghua Sun[1]; Chen Chen[1]; Tiantian Li[1,#]

Summary

What is already known about this topic?

Dramatic heatwaves frequently occurred simultaneously with the coronavirus disease 2019 (COVID-19) pandemic worldwide in 2020 and posed public health challenges. Public risk perceptions and behavioral responses to this compound risk need to be addressed.

What is added by this report?

During heatwaves, the proportion of individuals who perceived COVID-19 to be more concerning than heatwaves decreased by 9.4%, and the behavior of continuously wearing masks reduced by 20.6%. Heatwave exposures also corresponded to an average decline of 58% in the likelihood of continuously wearing masks and a decline of 41% in taking well-ventilated public transportation.

What are the implications for public health practice?

At-risk populations should be effectively prepared to respond to compounded risks from heatwaves occurring at the same time as COVID-19 outbreaks to better address threats caused by climate change.

The frequent simultaneous occurrence of the coronavirus disease 2019 (COVID-19) pandemic and heatwaves is a reminder that the combination of these 2 events is a global health issue. However, studies rarely explored how the public responds to this compounded risk of heatwaves and COVID-19. This study performed a retrospective survey in Beijing, China during the summer of 2020 to measure how the public changed their perceptions and behaviors to cope with this compounded risk. In periods of heatwaves, the proportion of people primarily concerned with COVID-19 reduced by 9.4% and the proportion of individuals continuously wearing masks decreased by 20.6%. Heatwave exposure corresponded to a 58% (95% CI: 50%–65%) decrease in the likelihood of wearing masks and a 41% (95% CI: 21%–56%) decrease in continuously taking well-ventilated public transportation. Heatwaves can disturb public compliance to COVID-19 preventative measures, and as the global incidence of COVID-19 is still on the rise, heatwave events in summers are a looming challenge in public health. This study could provide support to public health authorities to better prepare and implement optimal disease prevention strategies to address the compounded risks.

Heatwaves have occurred simultaneously with the COVID-19 pandemic in several countries worldwide during the past year (*1*–*3*), including a coinciding of the two during the current COVID-19 emergency in India with a rolling average of 378,000 new cases a day (*4*). People naturally tend to take actions to cool down to cope with extreme heat, such as dressing lightly and taking air-conditioned public transportation, which sometimes counters key COVID-19 prevention strategies such as wearing masks (*5*). Considering the increasing probability of heatwaves and COVID-19 epidemics occurring simultaneously, understanding public perceptions and responding to compound risks is crucial for promoting sustainable actions to adapt to climate change and minimizing the effects of the COVID-19 pandemic (*6*).

From May to September 2020, China experienced frequent heatwaves and announced 18,992 high-temperature warnings across the country. On June 11, 2020, an outbreak of COVID-19 started from the Xinfadi Wholesale Market in Beijing Municipality, which was followed by strict disease control actions and widespread communication to citizens to strengthen individual prevention. Simultaneously, Beijing was suffering from frequent heatwave events (Supplementary Figure S1 available in http://weekly.chinacdc.cn/), and 3 high temperature warnings (over 35 ℃) were issued for June 6–8, June 14–16, and July 23–25. Since the Chinese government has implemented strict measures to prevent the spread of COVID-19 (*7*) and has guided the public on implementing individual protective measures, mainly including wearing masks, staying in well-ventilated spaces, avoiding public gatherings, and maintaining personal hygiene, this study in Beijing provided insight on how people change their behaviors to respond to heatwaves during the COVID-19 pandemic.

A retrospective survey was conducted at the end of the Xinfadi COVID-19 outbreak in Beijing in early August 2020 using an online survey platform. Two periods of the survey were conducted to include heatwave and non-heatwave periods, and the identical questions on individual risk perceptions and COVID-19 prevention behaviors were investigated (Supplementary Table S1 available in http://weekly.chinacdc.cn/). First, based on the psychological measurement paradigm method (*8*), 4 factors measuring perceptions, including knowledge, concern, severity, and controllability, were investigated using a 5-point Likert scale ranging from 1 (not at all) to 5 (very). Risk perception dominance was then defined based on the scores of each perception factor question and was adopted to compare the risk perceptions of COVID-19 and of heatwaves. The study population were then categorized into the following 3 groups: 1) heatwave risk dominance (higher scores for heatwave related questions); 2) COVID-19 risk dominance (higher scores for COVID-19 related questions); and 3) equal dominance (equal scores for both of heatwave and COVID-19). The proportions of the three types of perception dominance were then calculated. Second, we considered two critical individual prevention behaviors against the infection of COVID-19: wearing masks and taking well-ventilated public transportation (a choice between taking enclosed air-conditioned public transportation or well-ventilated public transportation without air conditioner, which include buses whose windows can be opened manually). These two behaviors were measured by three choices, including "1=Continuously doing", "2=Sometimes doing" and "3=Never doing" (see Supplementary Table S1 available in http://weekly.chinacdc.cn/). In addition, a fourth option was given when asked about taking well-ventilated public transportation, "4=Ignore this issue"; respondents who selected this option were excluded from the analysis (about 17.6% of the study population).

Based on a three-step quality control process (see the Supplementary materials available in http://weekly.chinacdc.cn/), 1,000 valid responses were ultimately obtained. This study first compared differences in the proportion of risk perception dominance and individual choices of prevention behaviors between heatwave and non-heatwave periods using the chi-squared tests. Logistic regression models were then used to analyze the impact of exposure to compound heatwaves on individual COVID-19 prevention behaviors after controlling for demographic characteristics (age, gender, education, occupation, and income) in the total study population and different subgroups, in which we reorganized the outcome choices as a binary variable in two ways (Y1: "Continuously doing"=1, others including "Sometimes doing" and "Never doing"=0; Y2: "Never doing"=1, other including "Sometimes doing" and "Continuously doing"=0) to test the effect of heat exposure (binary variable, "heatwave period"=1, "non-heatwave period"=0) on individual adherence to COVID-19 preventions. Odds ratio (OR) and 95% confidence interval (CI) were calculated to present the results. Details have been presented in Supplementary Material (available in http://weekly.chinacdc.cn/). All the analyses were conducted using the R statistical software (version 4.0.3, the University of Auckland, Auckland, New Zealand).

The sample population was representative of the city's population structure in terms of gender and income but included less population over 40-years old and more high-level educated population (Table 1). Results of the chi-square test indicated significant differences in perception dominance and choices of prevention behaviors between heatwave and non-heatwave periods: as Figure 1A indicated, compared to the non-heatwave periods, the proportion of people expressing concern dominated by the risk of COVID-19 were reduced by 9.4% in heatwave periods, while people expressing concern dominated by heat risk increased by 3.9% during heatwave periods (χ^2=131.90, P<0.001); for masking wearing behaviors in Figure 1B, individuals who continuously wore masks decreased by 20.6% in heatwave periods (χ^2=87.23, P<0.001); for taking well-ventilated public transportation, continuously taking well-ventilated public transportation decreased by 9% (χ^2=20.86, P<0.001).

Table 2 showed the logistic regression results of the individual perception of COVID-19 risks during heatwave and non-heatwave periods for both the overall and subgroup populations. Compared to non-heatwave periods, the OR of the total population increasing perceived concern and severity of heatwaves were 1.93 (95% CI: 1.64–2.27) and 1.86 (95% CI: 1.59–2.18), respectively, and those of COVID-19 were 1.64 (95% CI: 1.38–1.94) and 1.63 (95% CI: 1.39–1.92), respectively. The OR of "continuously doing" for mask wearing [0.42 (95% CI: 0.35–0.50)]

TABLE 1. Descriptive statistics of the sample population and comparison to Beijing population proportion.

Item	Number of participants	Sample proportion	Beijing population proportion*	*P* value†
Gender				
Men	500	50.0%	50.9%	0.85
Women	500	50.0%	49.1%	
Age (years old)				
≤30	513	51.3%	30.9%	<0.001
30–40	402	40.2%	20.7%	
≥40	85	8.5%	48.4%	
Education level				
Senior high school and below	275	27.5%	61.1%	<0.001
University and above	725	72.5%	38.9%	
Occupation				
Office worker	512	51.2%	/	
Face to face service staffs	171	17.1%	/	
Self-employed	196	19.6%	/	
Other (including students and the retired)	171	10.9%	/	
Income level§ (CNY/year)				
Low income (<30,000)	323	32.3%	20.0%	0.02
Low and middle income (30,000–60,000)	187	18.7%	25.0%	
Upper middle income (60,000–100,000)	240	24.0%	25.0%	
High income (>100,000)	250	25.0%	20.0%	

Note: '/' means no available data.

* City population proportion was cited form the Beijing Yearly Statistic Book (2019).

† χ^2 test.

§ Income was classified according to the Beijing Yearly Statistic Book (2019).

and for taking well-ventilating public transportation [0.59 (95% CI: 0.44–0.79)] were all below 1, indicating that the possibilities of maintaining prevention behaviors declined during exposure to heatwaves. Subgroup analysis by gender, education level, income level, and occupation showed similar trends. In addition, the self-employed group [OR: 1.26 (95% CI: 0.33–4.80)] and face-to-face service staff [OR: 0.36 (95% CI: 0.14–0.91)] had lower likelihoods of wearing face masks less during heatwaves compared to other occupational groups.

DISCUSSION

This study provided quantitative evidence on how people in Beijing Municipality responded to compound heatwaves in the COVID-19 pandemic. We found both the perception of COVID-19 risk and 2 types of prevention behaviors of the studied sample were weakened during the heatwave period. The results of this study may be referenced by public health organizations to become better prepared for coping with the challenges brought by the COVID-19 pandemic and compound heatwave events.

