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Clinical Features of the Initial Cases of 2009 Pandemic Influenza A (H1N1) Virus Infection in China

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ABSTRACT

BACKGROUND

The first case of 2009 pandemic influenza A (H1N1) virus infection in China was documented on May 10. Subsequently, persons with suspected cases of infection and contacts of those with suspected infection were tested. Persons in whom infection was confirmed were hospitalized and quarantined, and some of them were closely observed for the purpose of investigating the nature and duration of the disease.

METHODS

During May and June 2009, we observed 426 persons infected with the 2009 pandemic influenza A (H1N1) virus who were quarantined in 61 hospitals in 20 provinces. Real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing was used to confirm infection, the clinical features of the disease were closely monitored, and 254 patients were treated with oseltamivir within 48 hours after the onset of disease.

RESULTS

The mean age of the 426 patients was 23.4 years, and 53.8% were male. The diagnosis was made at ports of entry (in 32.9% of the patients), during quarantine (20.2%), and in the hospital (46.9%). The median incubation period of the virus was 2 days (range, 1 to 7). The most common symptoms were fever (in 67.4% of the patients) and cough (69.5%). The incidence of diarrhea was 2.8%, and the incidence of nausea and vomiting was 1.9%. Lymphopenia, which was common in both adults (68.1%) and children (92.3%), typically occurred on day 2 (range, 1 to 3) and resolved by day 7 (range, 6 to 9). Hypokalemia was observed in 25.4% of the patients. Duration of fever was typically 3 days (range, 1 to 11). The median length of time during which patients had positive real-time RT-PCR test results was 6 days (range, 1 to 17). Independent risk factors for prolonged real-time RT-PCR positivity included an age of less than 14 years, male sex, and a delay from the onset of symptoms to treatment with oseltamivir of more than 48 hours.

CONCLUSIONS

Surveillance of the 2009 H1N1 virus in China shows that the majority of those infected have a mild illness. The typical period during which the virus can be detected with the use of real-time RT-PCR is 6 days (whether or not fever is present). The duration of infection may be shortened if oseltamivir is administered.

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In early April 2009, cases of human infection with 2009 pandemic influenza A (H1N1) virus were identified in the United States[1,2] and Mexico,[3] and the virus then spread rapidly to other regions of the world.[4,5] The 2009 H1N1 virus is a triple-reassortant influenza virus containing genes from human, swine, and avian influenza viruses.[6-8] After documentation of human-to-human transmission of the virus in at least three countries in two of the six world regions defined by the World Health Organization (WHO), the WHO raised the pandemic level from 5 to 6, the highest level.[9]

The first three cases of confirmed infection with the virus in China were documented between May 10 and May 15, 2009.[10] Since this was a new and potentially serious infectious disease, all patients with confirmed infection who had been hospitalized were quarantined in the hospital to isolate them from the general population. The hospital quarantine allowed us to closely monitor patients, tracking the incubation period of the disease, its clinical features, the results of laboratory and radiographic tests, and the nature and extent of viral shedding. This report describes the clinical and epidemiologic characteristics of the first 426 patients hospitalized in China from May to June 2009 with confirmed cases of 2009 pandemic influenza A (H1N1) virus infection.

Methods

Data Sources

On May 7, 2009, a national network was organized to monitor infection with the 2009 pandemic influenza A (H1N1) virus in China. The network included the Chinese Ministry of Health, the Chinese Center for Disease Control and Prevention, and all community and teaching hospitals in China. A national guideline, adapted from guidelines provided by the U.S. Centers for Disease Control and Prevention, was published on May 9 and used to direct the surveillance, reporting, diagnosis, and treatment of the disease. A suspected case was defined as an influenza-like illness (temperature ≥37.5°C and at least one of the following symptoms: sore throat, cough, rhinorrhea, or nasal congestion) and either a history of travel to a country where infection had been reported in the previous 7 days or an epidemiologic link to a person with confirmed or suspected infection in the previous 7 days. A confirmed case was defined by a positive result of a real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay performed at a laboratory operated under the auspices of the Chinese Center for Disease Control and Prevention. A close contact was defined as a person who lived with or was exposed to the respiratory secretions or other bodily fluids of someone with suspected or confirmed infection.