Heatwaves may play a significant driving factor in reducing compliance to COVID-19 prevention measures. Uncomfortable physical and psychological feelings produced by shortness of breath, sultry, and sweating during heatwaves may be the primary reason for reduction in mask-wearing compliance. Furthermore, increased exposure to heat could steer public risk perception, understanding, and awareness of seeking a guide to prevent heat-related risk (*9*), resulting in heat-related risks dominating public perception during heatwave periods and reducing attention paid to COVID-19. In addition, misconceptions that the pandemic would decline during hot weather may have also adversely shaped risk perceptions on COVID-19 and weakened prevention (*10*). This poses an urgent challenge to public health authorities: how should we correctly guide the general population to take safe cooling action during the COVID-19 pandemic? The compounded effects of extreme weather during a global pandemic should be

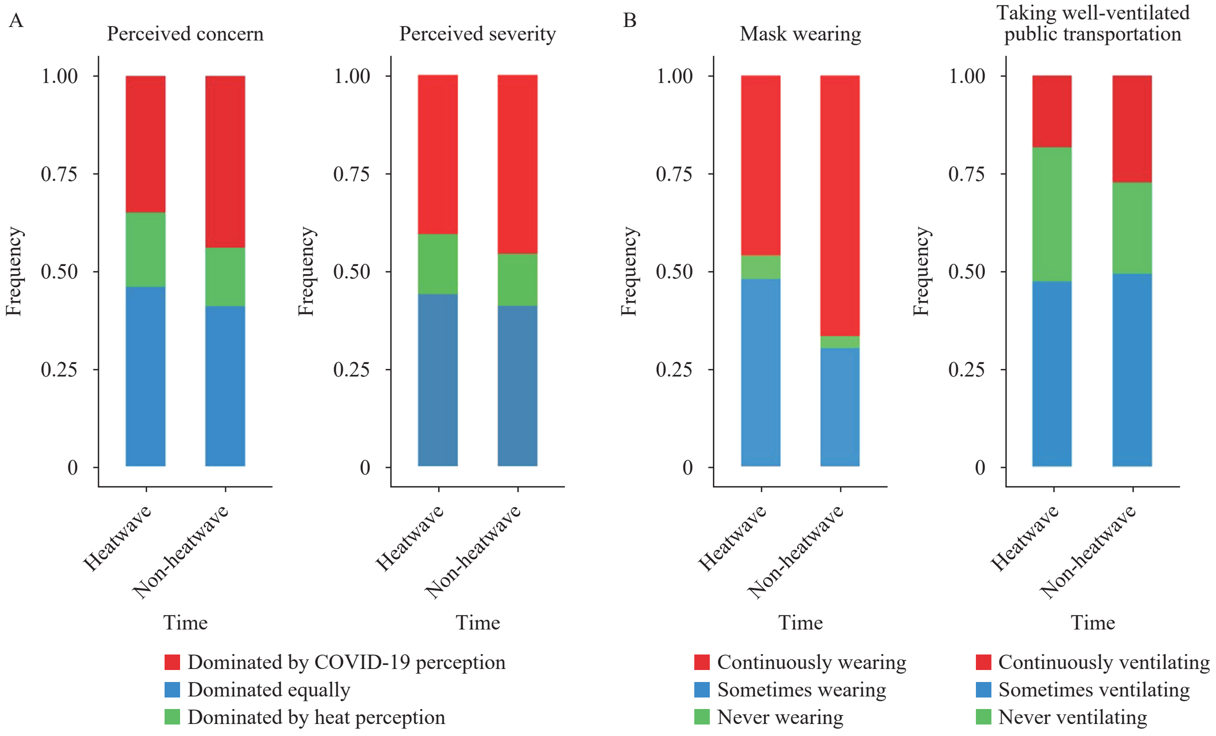

FIGURE 1. Comparisons of perceptions and behaviors between heatwave and non-heatwave periods in Beijing from June to July 2020. (A) Risk perception dominance; (B) Prevention behaviors.

addressed as a critical urgency.

The likelihood of keeping wearing masks or taking well-ventilated public transportation decreased by different levels in most of the subgroups, especially mask-wearing behaviors. Self-employed and face-to-face service staff had relatively lower likelihood of decline in "continuously wearing masks," reflecting China's strict regulation on service staff, especially those who could not avoid close contact to the public (e.g., supermarket cashier, courier, salesperson, etc.) in the COVID-19 prevention guide. However, office workers were likely to become high-risk groups because they relaxed COVID-19 behaviors and showed higher possibility of reducing prevention behaviors. As personal norms are key to taking preventative action (*11*), better adaptation to heatwaves during the COVID-19 pandemic and targeted strategies are needed to maintain the awareness of various population subgroups.

Public health prevention strategies should address two major aspects of the problem. To fight against COVID-19, information publicity and health-risk education for COVID-19 should be maintained to promote public awareness for disease prevention efforts. In addition, strict disease control regulation in public venues (public transportation, supermarket, etc.) and work places (office rooms, schools, etc.) should be strengthened by the responsible administrations. To better adapt to extreme weather conditions, action guidelines should be critically considered by public health authorities to guide people to safely adapt to climate anomalies during the pandemic. This study suggests strengthening education, increasing public understanding of compounded risks, and coordinating different sectors to integrate public health, environment, and social organizations to resist compounded risks due to climate change, such as integrating messages on the spread of COVID-19 risks during weather forecasts.

This study was subject to several limitations. First, this was a retrospective survey and may have been subject to recall bias. However, the survey was conducted immediately after the Xinfadi COVID-19 outbreak and was designed to accurately capture individual memories of perceptions and behaviors during the entire period. Second, this was a web-based survey in which sampling may focus on people who were web users. But according to the latest Statistical Report on China's Internet Development, as of June 2020, the number of web users exceeded 940 million and internet penetration rate reached 67% in China. Therefore, a web-based online survey could better

TABLE 2. Odds ratios for different choices of COVID-19 prevention behaviors and risk perceptions compared heatwave to non-heatwave periods in subgroup population [OR (95%CI)].

Item	COVID-19 prevention behaviors				Heat perception		COVID-19 perception	
	Continuously wearing	Never wearing	Continuously ventilating	Never ventilating	Perceived concern	Perceived severity	Perceived concern	Perceived severity
Total population	0.42 (0.35, 0.50)	2.11 (1.34, 3.33)	0.59 (0.44, 0.79)	1.63 (1.25, 2.13)	1.93 (1.64, 2.27)	1.86 (1.59, 2.18)	1.64 (1.38, 1.94)	1.63 (1.39, 1.92)
Gender								
Men	0.33 (0.25, 0.43)	5.73 (2.76, 11.91)	0.45 (0.29, 0.71)	1.59 (1.09, 2.32)	1.70 (1.36, 2.14)	1.76 (1.41, 2.21)	1.47 (1.16, 1.88)	1.60 (1.27, 2.01)
Women	0.52 (0.40, 0.67)	0.64 (0.31, 1.3)	0.72 (0.48, 1.07)	1.92 (1.27, 2.89)	2.24 (1.78, 2.83)	1.96 (1.56, 2.46)	1.82 (1.43, 2.31)	1.66 (1.32, 2.08)
Education level								
Senior high school and below	0.12 (0.08, 0.18)	1.17 (0.39, 3.54)	0.37 (0.19, 0.70)	1.59 (0.98, 2.58)	1.34 (0.99, 1.81)	2.41 (1.76, 3.31)	2.37 (1.70, 3.29)	2.23 (1.63, 3.05)
University and above	0.63 (0.51, 0.78)	2.39 (1.44, 3.95)	0.66 (0.48, 0.92)	1.81 (1.29, 2.55)	2.27 (1.87, 2.75)	1.71 (1.42, 2.06)	1.43 (1.17, 1.74)	1.47 (1.21, 1.77)
Income level								
Low income	0.60 (0.43, 0.82)	4.91 (1.39, 17.33)	0.78 (0.5, 1.24)	1.56 (0.96, 2.53)	2.12 (1.59, 2.82)	1.99 (1.50, 2.65)	1.39 (1.04, 1.87)	1.80 (1.36, 2.39)
Low and middle income	0.44 (0.28, 0.69)	2.46 (0.61, 9.87)	0.59 (0.31, 1.10)	2.33 (1.25, 4.32)	1.76 (1.21, 2.56)	2.40 (1.65, 3.49)	1.90 (1.28, 2.83)	1.72 (1.18, 2.5)
Upper middle income	0.39 (0.27, 0.56)	2.05 (0.69, 6.12)	0.28 (0.14, 0.56)	2.66 (1.51, 4.69)	1.60 (1.15, 2.22)	1.65 (1.19, 2.29)	2.01 (1.41, 2.86)	1.34 (0.96, 1.86)
High income	0.25 (0.17, 0.37)	1.66 (0.88, 3.12)	0.65 (0.31, 1.35)	0.95 (0.52, 1.77)	2.43 (1.75, 3.38)	1.64 (1.19, 2.25)	1.56 (1.11, 2.20)	1.72 (1.24, 2.39)
Occupation								
Office worker	0.27 (0.21, 0.35)	6.41 (2.8, 14.64)	0.47 (0.31, 0.71)	1.56 (1.09, 2.22)	1.68 (1.34, 2.10)	1.77 (1.42, 2.22)	1.72 (1.36, 2.19)	1.80 (1.43, 2.26)
Face to face service staffs	0.62 (0.40, 0.97)	1.26 (0.33, 4.80)	0.78 (0.40, 1.50)	1.51 (0.73, 3.14)	2.33 (1.57, 3.46)	1.66 (1.13, 2.46)	2.63 (1.72, 4.02)	1.93 (1.30, 2.86)
Self-employed	0.91 (0.60, 1.39)	0.36 (0.14, 0.91)	0.6 (0.29, 1.25)	4.35 (1.79, 10.59)	2.75 (1.89, 4.01)	2.68 (1.85, 3.87)	0.85 (0.58, 1.23)	1.19 (0.83, 1.70)
Other	0.37 (0.21, 0.64)	8.85 (1.08, 72.72)	0.88 (0.37, 2.12)	1.76 (0.69, 4.49)	1.78 (1.12, 2.84)	1.57 (0.99, 2.48)	2.19 (1.33, 3.60)	1.53 (0.96, 2.44)

adapt to people's daily lifestyle and cover population characteristics of the city, especially in Beijing. Third, only two prevention behaviors were included. Other actions (such as avoid gatherings, maintain hand hygiene, etc.) should be further studied. Fourth, individual perception on heatwave or COVID-19 may have been influenced if they recently experienced heat-related diseases or respiratory diseases, thus there may be some bias since we did not investigate individual health information. Finally, this study included 1,000 participants, which were likely not fully representative of Beijing residents. Although the structure of the sample was partially consistent with the city population, attention should be paid when interpreting the results.

In conclusion, the worldwide collision of heatwaves and COVID-19 is an emerging global health challenge. This study could aid in understanding and adapting to the compounded risk for future disease control and prevention strategies.

Conflicts of interest: No conflicts of interests.