Thermal scanners were installed at all airports and ports of entry to China. Persons suspected of being infected and persons identified as close contacts were quarantined for 7 days, during which time pharyngeal or nasopharyngeal swabs were collected for detection of the virus by means of a real-time RT-PCR assay. The average time between obtaining the samples and testing was 1 to 2 hours. There are 63 laboratories operated by the Chinese Center for Disease Control and Prevention across China, all of which are located in large cities. Persons with confirmed cases of infection were admitted to infectious diseases hospitals, where they could be quarantined.

The incubation period was defined as the time from exposure to the onset of illness. Patients were followed until discharge, with symptoms and signs recorded daily. The details of all investigations and treatments were recorded. Serial pharyngeal or nasopharyngeal swabs were analyzed daily for the presence of 2009 pandemic influenza A (H1N1) virus with the use of real-time RT-PCR testing. A return to normal body temperature was defined as a temperature of less than 37.3°C for 12 hours after the withdrawal of any antipyretic treatment. The criteria for discharge (as defined in the guideline) were two readings of normal body temperature taken on 2 consecutive days, the absence of respiratory symptoms, and negative results on the testing of samples from two consecutive pharyngeal or nasopharyngeal swabs.

Data collection and analysis were coordinated by the Chinese Ministry of Health. The medical records of patients discharged before June 30 were copied and sent to the data-collection center in Beijing. Data were reviewed by a trained team of physicians and medical students and entered in duplicate into a computerized database. Patient confidentiality was maintained by recording only the date of birth and sex on the data-collection form. The research ethics board at Beijing Ditan

Figure 1. Distribution of 426 Confirmed Cases of Human Infection with 2009 Pandemic Influenza A (H1N1) Virus Identified in China during the Study Period.

Numbers in parentheses indicate the number of confirmed cases from each region.

Hospital approved the study design. Approval by the institutional review boards at participating hospitals was not required because of the general acknowledgment that it was in the interest of the public health to collect data on an emerging pathogen.

LABORATORY CONFIRMATION OF INFECTION

The 2009 H1N1 virus was detected with the use of a real-time RT-PCR assay in accordance with the protocol from the U.S. Centers for Disease Control and Prevention, as recommended by the WHO.[11] The PCR products were sequenced for further confirmation with the use of the BigDye Terminator, version 3.1 Cycle Sequencing Kit (Applied Biosystems) in accordance with the manufacturer's instructions.

STATISTICAL ANALYSIS

Continuous variables were summarized as means (±SD) or medians (with interquartile ranges). For categorical variables, the percentages of patients in each category were calculated. Clinical characteristics were compared between subgroups of patients with and those without fever and between patients with and those without a diagnosis of pneumonia with the use of an unpaired Student's t-test, chi-square test, or Fisher's exact test, as appropriate.

Multiple logistic-regression analysis was used

to identify independent predictors of viral-shedding time among patients receiving treatment with oseltamivir. The outcome was predicted with the use of factors such as age, sex, severity or number of symptoms (e.g., fever, cough, sore throat, or cough with production of sputum), and the interval between symptom onset and initiation of oseltamivir therapy (less than or more than 48 hours). A P value of less than 0.05 was considered to indicate statistical significance. All analy-

Table 1. Characteristics, Underlying Medical Conditions, and Outcomes of 426 Patients Infected with 2009 Pandemic Influenza A (H1N1) Virus in China (May–June 2009).*