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Supplementary Materials

Study Design

We conducted a retrospective survey at the end of the COVID-19 outbreak in Beijing (in early August 2020), which was designed to effectively capture participants' accurate recall on their response to the compounded risks. In this retrospective survey, we repeated the investigation on individual risk perception and COVID-19 prevention behaviors in heatwave and non-heatwave periods to compare the variances of participant responses in the two periods. Based on the consideration of safety and effectiveness in this specific period, we applied an online survey supported by the ZHONGYAN Technology Company, which is the leading professional online survey high-tech enterprise in China covering over 400 million population samples distributed from the county-to-city-level regions across China.

Data Collection

Study population

A representative population aged over 18 years old was randomly selected from the online survey sample pool in Beijing. The questionnaire link was posted on the online survey platform, and each question was set as mandatory to avoid missing information. The participants answered the questionnaire using mobile phones or computers. Written informed consent of each respondent was received online before answering the questions. We obtained 1,000 valid responses in total.

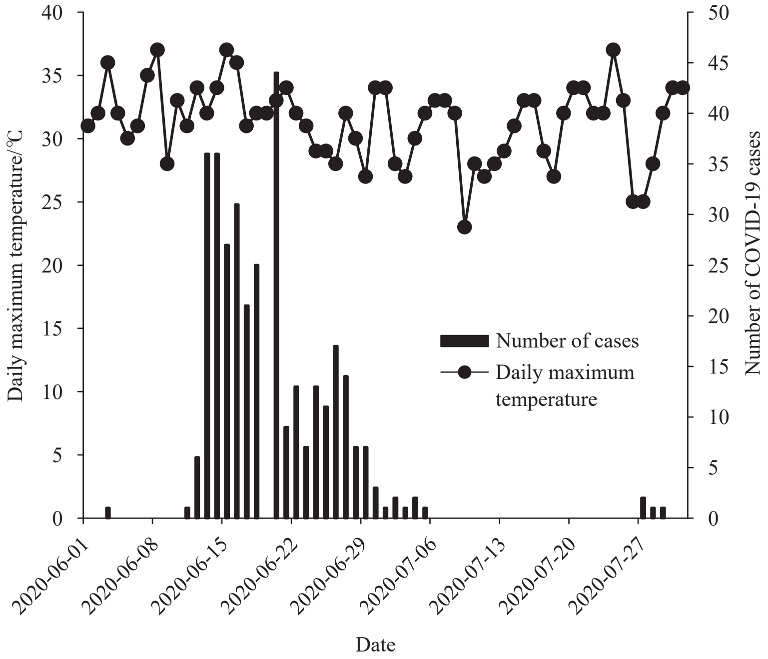
A three-step data quality control procedure was conducted to validate survey data. In the pre-control step ahead of the survey, the platform checked whether the participants were active users, and the questionnaire link could only be accessed once by the same ID to avoid duplicate answers from the same person; in the process-control step during the survey, the platform notified participants who gave an answer too quickly or continued duplicate selections in related questions; in the post-control step after the survey, a combination of artificial checks and computer checks was adopted to clean the data, and the platform would prepare an additional 5% of participants in addition to our required sample size as backup data to replace deleted study samples that did not meet requirements.

The questionnaire

The online questionnaire consisted of 3 parts: 1) demographic characteristics including gender, age, education level, income level, and occupation (Table 1); 2) individual risk perception on COVID-19 and heatwaves; and 3) individual COVID-19 prevention behaviors. The second and third parts were repeated in the investigations for heatwave and non-heatwave periods. Questions of risk perception and prevention behaviors were listed in Supplementary Table S1.

SUPPLEMENTARY TABLE S1. Questions of risk perception and prevention behaviors applied in the survey.

Variables	Questions
Risk perceptions	
Perceived concern	In your opinion, are you concerned about the risk in this period? From 1 = Not concerned at all to 5 = Very concerned
Perceived knowledge	In your opinion, how aware are you of the risk in this period? From 1 = Unknown to 5 = High level of knowledge
Perceived severity	In your opinion, is the risk serious to you in this period? From 1 = Not serious at all to 5 = Very serious
Perceived controllability	In your opinion, can you avoid the risk in this period? From 1 = Not controllable at all to 5 = Very controllable
Prevention behaviors	
Mask wearing	Do you keep wearing masks in this period? 1=Continuously wearing, 2=Sometimes wearing, 3=Never wearing.
Taking well-ventilated public transportations	Do you keep taking well-ventilated public transportations in this period? 1=Continuously ventilating, 2=Sometimes ventilating, 3=Never ventilating, 4=Ignore this issue



SUPPLEMENTARY FIGURE S1. Daily maximum temperature and number of cases in Beijing during June to July, 2020.

Outbreak Reports

A COVID-19 Outbreak Emerging in a Food Processing Company — Harbin City, Heilongjiang Province, China, January–February 2021

Lei Hou[1]; Hao Zhou[2]; Nanxi Meng[2]; Xue Yu[2]; Xin Wang[3]; Tuo Wang[4]; Jianfeng Zhang[5]; Yan Wang[2]; Shie Li[2]; Shuzhen Guo[2]; Jianxing Yu[3]; Muxin Chen[6]; Wenhui Shi[7]; Ning Xiao[6,#]; Chao Yang[2,#]; Jianxiang Liu[4,#]

Summary

What is already known about this topic?

The coronavirus disease 2019 (COVID-19) epidemic in China had been effectively controlled for several months, but as the ambient temperature dropped, large gathering-initiated epidemics occurred in northern China, including Hebei, Liaoning, and Jilin provinces.

What is added by this report?

A sudden epidemic emerged in Wangkui County, Suihua City, Heilongjiang Province, on January 9, 2021. An asymptomatically-infected resident of Harbin City returned from Suihua and triggered a large-scale outbreak in the Zhengda Food Processing Company in Harbin, Heilongjiang. The epidemic was associated with widespread community transmission inside and outside the company, eventually leading to 260 persons being infected (87.8% of 296 patients in Harbin).

What are the implications for public health practice?

This study demonstrates the importance of screening for infections in the COVID-19 prevention and control system, shares experiences identifying and managing asymptomatic infections, and recommends food processing enterprises like the Zhengda Company to improve preventative measures. Our evidence-based epidemiological analyses provide methods for finding high-risk settings and evaluating epidemic situations when many asymptomatic patients are identified in a short period of time.

Evidence supports the notion that community outbreaks of coronavirus disease 2019 (COVID-19) follow temperature gradients in a way that is consistent with outbreaks of other seasonal respiratory viruses (*1*). With the seasonal decrease in ambient temperature and prior to initiation of the current COVID-19 vaccination campaign, large gathering-based epidemics occurred in northern China in Hebei, Liaoning, and Jilin provinces (*2–3*). After 182 COVID-19 cases had been reported, the government of Harbin City, Heilongjiang Province, requested assistance investigating this outbreak and were assisted by the Joint Mechanism for COVID-19 Prevention and Control of the State Council on January 26, 2021, a working group that included China CDC professionals arrived in Harbin on January 27. China CDC and Harbin CDC jointly launched an epidemiological investigation and traced the outbreak. The joint investigation found that as of February 8, 2021, among the 296 known infected individuals, 292 (98.6%) were from Wangkui County, and the other 4 (1.4%), caused by the alpha variant of COVID-19, were from Daxing District, Beijing; 87.8% were associated with Zhengda Food Processing Company, a chicken processing facility, and 59.1% were asymptomatic but were able to be identified by various screening techniques (Figure 1). At the first sign of the epidemic, the local government had initiated their emergency measures, including containment, screening, and vaccination. After the joint epidemiological investigation, these measures were strengthened — isolation and quarantine, in particular, were utilized so that close contacts were isolated from their close contacts (secondary close contacts) for quarantine due to diverse infection risk and limited resources. These two different generations of contacts were quarantined in different hotels or in the same hotels with a partition between different contacts.

INVESTIGATION AND RESULTS

Based on the investigation of cases and fields, COVID-19 genome sequencing, and big data from mobile phone signals provided by the local public security bureau, a transmission chain was able to be elucidated. The chain started in Suihua City where Wangkui County was the epidemic center in

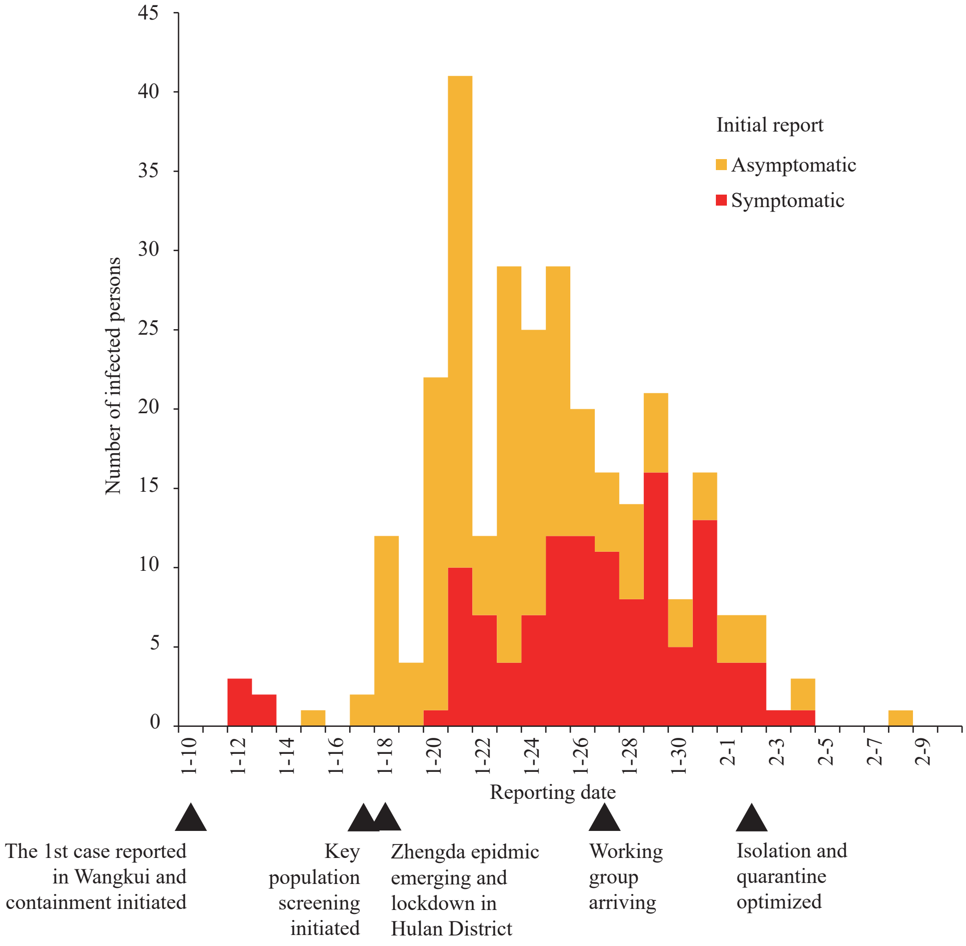


FIGURE 1. COVID-19 epidemic circumstances of infections in Harbin City, January–February, 2021.
Note: Classification of cases was based on the initial report. There were 296 cases identified from January 12 to February 8, among which 175 were initially asymptomatic, and of these, 25 developed eventually symptoms.