Characteristic	Value
Male sex — no. (%)	229 (53.8)
Age — yr	
Mean	23.4±14.3
Range	0.6–74.8
Age group — no. (%)	
<5 yr	15 (3.5)
5–14 yr	100 (23.5)
15–30 yr	207 (48.6)
31–50 yr	78 (18.3)
51–65 yr	21 (4.9)
>65 yr	5 (1.2)
Race or ethnic group — no. (%)†	
Chinese Han	345 (81.0)
White	65 (15.3)
Southeast Asian	16 (3.8)
Coexisting conditions — no. (%)	
Hypertension	15 (3.5)
Asthma	7 (1.6)
Diabetes	3 (0.7)
Cancer	2 (0.5)
Coronary heart disease	2 (0.5)
Chronic obstructive pulmonary disease	1 (0.2)
Chronic nephritis	1 (0.2)
Venue in which case was identified — no. (%)	
Fever clinic at general hospital	200 (46.9)
At port of entry	140 (32.9)
During quarantine	86 (20.2)
Recent travel to infected region — no. (%)‡	
None	100 (23.5)
United States	183 (43.0)
Canada	64 (15.0)
Australia	58 (13.6)
Singapore	4 (0.9)
Philippines	4 (0.9)
Argentina	3 (0.7)
Other	10 (2.3)

Table 1. (Continued.)

Characteristic	Value
Incubation period — days§	
Median	2
Range	1–7
Exposure site — no./total no. (%)	
Airplane	60/148 (40.5)
Home	25/148 (16.9)
Classroom or office	13/148 (8.8)
Car, train, or bus	20/148 (13.5)
Restaurant	4/148 (2.7)
Outcomes — days	
Duration of fever	
Median	3.0
Range	1–11
Viral shedding verified with real-time RT-PCR testing	
Median	6
Range	1–17
Interval between temperature returning to normal and negative real-time RT-PCR test result	
Median	3
Range	<1–13
Adverse events — no. (%)¶	
Abnormal liver function	2 (0.5)
Nausea and vomiting	2 (0.5)
Rash	1 (0.2)

* Plus–minus values are means ±SD. RT-PCR denotes reverse-transcriptase–polymerase-chain-reaction.
† Race and ethnic group were self-reported. Southeast Asia includes the regions south of China and Taiwan, east of India, and north of Australia.
‡ An infected region was defined as an area where one or more confirmed cases of 2009 pandemic influenza A (H1N1) virus infection had been found in the preceding 7 days. The category of Other included England (two patients), Indonesia (two), Korea (one), New Zealand (one), Greece (one), Israel (one), Yemen (one), and Venezuela (one).
§ Data on the incubation period were available for 125 patients who could clearly recall their exposure history. The incubation period was defined as the time from exposure to the onset of illness.
¶ Among the five patients who had adverse events, two were taking oseltamivir alone and three were taking oseltamivir plus levofloxacin or azithromycin. In the two patients with abnormal liver function, one was taking oseltamivir alone and one oseltamivir plus levofloxacin. In the two patients with nausea and vomiting, one was taking oseltamivir alone and one oseltamivir plus levofloxacin. The patient with a rash was taking oseltamivir and azithromycin.

ses were carried out with the use of SPSS software for Windows (release 13.0).

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS

Sixty-one major hospitals located in 20 provinces across the country were involved in the emergency public health response. The first case of confirmed imported infection was identified on May 10, 2009, and the first secondary case of confirmed infection (in a patient with known exposure to a person with imported infection) was identified on May 29. The first domestic case — in which the person infected had no clear history of exposure — was reported on June 13. On mainland China, there were 22 laboratory-confirmed cases in May and 544 such cases in June. By August 10, a total of 20,329 close contacts had been tested for 2009

Table 2. Clinical Features of Infection in the 426 Patients.*

Symptom or Sign	Present on Admission	Median Duration
	no./total no. (%)	*days (IQR)*
Symptom		
Elevated temperature		3 (2–4)
37.3–38.0°C	134/426 (31.5)	
38.1–39.0°C	114/426 (26.8)	
>39.0°C	39/426 (9.2)	
Cough	296/426 (69.5)	5 (3–6)
Sore throat	156/426 (36.6)	4 (2–5)
Sputum production	104/426 (24.5)	4 (2–6)
White sputum	54/104 (51.9)	NA
Yellow sputum	50/104 (48.1)	NA
Rhinorrhea	101/426 (23.7)	3 (2–5)
Headache	83/426 (19.5)	2.5 (1–4)
Nasal congestion	68/426 (16.0)	3 (2–4)
Fatigue	44/426 (10.3)	3 (1–4)
Myalgia, arthralgia	43/426 (10.1)	3 (2–4)
Chill	32/426 (7.5)	NA
Conjunctival congestion	12/426 (2.8)	2 (1–3)
Diarrhea	12/426 (2.8)	1.5 (1–3.5)
Nausea, vomiting	8/426 (1.9)	NA
Chest pain	2/426 (0.5)	6.5 (6–7)
Sign		
Congestion of throat	319/426 (74.9)	4 (3–6)
Swelling of tonsils	319/426 (74.9)	4 (3–6)
Enlargement of lymph nodes	3/426 (0.7)	5 (4–5)

* IQR denotes interquartile range, and NA not available.

pandemic influenza A (H1N1) virus infection during quarantine; test results were positive for 797 persons (3.9%). By August 23, a total of 56 million travelers had been screened at ports of entry, and 17,909 with a febrile respiratory illness were tested for infection with the virus; test results were positive for 757 persons (14 per 1 million).

Data from the first 426 patients with confirmed cases of infection who were hospitalized in May or June were available for analysis; 153 patients were from Beijing, 71 from Guangdong, 69 from Shanghai, 40 from Fujian, and 93 from various other provinces (Fig. 1). (Demographic details, underlying medical conditions, and outcomes are listed in Table 1.) The majority of the patients (81%) were Han Chinese, and 15.2% were white. The median incubation period was 2 days (range, 1 to 7). As shown in Table 2, 67.4% of patients had a fever. Less common symptoms included nausea, vomiting, and diarrhea. (A comparison of symptoms and duration of disease in patients with fever and those without fever is presented in Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.) Headache and lymphopenia were more common in patients with fever.

LABORATORY AND RADIOGRAPHIC FINDINGS

Mild leukopenia was observed in 21.4% of 412 patients, and lymphopenia in 68.1% of adult patients and 92.3% of children (Table 3). Data on the ratio of CD4 cells to CD8 cells were available

Table 3. Laboratory and Radiographic Findings on Admission.*

Variable	Value
Leukocyte count	
Mean count — per mm³	3440±220
<4000/mm³ — no./total no. (%)	88/412 (21.4)
>10,000/mm³ — no./total no. (%)	12/412 (2.9)
Lymphocyte count	
Mean count — per mm³	1399.34±776.73
<1500/mm³ in adults — no./total no. of adults (%)†	201/295 (68.1)
<3000/mm³ in children — no./total no. of children (%)	96/104 (92.3)
CD4 T-lymphocyte count — per mm³	576.65±295.27
CD8 T-lymphocyte count — per mm³	436.11±263.26
CD4:CD8 ratio <1.4 — no./total no. (%)	106/212 (50)
Hemoglobin — g/liter	135.12±14.89
Platelet count — per mm³	201,200±59,000
Creatine kinase >200 U/liter — no./total no. (%)	16/115 (13.9)
Creatine kinase MB fraction >25 U/liter — no./total no. (%)	12/88 (13.6)
Lactate dehydrogenase — U/liter	184.83±47.75
Glucose — mmol/liter	5.51±3.23
Alanine aminotransferase >40 U/liter — no./total no. (%)	31/352 (8.8)
Aspartate aminotransferase >40 U/liter — no./total no. (%)	35/345 (10.1)
Total bilirubin >17.1 μmol/liter — no./total no. (%)	19/326 (5.8)
Potassium	
Mean value — mmol/liter	3.78±0.38
<3.5 mmol/liter — no./total no. (%)	88/347 (25.4)
Sodium — mmol/liter	139.27±4.29
Chloride — mmol/liter	102.65±3.76
Erythrocyte sedimentation rate — no./total no. (%)	
>15 mm/hr in male patients	8/41 (19.5)
>20 mm/hr in female patients	11/36 (30.6)
C-reactive protein >10 mg/liter — no./total no. (%)	68/217 (31.3)
Creatinine — μmol/liter	67.17±20.16
Abnormalities on chest radiograph — no./total no. (%)	14/273 (5.1)
Local patchy shadowing	12/14 (85.7)
Ground-glass opacities	1/14 (7.1)
Interstitial abnormality	1/14 (7.1)
Abnormalities on chest CT — no./total no. (%)	6/82 (7.3)
Local patchy shadowing	5/6 (83.3)
Ground-glass opacities	1/6 (16.7)