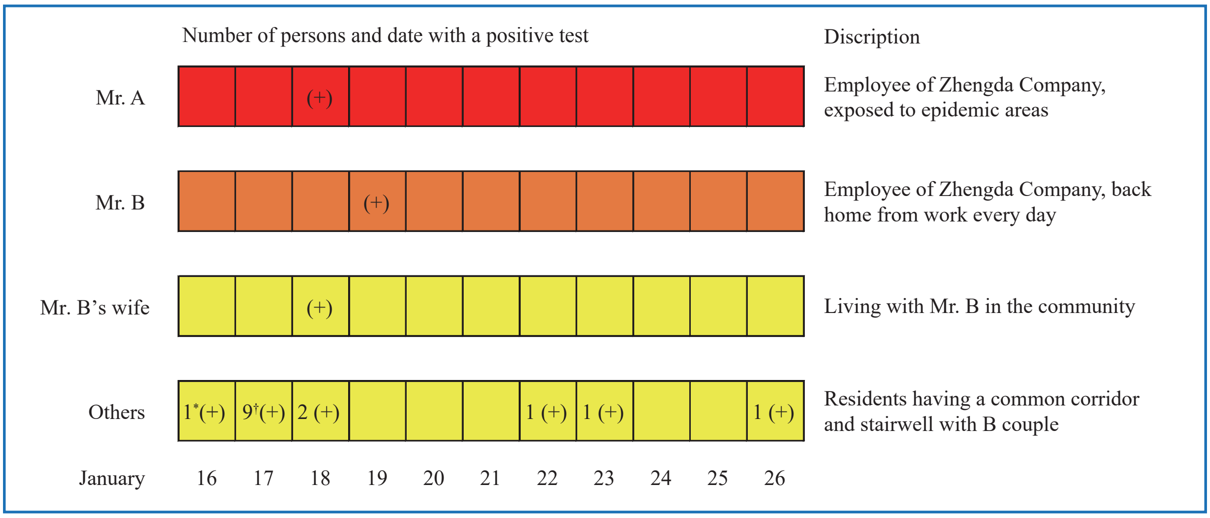
Heilongjiang Province since the end of 2020; Wangkui was locked down on January 11, 2021. The transmission chain led to communities in Harbin through Zhengda. In this article, we illustrate the chain hypothesized through two representative examples with available evidence — one example was from Suihua to Zhengda Company (Mr. A, B, and F working at this company) by Mr. A to Mr. B then to Mr. B's community; the second one was from Zhengda Company to individuals not related to the company by Mr. F.

Example One

In this example (Figure 2), the first-identified infected individual was asymptomatic, living in Mr. B's building that shared a common stairwell. This individual was diagnosed as infected through routine polymerase chain reaction (PCR) testing on January 16 when going to a hospital for unrelated treatment. On January 17, following a positive PCR report, all residents in the building sharing a common stairwell were quarantined and screened with PCR; more cases were found through this screening. On January 18, the Zhengda-Company-based epidemic was identified by a screening program organized by the local government. Mr. A and Mr. B were key patients in the 2 outbreak areas (the company and the building) (Table 1).

Stage 1: Mr. A was infected in Suihua City between January 1 and 5

Mr. A tested positive on January 18 and was diagnosed with COVID-19 after becoming symptomatic on January 21. His wife had a slight cough before January 19 and tested positive on January 28; she had a history of traveling and living in Suihua during January 1 and 5 where she and her husband, Mr. A, attended a funeral for Mr. A's father-in-law. The couple may have had close contact with an asymptomatically-infected individual for approximately 10 minutes at a station entrance outside of Wangkui County on January 5, 2021.



	Number of persons and date with a positive test											Discription
Mr. A			(+)									Employee of Zhengda Company, exposed to epidemic areas
Mr. B				(+)								Employee of Zhengda Company, back home from work every day
Mr. B's wife			(+)									Living with Mr. B in the community
Others	1[*](+)	9[†](+)	2 (+)				1 (+)	1 (+)			1 (+)	Residents having a common corridor and stairwell with B couple
January	16	17	18	19	20	21	22	23	24	25	26	

FIGURE 2. COVID-19 transmission relationships for Example One, Zhengda Company, Harbin City, January, 2021.

[*] Asymptomatic index case in this community who was found when seeing an orthopedic doctor on January 16 and who had been in Harbin City during this epidemic.

[†] Includes three symptomatic patients. The dates are of collecting positive samples.

Furthermore, as shown in Figure 1, most individuals infected before Mr. A was infected had an epidemiological history of being in Wangkui County; none were associated with the Zhengda Company. Other cases in Mr. A's community were found after January 21 and mostly were Zhengda employees, living in different buildings, with different job positions.

Finally, viral genome sequencing showed that Mr. A had been infected with a strain from Wangkui County, Suihua City. Positive IgG and IgM testing on January 29 provided evidence that infection likely occurred at the beginning of January.

Stage 2: Mr. A transmitted the virus to Zhengda Company employees between January 6 and 17

First, Mr. A returned from Suihua City on January 5 and went to work on the evening of January 6 in the Zhengda Company slaughterhouse. His and his colleagues' dressing room was in the clean area of the workshop and was about 7–8 square meters (m^2) in size. The dressing room was not routinely disinfected; disposable work clothes were not used by staff. The dressing room was used for changing and resting by all employees working in this area. Our environmental sample identified COVID-19-positive areas in the men's room and outside the women's room. 70% (90/129) of the Zhengda employees infected had an association with the clean area of the workshop.

Second, Mr. A usually worked the night shift but occasionally worked the day shift during January 6–17. Infections were more common among night-shift workers than day-shift workers (48.3% *vs.* 8.2%, $P<0.001$). The night-shift exposure infection odds ratio (OR) was 10.51, with a confidence interval (CI) of 5.90–18.71. The attack rate among Mr. A's 10 material preparation team colleagues was 60.0%, compared with 45.8% for other night shift workers.

Finally, viral genome sequencing showed that Zhengda cases including Mr. A and Mr. B were highly homologous with the Wangkui strain.

Stage 3: Mr. B was infected in the men's dressing room or on a Zhengda commuter bus between January 7 and 17

First, Mr. B and Mr. A both worked in the clean area during January 7 and 17, and despite working on different shifts or locations, they used the same men's dressing room. There was a 77% increased risk of infection among men compared to risk among women (OR=1.77, 95% CI: 1.17–2.68; attack rate 17.1% *vs.* 10.4%, $P=0.006$). The OR of infection in the clean area compared with a dirty area that has its own dressing room was 3.68 (95% CI: 1.33–10.20).

Second, Mr. B took the commuter bus to and from work at 05:40 and 17:30 every day. Mr. B stated that he heard people coughing on the bus around January 14. A survey showed that the attack rate among bus line passengers was 9.5%, similar to the 8.2% attack rate at the clean work area during day shifts ($P=0.859$). Another possible exposure location for Mr. B was the staff dining hall, but comparable data are not available.

Stage 4: Mr. B infected others in his community between January 7 and 17

First, no individuals in Mr. B's community in

TABLE 1. Comparisons of the first example transmission chain in the COVID-19 outbreak in Harbin City, Heilongjiang Province, China, January 2021.

Groups per links in the transmission chain	Number of persons		Total*
	Infected	Not infected	
Mr. A to Zhengda Company			
Shifts in Mr. A's workshop			
Night shift (Mr. A's shift)	28	30	58
Day shift (non-Mr. A's shift)	62	698	760
OR (95% CI)	–	–	10.51 (5.90–18.71)
Night shift in the clean work area			
Mr. A's team (material preparation)	6	4	10
Non-Mr. A's team (packing and cleaning)	22	26	48
OR (95% CI)	–	–	1.77 (0.44–7.09)
Zhengda Company to Mr. B (Mr. A and Mr. B said that they had to change clothes before entering the workshop every time and they did not know each other due to working in different shift)			
Work areas in Mr. A's workshop			
Clean area (Mr. A's)	90	728	818
Dirty area (not Mr. A's)	4	119	123
OR (95% CI)	–	–	3.68 (1.33–10.20)
Dressing room in the clean area			
Men's room (multiple indoor environmental samples positive)	49	237	286
Women's room (one outdoor environmental sample positive)	57	489	546
OR (95% CI)	–	–	1.77 (1.17–2.68)
Mr. B to his community			
Possible exposure sites			
Commuter car (non-Mr. A's)	8	76	84
Clean work area at the day shift	62	698	760
OR (95% CI)	–	–	1.19 (0.55–2.57)
Residents sharing the common corridor and stairwell with Mr. B			
Go out often	10	5	15
Stay at home occasionally; go out occasionally or never go out	5	19	24
OR (95% CI)	–	–	7.60 (1.77–32.63)

*: Numbers of exposed persons were obtained by asking for Zhengda Company and checking name lists in duty rosters. Odds ratios (ORs) with 95% confidence intervals (CIs) were based on a chi-square test.

Hulan District of Harbin had ever been to a COVID-19 high-risk area, and no individuals from Suihua entered the community within the previous month. Mr. B commuted between home and Zhengda every day.

Second, Mr. B's wife tested PCR positive on January 18, with a strain shown to be the Wangkui strain. She was infected despite being vaccinated (two HB02 vaccines, provided by Beijing Institute of Biological Products Co, Ltd, about one month before infection) and paying great attention to personal protection for occupational reasons. This observation supports an intrafamily infection from Mr. B to his wife.

Finally, the common corridor was usually closed, and its door handle tested negative for COVID-19.

Stage 5: Virus spread in Mr. B's building between January 7 and 17

First, there were no cases other than families using the common stairwell among the families of this building or this community. Of total of 15 infected individuals, 13 had a history of going out; 1 individual, who never went out, lived with his mother who was infected; and the last individual had 4 infected neighbors living in different houses on the same floor.

Second, a supplementary investigation conducted on February 1 among 39 residents, excluding a couple including Mr. B, sharing the common stairwell showed that the attack rate of people who often went out was higher than the attack rate among people who did not often go out (66.7% *vs*. 20.8%; OR=7.60, 95% CI: 1.77–32.63; *P*=0.005).

Example Two

In this example, none of the persons infected had a history of travel outside of Harbin during the outbreak, but social activities outside Zhengda resulted in new infections that were not among Zhengda employees or their relatives (Figure 3).

Stage 1: Mr. F was infected in Zhengda between January 6 and 17

First, Zhengda employee Mr. F experienced cough, headache, sore throat, and a runny nose; he self-medicated on January 15 and tested positive on January 20; he was diagnosed with COVID-19 pneumonia on January 22. Mr. F worked the night-shift in the clean area from January 6 to 17. His frequent use of the men's dressing room and night-shift work placed him at high-risk of infection.

Second, Mr. F was a close contact of his mother suffering COVID-19 pneumonia, who had been diagnosed on January 21; she was a Zhengda employee on the same team as Mr. F, working the same shift.

Stage 2: Mr. G was infected by Mr. F on January 15

First, on the evening of January 15, the date that Mr. F developed symptoms and was likely most infectious, Mr. F took a bus (defined as a closed space) with Mr. G after work for 7 stops (Hulan District Government to Zhengda). A surveillance system on the vehicle showed that Mr. G was sitting in front of the lower door while Mr. F passed by, stood at the lower door, pulled down his mask, and shouted towards the front.

Second, on the evening of January 21, Mr. G tested positive, and a virus isolated from his throat swab had a genetic sequence identical to Mr. F's virus sequence — the Wangkui strain that showed Mr. G's infection was later than Mr. F.

Stage 3: Ms. H was infected by Mr. G on January 20

First, Mr. G was a bank security guard; at 10∶24 on January 20, Mr. G opened a door and scanned a QR code for Ms. H, a customer of the bank, who tested positive test with a confirmed diagnosis on January 25.

Second, the viral genome sequencing showed the virus isolated from Mr. G and the virus isolated from Ms. H were Wangkui-strain viruses with identical mutation sites (C24621T).

DISCUSSION

A major challenge COVID-19 prevention and control is the detection of asymptomatic infections and infections having long incubation periods. This challenge can be overcome by early and timely screening with PCR. In this outbreak, the first person known to be infected was asymptomatic and was identified in a clinic focusing on non-infectious diseases on January 16. The infected person had neither contact with the Zhengda Company nor travel to high-risk areas outside Harbin. Identification of an asymptomatic index case contrasts with initial diagnoses in other outbreaks, such as the Huanan Seafood Wholesale Market in Wuhan and the Xinfadi Wholesale Market in Beijing (*4*–*5*), in which the index cases were symptomatic and were found by infectious diseases clinics. The 12 days of silent transmission were interrupted by key population screening, resulting in identification of many infections with unclear transmission patterns and quarantine of Zhengda

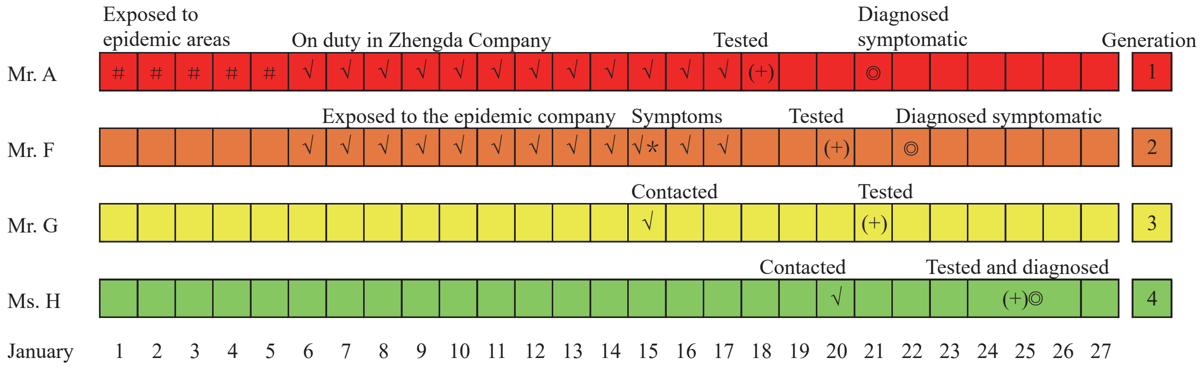


FIGURE 3. COVID-19 transmission chain generations for Example Two, in Harbin City, January, 2021.

employees. Despite the identification of initial cases, at least 3 generations of secondary cases occurred in the company, in residential areas, and in other companies. Respiratory droplets or contaminated air in confined spaces, such as dressing rooms, dining halls, resident corridors, and vehicles, played an important role in the chain of infection.

Food processing companies like Zhengda usually have “clean” areas that can provide an environment suitable for COVID-19 transmission. Our study showed that some measures, such as actively reporting to one’s own community a history of having returned from an epidemic area, key-population screening, symptom reporting and monitoring, ventilation of confined spaces, regular disinfection of indoor environments and coveralls in dressing rooms, and good personal protection habits, can slow the epidemic spread.

Among the earliest cases in the company, a night shift worker in the clean area developed his first symptoms on January 13, preceding the January 16 diagnosis in which the asymptomatic index case was found. Residents sharing a common stairwell with the index case were quarantined and tested; they did not have a history of contact in Zhengda. This means that it is unlikely to have been backpropagation. We searched but did not find evidence of infection to humans from chickens, including live chickens and chicken products. In the most important transmission settings — the men’s dressing room and adjacent corridor, the transmission mode appeared to be from the human respiratory system. This suggests that it is more important to guard against person-to-person infection than infection from fomites.

China CDC developed a method for analyzing generations of infection, as shown in Figure 3 (*6*). Our evidence-based examples supplemented standard epidemiological methods for finding high-risk areas and evaluating epidemic situations (Table 1). The method was comparable to John Snow’s investigation of the cholera epidemic in London in the mid-19th century. When transmission links are uncertain, for example after identifying many unrelated cases following wide-scale population screening with PCR, this method is useful. Nevertheless, analysis depending on accurate and detailed investigations usually lags behind an outbreak, and onsite fast disposal following field investigations are vital.

This study was subject to some limitations. The investigation was conducted under a state of emergency, with a priority for first controlling the epidemic. Some data, such as on dining hall contacts, could not be fully collected. Within Zhengda, the transmission relationship was complex (e.g., from person to person or from environment to person), making it difficult to judge the transmission of intergenerational relationships. We obtained little information on vaccine effectiveness, even though the local government prioritised vaccinating key populations, including medical staff and cold chain practitioners. Our study was conducted in the middle and late stages of the epidemic. An earlier, rapid but imperfect epidemiological investigation, nevertheless, may be superior to a later but more thorough investigation for controlling the epidemic.

In conclusion, the Zhengda epidemic was quickly contained within three weeks of its discovery, showing the effectiveness of China’s precision containment strategy. However, the COVID-19 prevention and control can be improved, for example by strengthening supervision and management of food-processing and cold-chain storage companies, outpatient services, and confined spaces. Our experience and findings will be useful next winter, and our quarantine practices for close contacts and their close contacts should be implemented with standardized guidelines for COVID-19 prevention and control.

Conflicts of interest: No conflicts of interest.

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Notes from Field

An Immunocompetent Patient with High Neutralizing Antibody Titers Who Shed COVID-19 Virus for 169 days — China, 2020

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Few reports are available about prolonged shedding of coronavirus disease (COVID-19) virus, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), by immunocompetent patients. We report a case of an infected, immunocompetent person with 169 days of COVID-19 virus shedding during which time he had two brief periods when he tested negative for COVID-19 followed by again testing positive. We describe relevant clinical, immunological, and genomic features. We found that continuous and prolonged viral replication and infectivity existed in an immunocompetent COVID-19 patient, despite having high neutralizing antibody titers.

INTRODUCTION

Previous case reports have described immunocompromised patients shedding COVID-19 virus RNA for 105 days and 153 days, and to our knowledge, the longest reported duration of COVID-19 virus shedding in an immunocompetent COVID-19 patient was 61 days (*1*–*3*). In this report, we describe an immunocompetent COVID-19 case in Beijing with 169 days of viral shedding.

CASE REPORT

A 64-year-old man with coronary atherosclerotic heart disease, hypertension, and type-2 diabetes, with a 40-year history of smoking and alcohol consumption, was confirmed as a COVID-19 case on February 12, 2020. He was identified in a family cluster of COVID-19 virus infection (Figure 1A), in which 4 of 7 family members were confirmed to be COVID-19 cases and whose COVID-19 virus viral sequences were highly homologous. Overall, 3 family members recovered and were discharged by March, but the subject of this case report, who had moderately severe COVID-19, was isolated at the hospital due to persistent COVID-19 virus positivity until August of 2020, with an exception of two 2-week periods when he tested negative (*4*) (Figure 1A, Supplementary Table S1 available in http://weekly.chinacdc.cn/).

The patient had chills, fever (38.6 °C), sore throat, and loss of appetite from February 1 to his admission on February 12. Clinical examination revealed decreased white blood cell (WBC) and lymphocyte counts (Supplementary Table S2 available in http://weekly.chinacdc.cn/). Chest computed tomography (CT) showed patchy ground-glass opacities in the upper and the lower lobes under the pleura of both lungs and in the middle lobe of the right lung (Supplementary Figure S2 available in http://weekly.chinacdc.cn/). Throughout his hospitalization, no abnormalities were observed in his liver or kidney function or in routine blood examinations (Supplementary Table S3 available in http://weekly.chinacdc.cn/). Supportive evidence that he was immunocompetent was that all absolute cluster of differentiation 4 (CD4) counts were above 350/μL, the CD4/cluster of differentiation 8 (CD8) ratio was above 1, and he was HIV negative; however his CD8 cell counts and natural killer (NK) cell counts were low at times (Supplementary Table S3).