* Plus–minus values are means ±SD. To convert the values for glucose to milligrams per deciliter, divide by 0.05551. To convert the values for bilirubin to milligrams per deciliter, divide by 17.1. To convert the values for creatinine to milligrams per deciliter, divide by 88.4. CT denotes computed tomography.
† An adult was defined as a patient who was 14 years of age or older.

for 212 patients, half of whom had an abnormal CD4:CD8 ratio (<1.4). Among the patients with leukopenia, the condition developed 2 days (range, 1 to 3) after the onset of illness, and white-cell counts returned to normal 7 days (range, 6 to 9) after the onset of illness. Abnormalities in chest radiography were detected in 19 of 273 patients on admission or after hospitalization. The most common features of these abnormalities appeared as local patchy shadowing on radiography (see Fig. 1 in the Supplementary Appendix). Diarrhea was more common in patients with pneumonia, but no significant variation in clinical features between patients with and those without pneumonia was found (see Table 2 in the Supplementary Appendix). Hypokalemia was present in 25.4% of the patients.

CLINICAL OUTCOMES

All 426 patients were discharged home. The median duration of fever was 3 days (range, 1 to 11). The median time from the onset of the first symptoms of illness to the first positive real-time RT-PCR test result for the virus was 1 day (range, 0 to 2). Treatment with oseltamivir was administered in a total of 351 patients and was administered to 254 of these patients (72.4%) within 48 hours after the onset of illness.

The results of serial virologic testing of samples from pharyngeal or nasopharyngeal swabs with the use of real-time RT-PCR were available for 421 patients. The median time from the onset of illness to a negative test result for real-time RT-PCR was 6 days (range, 1 to 17). The median interval from the time the temperature returned to normal to the time at which a negative test result was obtained was 3 days (with an interval of <1 day for 10.9% of patients; 1 to 2 days, 31.9%; 3 to 5 days, 45.0%; 6 to 7 days, 8.2%; and >7 days, 4.0%). In total, 96.0% of patients had a negative test result on real-time RT-PCR within a week after their temperature returned to normal. The results of a univariate analysis of the risk of persistent real-time RT-PCR positivity for the virus (>5 days) are shown in Table 3 in the Supplementary Appendix. Multivariable logistic-regression analysis showed that the following were independent risk factors for prolonged infection with the virus on the basis of real-time RT-PCR test results: an age of less than 14 years (odds ratio, 1.94; 95% confidence interval [CI], 1.13 to 3.31; P=0.02), male sex (odds ratio, 1.69; 95% CI, 1.07 to 2.66; P=0.02), and a period of more than 48 hours between the onset of disease and treatment with oseltamivir (odds ratio, 4.46; 95% CI, 2.58 to 7.72; P<0.001) (Table 4).

Adverse events occurred in five patients, two of whom were taking oseltamivir alone and three of whom were taking oseltamivir plus levofloxacin and azithromycin. Nausea and vomiting occurred in one patient taking oseltamivir alone and one patient taking oseltamivir plus levofloxacin, and oseltamivir was discontinued in both patients. Abnormal liver function (elevated levels of serum liver enzymes or bilirubin) occurred in one patient taking oseltamivir and one patient taking oseltamivir plus levofloxacin, and rash occurred in one patient taking oseltamivir plus azithromycin. All complications were mild and resolved spontaneously before discharge.

DISCUSSION

We describe a cohort of 426 patients identified in 20 provinces in China who were hospitalized for 2009 pandemic influenza A (H1N1) virus infection between May and June 2009. The decision to undertake stringent quarantine and isolation measures regarding these patients was based on the unknown biologic action of the virus and the absence of effective vaccination. Since July 10, 2009, hospitalization for the purpose of isolation has not been mandated in China. Public health measures have instead focused on managing clusters of infection and complications of the illness in certain patients.