The patient's neutralizing antibody titer was 1∶2,048 measured 13 days after illness onset; the titer peaked at 1∶8,192 on day 24 and subsequently declined, staying at 1∶384 for over 9 months (Figure 1B; Supplementary Table S4 available in http://weekly.chinacdc.cn/). The highest viral loads, as assessed by PCR cycle thresholds (Ct) in sputum (Ct=17.4) and nasopharyngeal specimens (Ct=23.4), occurred 4 to 5 months (days 114 and 132) after illness onset (Figure 1C, Supplementary Tables S5–S6 available in http://weekly.chinacdc.cn/). Overall, 3 sputum samples (days 107, 112, and 131) were positive for sub-genomic RNA (sgRNA), with respective Ct values of 32.25, 38.15, and 38.30 (Figure 1C). Detailed methods are in Supplementary Materials (available in http://weekly.chinacdc.cn/).

Phylogenetic analyses showed that all viruses

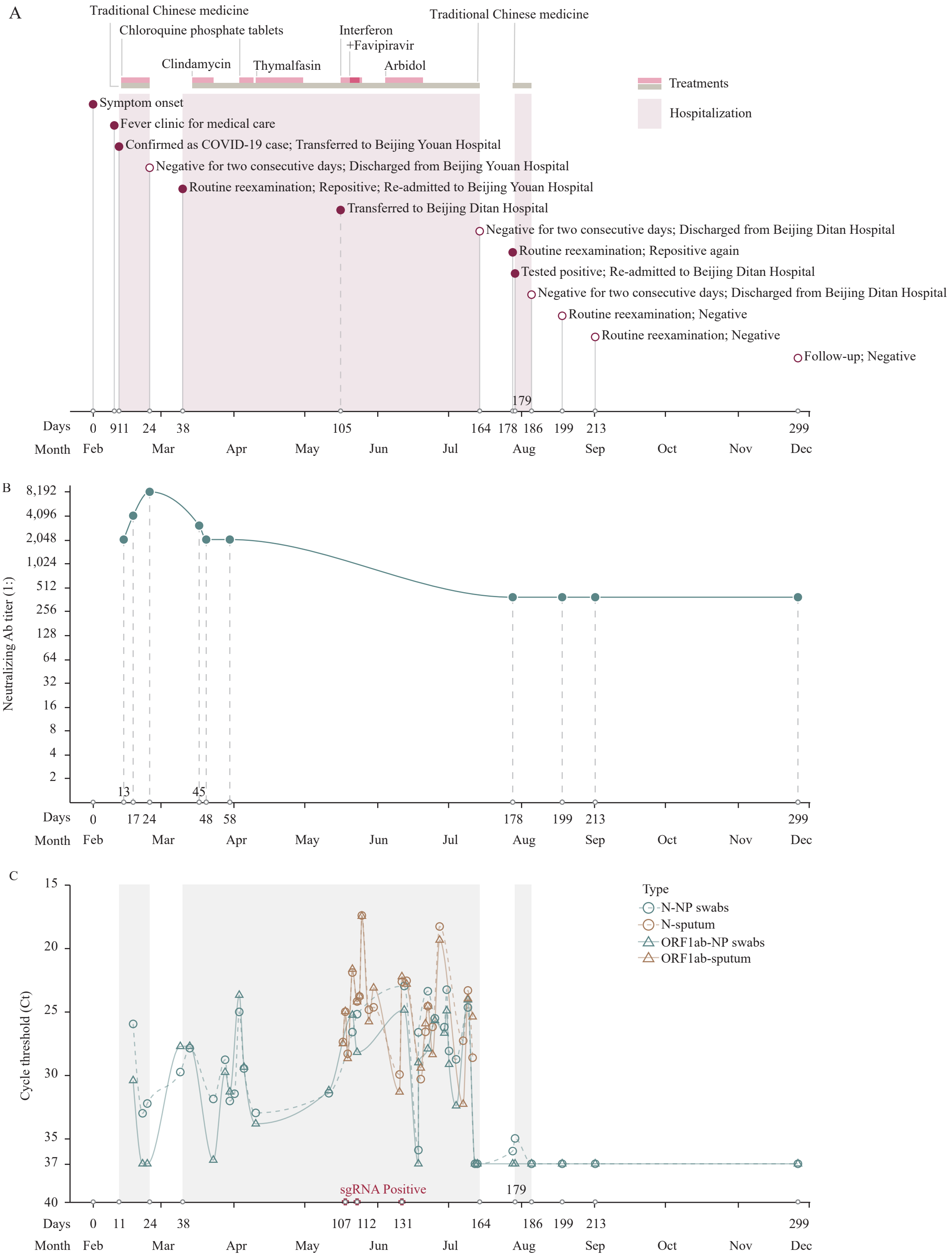

FIGURE 1. The timeline of the course of treatment and conducting assays for neutralizing antibody titers and PCR cycle threshold values of the COVID-19 patient from illness onset to 299 days after illness onset. (A) Time course of diagnosis and treatments of the patient. (B) Geometric mean titer (GMT) of neutralizing antibodies; 10 blood samples (days 13, 17, 24, 45, 48, 58, 178, 199, 213, and 299) were tested in triplicates. (C) Cycle threshold (Ct) values from detecting N and ORF1ab genes of COVID-19 virus from 33 nasopharyngeal (NP) swabs and 20 sputum samples.

Note: PCR was considered negative when the Ct value was ≥37. Days with positive sgRNA assessed in three sputum samples are noted with red circles. N denotes N gene; NP denotes for nasopharyngeal samples, sputum denotes for sputum samples. ORF1ab denotes for open-reading-frame 1ab gene.

belonged to lineage B (*5*) and were 99.95% to 99.98% homologous with reference strain NC 045512 — evidence that is incompatible with reinfection (Supplementary Figure S1A available in http://weekly.chinacdc.cn/) (*6*). Five single nucleotide variants (SNVs) were observed when the case report subject was diagnosed, and sequences among two other family members were identical (the viral load of the third family member was too low to be sequenced). Mutations accumulated across the COVID-19 virus genome, increasing to 14 mutation sites on Day 151. In total, 3 amino acid substitutions in the S protein were observed in serial samples, including H655Y, Y200C, and D614G substitutions. The mutations effectively changed the lineage from B to B.1.1 (Supplementary Figure S1B–C).

Previous case reports have described immunocompromised patients shedding COVID-19 virus RNA for 105 days and 153 days; the longest, previously-reported duration of COVID-19 virus shedding in an immunocompetent COVID-19 patient was 61 days (*1–3*). To our knowledge, the patient we describe has the longest duration of viral shedding (169 days) with intra-host variants (151 days). The intra-host mutation rate was comparable to that seen with inter-host variants (*7–8*). However, unlike previous studies, which describe shorter infection periods, the mutations identified in this case appeared across the entire genome rather than in select hotspots, such as S and ORF8 genes (*1–2*).

Although previous studies suggested that COVID-19 patients positive for COVID-19 virus RNA following a period of being negative have little or no infectiousness (*9–10*), our evidence suggests infectiousness may last up to 151 days after symptom onset. Although lack of laboratory facilities precluded virus isolation and culture, the observed accumulated mutations and positive sgRNA 3–4 months after infection suggests continuous, on-going viral replication and therefore potential for transmission (*1*). We believe that more attention to the infectiousness of patients testing positive after a period of testing negative is warranted.

The patient did not have severe clinical symptoms, indicating that prolonged viral shedding can occur in moderately ill cases (*11–12*). Because frequent nucleic acid testing is normally only done in people with COVID-19-like symptoms, we may be under-detecting occurrence of long-term virus shedding (*4*).

We anticipate additional follow-up of this individual. Although a single case report may have limited generalizability, our observation that he shed virus despite his neutralizing antibody titers being much higher than titers we have seen with other patients at our facility (*13*) suggests that immune responses other than humoral responses may have important roles in virus clearance. Perhaps cellular immune responses and innate immune functions are important for eventual clearance of persistent infections. The low CD8 T-cell and NK cell counts may have prolonged the time required for virus elimination or may indicate an exhausted immune response; however, it is not clear which of these two possibilities is at play. Dynamic interactions of killer T-cells, COVID-19 virus infection, and the individual's immunological function need to be evaluated holistically to understand risk factors for prolonged and infectious COVID-19 virus shedding. It may also be important to evaluate the role of the genetic background of the patient or of virus-host interactions and their contributions to prolonged viral shedding (*14*).

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Ethics: This study has obtained consent from participant and is approved by the Medical Ethical Committee of Beijing YouAn Hospital, Capital Medical University (approval number [2020]036).

Conflicts of Interest: No potential conflicts of interest was reported by the authors.

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SUPPLEMENTARY MATERIALS

Clinical Presentations

All available data on white blood cell (WBC), lymphocyte, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), direct bilirubin (DBIL) from liver function tests; albumin (ALB), blood urea nitrogen (BUN) and creatinine level (Cr) from kidney function tests, and computerized tomography (CT) images were obtained from clinical charts and tests results.

Laboratory Examinations

Neutralizing Antibody

Ten blood samples were collected. Antibodies were assessed with a modified cytopathogenic neutralization assay (NA) using live COVID-19 virus. The dynamics of neutralizing antibody levels at different time points were analyzed. We conducted neutralization assay (NA) to evaluate antibody level according to the Reed-Muench method on day 5. Serum samples were inactivated at 56 °C for 30 minutes and serially diluted with cell culture medium in 2-fold steps. Diluted sera were mixed with a virus suspension of 100 median tissue culture infective dose in 96-well plates at a ratio of 1∶1, followed by 2 hours of incubation at 36.5 °C in a 5% carbon dioxide (CO_2) incubator; 1–2 × 10^4 Vero cells were then added to the serum-virus mixture, and the plates were incubated for 5 days at 36.5 °C in a 5% CO_2 incubator. Cytopathic effects in each well were recorded by microscope; neutralizing titers were calculated by the dilution number yielding a 50% protective condition. A titer of ≥1∶4 indicated seropositivity.

Viral Load

Viral loads were obtained from 33 nasopharyngeal swabs and 20 sputum samples collected at different time points during the patient's hospitalization. All available Cycle threshold (Ct) values for determining viral load were abstracted from 7500 software v2.3 from the 2 hospitals (Thermo Fisher Scientific, Beijing, China).

In addition, sub-genomic RNA (sgRNA) was monitored to evaluate transcription of COVID-19 virus. Fifteen nasopharyngeal swabs and four sputum samples collected from Day 100 to Day 157 were analyzed.

Phylogenetic Analysis

Longitudinal nasopharyngeal swabs and sputum samples were collected after diagnosis and then sequenced by Next Generation Sequencing (NGS). A total of 14 viral genome sequences were obtained from serial samples, including 9 genomes from sputum samples and 3 genomes from nasopharyngeal swabs collected from the study case, and 2 from nasopharyngeal swabs collected from his 2 family members.

Viral Genomic RNA and Subgenomic RNA Detection

A series of nasopharyngeal swabs and/or sputum samples were collected after diagnosis. Viral RNA was extracted by automated nucleic acid purification (KingFishe Flex Purification System, Thermo, Waltham, MA, USA) and diluted in 90 μL RNase-free H_2O. The viral genomic RNA (gRNA) was amplified by real-time RT-PCR assay using 5 μL input RNA and commercial kits (Bojie, Shanghai, China). The subgenomic RNA (sgRNA) was detected by real-time RT-PCR assay using 5 μL of RNA, TaqMan Fast Virus 1-Step Master Mix (Thermo), and sgRNA specific primer/probe sets. The results were determined according to the manufacturer's instruction. Negative and positive controls were applied to ensure the quality of the tests.

Next Generation Sequencing

Viral RNA was extracted from patient nasopharyngeal swabs and sputum samples using automated nucleic acid purification (KingFisher Flex Purification System). First strand cDNA synthesis was performed with the SuperScript IV First Strand Synthesis System (Invitrogen, MA, USA), using 8 μL input RNA and random hexamers. Then tiled-PCR amplicons were generated by 25–32 PCR cycles using ARTIC nCoV-2019 sequencing protocol v3 (https://www.protocols.io/view/ncov-2019-sequencing-protocol-v3). The primers for Pool 1 and 2 were synthesized by Sangon (Shanghai, China). NGS libraries were prepared by Nextera XT Library Prep Kit (Illumina, San Diego, CA, USA) and sequenced on MiniSeq using 2 × 150 paired-end sequencing kits (Illumina). Negative control samples were processed and sequenced in parallel for each sequencing run as contamination control.

COVID-19 Virus Genome Analysis

Quality control and adaptor trimming was done CLC Genomics Workbench (v10.0, Qiagen, Germany). The clean reads were mapped to the reference COVID-19 virus genome (GenBank: MN908947.3) using Bowtie2 and SAMtools. Variant calling was performed using Genome Analysis Toolkit (GATK, version 4.0.10). Single nucleotide polymorphic variants were filtered for quality (QUAL) >200 and quality by depth (QD) >20 and indels were filtered for QUAL >500 and QD >20 using the filter tool in bcftools, v1.9. Phylogenetic analysis was conducted using MAFFT v7. A maximum likelihood tree was inferred by N-J model with bootstrap of 1000, including the patient COVID-19 virus genomes, the reference genome sequence (GenBank: MN908947.3) and 494 representative genomes randomly selected from NCBI virus dataset by regions of interest. The final figure was made using iTOl (https://itol.embl.de/). The viral genomes reported in this study have been deposited in GISAID (https://www.gisaid.org).

SUPPLEMENTARY TABLE S1. The timeline of the course of patient treatment from illness onset to 299 days after onset.

Date	Days from illness onset	Event
2/1/20	0	Symptom onset
2/10/20	9	Fever clinic for medical care
2/12/20	11	Confirmed as COVID19 case; transfer to Youan Hospital
2/26/20	24	Negative for two consecutive days; discharged from Youan hospital
3/13/20	38	Routine reexamination; positive again; re-admitted to Youan Hospital
5/16/20	105	Transfer to Ditan hospital
7/14/20	164	Negative for two consecutive days; discharged from Ditan hospital
7/28/20	178	Routine reexamination; positive again
7/29/20	179	Last day tested positive; re-admitted to Ditan hospital
8/5/20	186	Negative for two consecutive days; discharged from Ditan hospital
8/18/20	199	Routine reexamination; negative
9/1/20	213	Routine reexamination; negative
11/26/20	299	Follow-up; negative

SUPPLEMENTARY TABLE S2. Clinical laboratory information of the patient from past tests.

Date	Days from illness onset	WBC (10^9/L)	N (10^9/L)	L (10^9/L)	L (%)	NLR	HB (g/L)	ALT (U/L)	AST (U/L)	TBIL (μmol/L)	DBIL (μmol/L)	ALB (g/L)	BUN (mmol/L)	Cr (μmol/L)
2/13	12	1.96*	1.32*	0.36*	18.3*	3.7	121	51*	145*	25.8*	7.3*			
2/18	17	3.3*	1.96*	1.02	30.9	1.9	129	70*	123*	11.5	3.6			
2/25	24	3.68*	2.33	1.08	29.3	2.2	143	19	40	12.8	2.5			
3/12	40	3.92*	2.4	1.05	26.8	2.3	156	24	23	22.7*	4.8			
3/13	41	3.91*	2.62	0.88*	22.5	3.0	135	11	22	16.9	5.3			
3/16	44	4.8	2.77	1.42	29.6	2.0	154	34	22	22.6*	4.6			
3/17	45	3.32*	2.19	0.81*	24.4	2.7	143							
3/20	49		2.19					36	25	20.6*	4.9			
3/30	58	2.24*	1.07*	0.76*	33.9	1.4	136	16	30	17.5	2.1			
5/17	106	3.26*	1.75*	1.14	35	1.5	148	16.1	21.2	31.4*	11.0	49	3.1	49.1*
5/21	109	3.33*	1.95*	0.91*	27.3	2.1*	147	15.6	21.9	21.2*	8.9*	45	3.8	51.8*
5/25	113	3.81*	2.19	1.12	29.4	2.0	154	23.1	28.8	21.7*	8.8*	49	4.1	51.9*
5/27	116												4.6	49.2*
5/30	119												4.5	51.2*
6/4	124	3.76*	2.16	1.27	33.8	1.7	161*	47.1	45.6*	21.3*	7.2*	47	4.5	48.7*
6/16	136	3.25*	2.18	0.84*	25.8	2.6*	146	47.5	49.7*	16.5	7.2*	42	4.5	45.1*
6/28	147							21.7	31.6	25.3*	10.9*	44	4.1	49.3*
7/28	178	3.86*	2.82	0.68*	17.6*	4.2*	152	30.8	30.2	22.1*	8.7*	46	3.7	46.4*
8/3	184	3.53*	2.07	1.05	29.7	2.0	161*						5.3	55.5
Reference*		4–10	2–8	1–5	20–40	1.5–2.0	120–160	9–50	15–40	0–18.8	0–6.8	40–55	3.1–8	57–97

Abbreviations: WBC=white blood cell; N=neutrophil; L=lymphocytes; HB=hemoglobin; ALT=alanine aminotransferase; AST=aspartate aminotransferase; TBIL=total bilirubin; DBIL=direct bilirubin; ALB=albumin; BUN=blood urea nitrogen; Cr=creatinine.

* Laboratory values that are outside of the normal reference values for general population at Ditan Hospital.

SUPPLEMENTARY TABLE S3. Immune cells information in the peripheral blood from the patient.

Phenotype	Results of different date surveillance				Normal reference
Date (days after onset)	5/18 (107)	5/25 (114)	6/19 (139)	7/1 (151)	
CD3+ T cells	698*	801*	1,008*	767*	1,027–2,086 cells/μL
CD8+ absolute counts	297*	277*	227*	294*	320–1,250 cells/μL
CD8+/CD45+	28.1%	25.7%	15.8%	25.7%	15%–34%
CD4+ absolute counts	375*	487*	791	454*	706–1,125 cells/μL
CD4+/CD45+	35.4%	45.2%	54.8%*	39.7	30%–54%
CD4+/CD8+ ratio	1.3	1.8	3.5*	1.6	1–2
CD16+CD56+ absolute counts	113	140	48	NA	90–590 cells/μL
CD16+CD56+/CD45+	11	13	4*	NA	5%–27%
CD19+ absolute counts	111	87*	165	NA	90–660 cells/μL
CD19+/CD45+	11	8	13	NA	6%–25%

Note: For acquired immunodeficiency HIV patients, CD4 >350 cells/μL indicates immunocompetence.

Abbreviation: NA=not applicable.

* Values outside of the reference range in general population.

SUPPLEMENTARY TABLE S4. Neutralizing antibody titer in Geometric Mean Titers (GMT) from 10 blood samples from the patient.

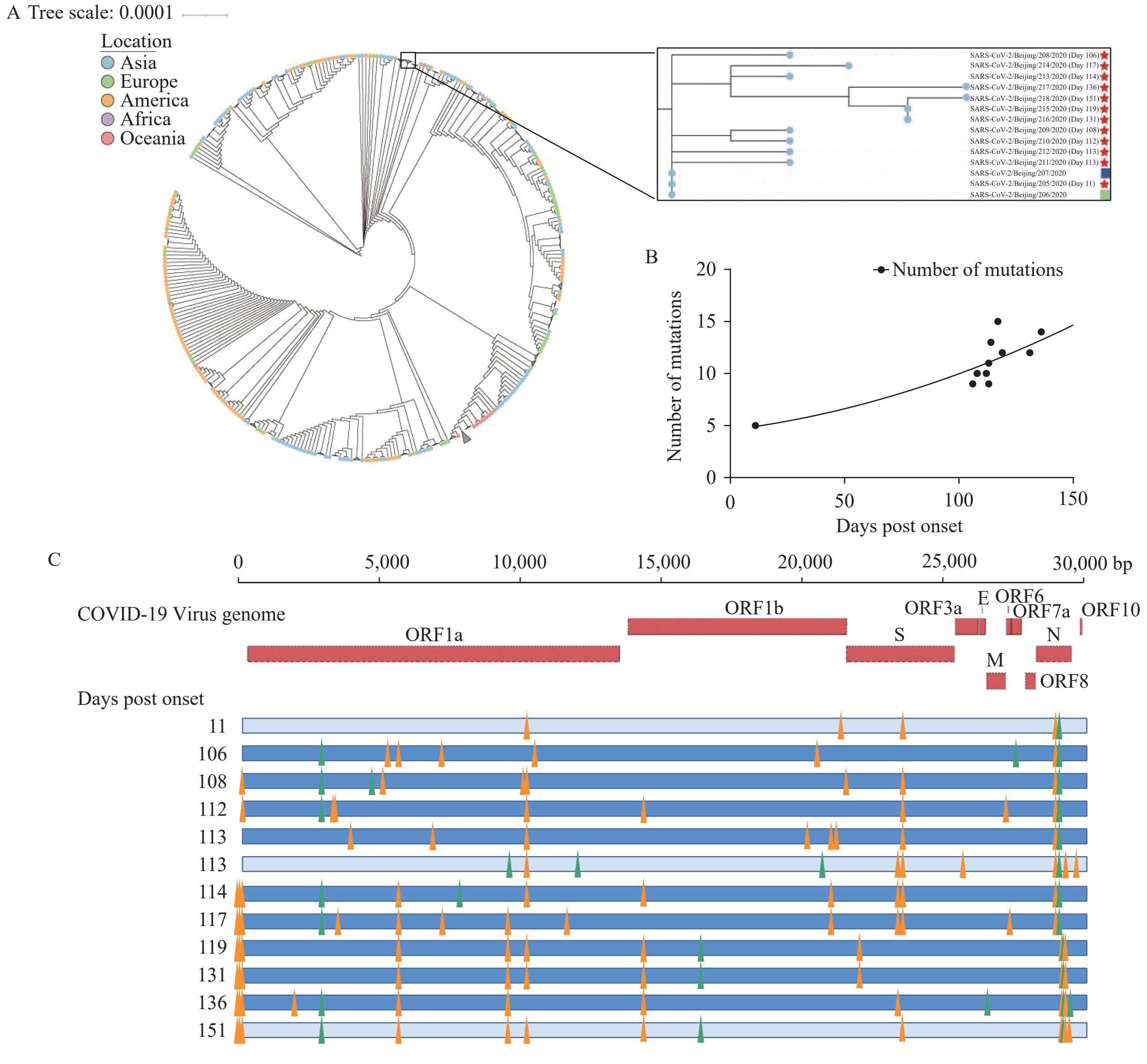
Date	Days from illness onset	Neutralizing Ab titer (1:)
2/14/20	13	2048
2/18/20	17	4,096
2/25/20	24	8,192
3/17/20	45	3,072
3/20/20	48	2,048
3/30/20	58	2,048
7/28/20	178	384
8/18/20	199	384
9/1/20	213	384
11/26/20	299	384