To date, it has been difficult to define the true incubation period of the virus.[6,12-14] Analysis of 642 cases from the United States[6] suggested an incubation period of 2 to 7 days. Close observation of confirmed cases in China provided the opportunity to investigate the incubation period in 125 patients with an exact date of onset of illness. The median incubation period was 2 days, with a range of 1 to 7 days.

As compared with patients in the United States[6] and Japan[13] and those in Mexico and other countries,[14] fewer patients in our cohort (67.4%, vs. 94% in the United States) presented with fever. The incidence of nausea, vomiting, and diarrhea was also much lower than previously reported. In our cohort, 21.4% of 412 patients had leukopenia (white-cell count, <4000 per cubic millimeter), and 68.1% of adults and 92.3% of children had lymphopenia (total lymphocyte count, <1500 per cubic

millimeter in adults and <3000 in children). None of the patients had thrombocytopenia (total platelet count, <100,000 per cubic millimeter). The lymphopenia was transient. Both leukocytosis and leukopenia were reported in hospitalized patients in California.[15] An abnormal ratio of CD4:CD8 cells (<1.4) was present in half of our patients. These transient alterations in the numbers of peripheral-blood leukocytes are similar to those seen in cases of seasonal influenza; Fas–Fas ligand signaling, which induces apoptosis, plays a major role in the mechanisms regulating the leukocyte population.[16] Hypokalemia was documented in 25.4% of our patients as compared with 43 to 90% of patients with severe acute respiratory syndrome (SARS) during hospitalization.[17,18] The mechanism of hypokalemia is unknown.

Nineteen patients had abnormalities on chest radiography, but, unlike patients with the H1N1 virus in Mexico,[19] none had severe pneumonia. The viral infection in patients with pneumonia had no distinguishing epidemiologic, clinical, or laboratory features. However, the sample was small. Patients with pneumonia recovered quickly. This may be due in part to early laboratory diagnosis and early treatment with oseltamivir. With the use of real-time RT-PCR testing at both local branches and the laboratory at the Chinese National Influenza Center in Beijing, the Chinese Center for Disease Control and Prevention requires a median time of just 1 day from the onset of illness to confirm the diagnosis.

Of the 19 patients with pneumonia, 18 were given oseltamivir within 48 hours after the onset of illness. In Mexico,[19] the time between the onset of symptoms and admission to the hospital ranged from 4 to 25 days (median, 6), all patients had an influenza-like illness at presentation that progressed over a period of 5 to 7 days, none of the patients received oseltamivir before admission, and 11 began receiving oseltamivir 8 days after the onset of symptoms. According to the WHO guidelines on the pharmacologic management of influenza virus, patients who are at risk for pneumonia should be treated with oseltamivir or zanamivir as soon as symptoms develop, if possible.[20] At present, however, the quality of the evidence supporting such recommendations is low. Observational studies of seasonal influenza have shown a reduction in progression to severe disease and hospitalization in patients treated with antiviral drugs, but additional randomized controlled trials are needed to evaluate the efficacy of these drugs in the treatment of both the seasonal flu and 2009 pandemic influenza A (H1N1) virus infection. The benefits of antiviral treatment should also be balanced against feasibility (i.e., the availability of the drug), the risk of resistance, and the cost to and demand on the health care system.

Table 4. Risk of Viral Shedding for More Than 5 Days.*

Variable	Viral Shedding for More Than 5 Days (N=350)	
	Odds Ratio (95% CI)	P Value
Age		0.02
<14 yr	1.94 (1.13 –3.31)	
≥14 yr	1.00	
Sex		0.02
Male	1.69 (1.07–2.66)	
Female	1.00	
Fever		0.82
Yes	1.10 (0.50–2.41)	
No	1.00	
Cough, sore throat, or sputum production		0.09
Yes	1.58 (0.93–2.70)	
No	1.00	
Interval from symptom onset to oseltamivir therapy		<0.001
>48 hr	4.46 (2.58–7.72)	
≤48 hr	1.00	

* Data are from a multivariate logistic-regression analysis. Viral shedding was assessed on the basis of the results of reverse-transcriptase–polymerase-chain-reaction testing.