SUPPLEMENTARY TABLE S6. Cycle Threshold (Ct) values from 20 sputum samples of the patient.

Date	Date from illness onset	N gene	ORF 1ab gene
5/17/20	106	27.4	27.53
5/18/20	107	25.02	24.99
5/19/20	108	28.33	28.7
5/21/20	110	21.93	21.66
5/23/20	112	24.21	24.23
5/24/20	113	23.81	23.77
5/25/20	114	17.43	17.49
5/28/20	117	24.86	25.8
5/30/20	119	24.67	23.14
6/10/20	130	29.96	31.34
6/11/20	131	22.65	22.25
6/13/20	133	22.58	22.84
6/19/20	139	30.33	29.45
6/21/20	141	26.6	25.96
6/22/20	142	24.58	24.57
6/24/20	144	26.21	28.39
6/27/20	147	18.3	19.37
7/7/20	157	27.3	32.3
7/9/20	159	23.34	23.99
7/11/20	161	28.64	25.42

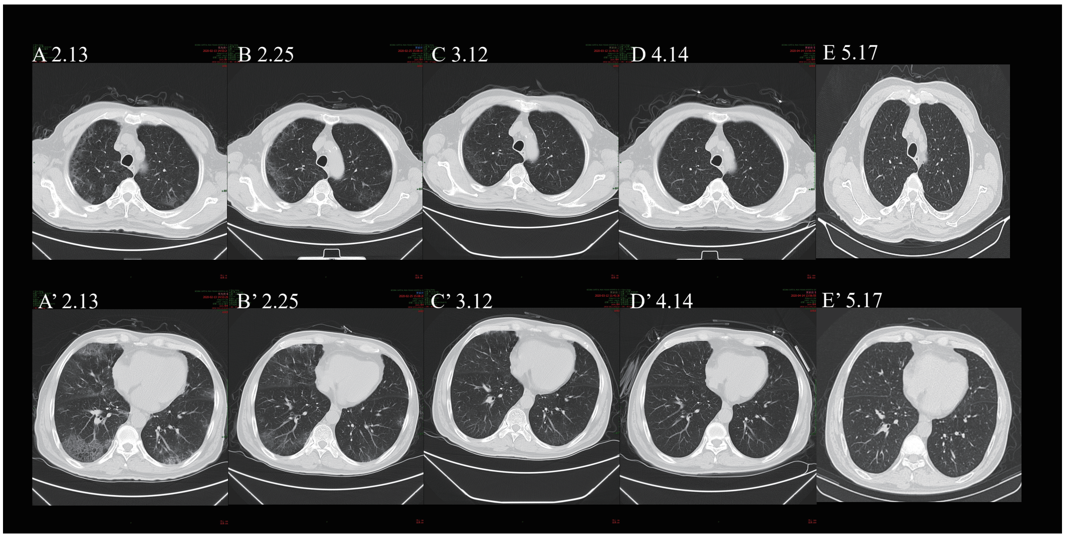
SUPPLEMENTARY TABLE S5. Cycle Threshold (Ct) values from 33 nasopharyngeal swab samples from the patient.

Date	Days from illness onset	N gene	ORF 1ab gene
2/18/20	17	25.98	30.44
2/22/20	21	33.02	>37
2/24/20	23	32.25	>37
3/12/20	37	29.77	27.75
3/13/20	41	27.89	27.74
3/23/20	51	31.89	36.71
3/28/20	56	28.8	29.79
3/30/20	58	32.05	31.33
4/1/20	60	31.48	>37
4/3/20	62	25.03	23.71
4/5/20	64	29.49	29.38
4/10/20	69	32.99	33.85
5/11/20	100	31.44	31.23
5/21/20	110	26.62	25.28
5/23/20	112	25.21	28.21
6/12/20	132	22.99	24.88
6/18/20	138	35.92	>37
6/18/20	138	26.64	29.03
6/22/20	142	23.4	27.94
6/25/20	145	25.54	25.71
6/29/20	149	26.23	26.7
6/30/20	150	23.28	24.94
7/1/20	151	28.11	29.16
7/4/20	154	28.77	32.43
7/9/20	159	24.68	24.08
7/12/20	162	>37	>37
7/13/20	163	>37	>37
7/28/20	178	36	>37
7/29/20	179	35	>37
8/5/20	186	>37	>37
8/18/20	199	>37	>37
9/1/20	213	>37	>37
11/26/20	299	>37	>37



SUPPLEMENTARY FIGURE S1. Genomic features of COVID-19 virus in serial samples of the patient from Day 11 to Day 151 after illness onset. (A) Phylogenetic tree of COVID-19 virus in serial samples from the study case (red stars) and single specimens 2 two of his family members (blues and green squares). The tree was constructed by the N-J method with bootstrap values determined with 1,000 replicates. (B) The number of mutations in serial samples derived from study case. (C) The distribution of mutations across the full COVID-19 virus genome.

Note: Missense mutations and synonymous mutations were indicated in orange and green, respectively. Sputum samples and throat swab samples are shown in dark blue and light blue, respectively.



SUPPLEMENTARY FIGURE S2. Computerized tomography scans change of the patient from February 13, 2020 to May 17, 2020 in 2 hospitals in Beijing. (A) and (A’), CT scans of the patient’s upper and lower lung on Feb 13. (B) and (B’), CT scans of upper and lower lung on Feb 25. (C) and (C’), CT scans of upper and lower lungs on March 12, the second hospital admission. (D) and (D’) CT scan of upper and lower lungs on April 14. (E) and (E’) CT scans of upper and lower lung on May 15.
Note: No signs of pneumonia were observed.

Commentary **Commemoration**

In Memory of Professor Hans Dieter Klenk

MOE & NHC Key Laboratory of Medical Molecular Virology Team[1]

Dr. Hans Dieter Klenk, an international renowned virologist, former President of the German Society of Virology, and a great friend and collaborator of scientists in China, passed away on June 02, 2021.

Hans Dieter Klenk studied medicine and biochemistry in Tübingen, Vienna, and Cologne. From 1967 to 1970, he was a visiting scientist in the laboratory of Purnell Choppin at Rockefeller University in New York. In 1973 and in 1985 he was a professor of virology at the Philipps University in Marburg and became Director of the Institute of Virology until his retirement in 2007.

Prof. Klenk's successful research concentrated on the role of the surface proteins hemagglutinin and neuraminidase in the pathogenesis of influenza. He was also interested in other emerging viruses that threaten public health and has established the central research direction of the Marburg Institute of Virology, which is still actively pursued today.

Prof. Klenk received numerous highly respected scientific awards, such as the Robert Koch Medal, the Ernst Jung Medal for Medicine, and the Emil von Behring Prize. He was awarded the Federal Cross of Merit 1st Class and the VCanBio International Collaboration Award.

Hans Dieter Klenk had a decisive influence on the Marburg Institute of Virology and established its international orientation and visibility. Under his leadership, numerous young scientists had the opportunity to develop their own scientific profile and to be appointed to leading positions nationally and internationally.

He coordinated numerous scientific consortia including the Collaborative Research Center 286 of the German Research Foundation and was active as chairman for the scientific advisory boards of several research institutions including Georg-Speyer-Haus, Feldberg Foundation for Anglo-German Scientific Exchange, Shanghai-Pasteur Institute, and the Key Laboratory Institute on Medical Molecular Virology of China.

During the outbreak of SARS, he led a group of Germen scientists to initiate Sino-German collaboration in studies on emerging infectious diseases. Furthermore, he served with Professor Yumei Wen as the founding co-editors-in-chief of the journal *Emerging Microbes & Infections*, which is now a well-recognized international scientific journal published by Taylor & Francis online.

Prof. Klenk leaves behind a huge legacy on a professional and personal level. His many publications, honors, and recognitions bear witness to his astuteness, precision, and nature of always questioning and seeking answers. His devotion to help others and his ardent pursuit for scientific problems has been a respectful model for all of us, and his memory will live on.

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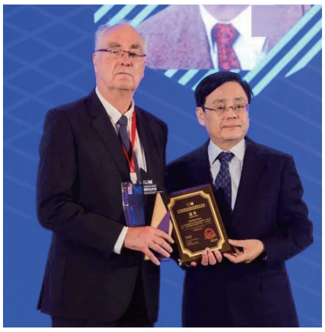
Prof. Hans Dieter Klenk gave a talk at a symposium in Shanghai, China (2018)

Prof. Hans Dieter Klenk with Prof. Yumei Wen in Tianjin, China

Prof. Hans Dieter Klenk with Prof. George F. Gao at VCanBio Award Ceremony (2018)



Prof. Wei He awarding Prof. Hans Dieter Klenk the VCanBio Award (2018)

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