Our study shows that the average duration of 2009 pandemic influenza A (H1N1) virus shedding, according to the results of PCR testing, is 6 days. Although a positive result of real-time RT-PCR testing does not necessarily indicate shedding of infective virus, PCR is more sensitive than culture for viral detection.[21] Using a positive result of real-time RT-PCR testing for 2009 pandemic influenza A (H1N1) virus infection within 5 days after symptom onset as a primary outcome, our study shows that beginning oseltamivir therapy within 48 hours after the onset of symptoms can reduce the duration of viral shedding (as measured by real-time RT-PCR assay).[22] The median interval from normalization of body temperature to a negative real-time RT-PCR test result was 3 days,

with negative results obtained within 5 days for 87.9% of the study patients and within 7 days for 96.0%. This suggests that 96.0% of patients are no longer infectious and can return to work or school within a week after their temperature returns to normal.

Our study has some limitations. First, the cases of infection in our patients are not clinically comparable with those in hospitalized patients in the United States or Mexico because of differences in hospitalization practices. Second, patients who became infected in their community and did not go to the hospital were not included in our study. Finally, although early treatment with oseltamivir did reduce the duration of viral shedding, the feasibility of its use, the risk of resistance, and the potential cost to and demand on the health care system remain concerns.

In conclusion, close observation of patients infected with the 2009 pandemic influenza A (H1N1) virus provided us with an accurate estimate of the incubation period and the duration of positive results of real-time RT-PCR testing. Late initiation of oseltamivir therapy (>48 hours after the onset of illness) was an independent risk factor for prolonged RT-PCR positivity.

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APPENDIX

The National Influenza A Pandemic (H1N1) 2009 Clinical Investigation Group of China functions under the auspices of the Chinese Ministry of Health to guide efforts on the surveillance, reporting, diagnosis, and treatment of 2009 pandemic influenza A (H1N1) virus infection in China. The group members and their affiliations are as follows: L. Guo, S. Zhang, B. Zhang, L. Lu, Y. Mao, X. Li (Beijing Ditan Hospital, Institute of Infectious Diseases, Capital Medical University); J. Wang (Eighth Hospital of Guangdong); H. Lu (Shanghai Public Health Clinical Center); H. Wen (Fuzhou Pulmonary Hospital of Fujian); Y. Chen (Fujian Provincial People's Hospital); Z. Liang (West China Medical School, West China Hospital, Sichuan University); K. Hu (Hubei Provincial People's Hospital); J. Yan (Zhejiang Provincial People's Hospital); M. Wu (Hainan Provincial People's Hospital); Z. Du (Tianjin Haihe Hospital); J. Du (Affiliated Hospital of Guizhou Medical College); W. Zhao (Second Hospital of Nanjing); Z. Li (Shengjing Hospital of China Medical University); D. Gao (Jinan Chest Hospital); D. Tan (Xiangya Hospital of Central-South University); M. Fan (Fourth Hospital of Taiyuan); W. Zhang (First Hospital of Nanchang University); X. Ma (Henan Provincial People's Hospital); W. Huang (First Affiliated Hospital of Chongqing Medical University); H. Li (Yunnan Provincial Infectious Disease Hospital); G. Wang, X. Xu (Peking University First Hospital); H. Wu (Beijing Youan Hospital, Capital Medical University); Z. Gao (Peking University People's Hospital); M. Zhao (Peking University Third Hospital); W. Zhang, Y. Zhang (Chinese Center for Disease Control and Prevention); Y. Shu, D. Wang (Chinese National Influenza Center, Chinese Center for Disease Control and Prevention); G. Deng (Peking Union Medical College Hospital); M. Zhao (Military Hospital 302, Beijing); D. Ma (Beijing Youyi Hospital, Capital Medical University); B. Cao, L. Liang, L. Gu, Z. Cao, T. Yang, X. Zhai, C. Wang (Beijing Chao-Yang Hospital, Beijing Institute of Respiratory Medicine, Capital Medical University) — all in China.

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