Interventions and Respiratory Specimen Screening of Close Contacts to Control an Outbreak of Pandemic Influenza A (H1N1) Virus in a Tour Group, China, 2009

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Introduction

Pandemic influenza A (H1N1) (2009 H1N1) has emerged and spread rapidly among people worldwide since mid-Apr 2009, with over 18,036 deaths reported from 214 countries as of 9 May 2010[1]. Based on the epidemiologic data, 2009 H1N1 is believed to spread in similar ways as seasonal influenza virus, mainly through droplet route and close contact with infected cases during the infectious period[2], yet clinically indistinguishable from seasonal influenza. However, when outbreaks caused by the virus spread globally[3-4], a quick response and appropriate interventions are necessary.

In mainland China, the first case of 2009 H1N1 virus infection was identified in Sichuan Province on 9 May 2010[5]. The province subsequently experienced a rapid increase in infected cases, notably involving a tour group with 30 members during 2-8 Jun 2009[6]. As a response, close contact tracing and 7-days medical observation were implemented as soon as the outbreak was detected. Meanwhile, respiratory specimen screening was also conducted among close contacts to control spreading of infection. The results of that effort were reported and measures imposed on this 2009 H1N1 outbreak of the tour group were described to provide as a reference and experiences for response to similar outbreaks.

Methods

Outbreak Investigation[6]

The tour group departed on 3 Jun 2009 from Chengdu to Jiuzhaigou, and returned on 5 Jun 2009. During the three-day trip, air-conditioned bus was the major vehicle that took the tour group members to each scenic spot. There were no assigned seats on the bus and seating changes became possible after each stop.

The index case-patient of 2009 H1N1 infection developed illness during flight from Chengdu to Jiuzhaigou, and joined the tour group with her husband and daughter the next day. She stayed together with the tour group most of the time. She presented at a hospital on 5 Jun 2009, accompanied by her family, and was reported and isolated for treatment on the same day.

Secondary cases were nine (30%) tour group members who had talked with the index case-patient, and one airline passenger who was not a tour group member and sat two rows away from her in the flight. None of the 14 tour group members who had not talked with the index case-patient became ill.

Definition and Classification of Close Contact

Generally, once the index case is detected, the case definition for outbreak control and close contact tracing should be established[7]. The infectious period of a confirmed case-patient is defined to be one day prior to and through seven days after onset of illness or resolution of symptoms, whichever is longer[8]. Here, the infectious period for the index case-patient was from 1 to 5 Jun 2009, when the index case-patient was isolated. Potential close contacts were classified into five categories according to WHO guideline[9]: health care workers (HCW), household, tour group, passengers and social contacts. In order to compare the interventions taken with the close contacts, the five categories were, then, grouped into three groups according to the documented or general perception of decreased risk of infection.

Group I (HCW): Any doctor, nurse or staff who worked in the hospital and provided direct medical service to a confirmed case-patient without appropriate Personal Protective Equipments (PPEs).

Group II (Household and tour group close contacts): Tourists and the tour guide traveling together every day who had higher chance to closely contact with other group members, including direct physical contact, indirect close contact (<2 m) and face-to-face conversations. A household close contact was defined as a relative or family member living together with confirmed case-patient.

Group III (Passengers and close social contacts): A passenger close contact was defined as any crew who provided face-to-face service to confirmed case-patient or any passenger seated in the same row or within three rows in front of or behind confirmed

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case-patient. A social close contact was defined as a person, besides the previous four types of close contacts, known to have been within two meters of the index case-patient or of a secondary case for any length of time during infectious period, including bus passengers, co-workers, restaurant waiters and taxi drivers.

Close Contact Tracing and Medical Observation

Information from HCW close contact was collected during field investigation in hospital and was double-checked with information obtained from interview with case-patients. Information of household close contact was obtained directly from interview with case-patients. Registration and contact information of tour group close contacts was collected from interview with case-patients and the travel agency. The information of passengers and air crews was gathered from the airports and airline company.

Detailed information on exposure was double-checked with information from interview of case-patient. Close social contact information was collected from related institutions and agencies, such as bus and taxi companies, where case-patients had worked, visited, or used their vehicles. Subsequently, China CDC staff tried to contact the identified close contacts and double-checked the information by telephone. If no telephone number was available, CDC staff would visit the close contacts in person.

Afterwards, close contacts were gathered at designated places, such as hospital or hotel, for seven-day medical observation. A set of structured questionnaire was used to collect demographic and exposure information from each close contact during medical observation. Some close contacts were instructed to stay at home for seven days. Interview with the questionnaire was conducted by face-to-face interview or telephone.

Contacts who developed febrile respiratory illness within seven days were considered as suspected cases of 2009 H1N1, which was defined as a patient with fever (temperature 37.5°C), and/or recent onset of at least one of the followings: rhinorrhea, nasal congestion, sore throat, or cough, and were immediately admitted to a designated hospital and placed in a private room or a room with negative pressure if available, for isolation and antiviral treatment. All HCW caregivers followed standard precautions of contact and respiratory infection control such as wearing N95 mask and PPE for possible risk of aerosol transmission of virus[10]. A confirmed case was defined as a suspected case with laboratory evidence of 2009 H1N1 virus infection diagnosed by real-time Reverse Transcriptase Polymerase Chain Reaction (rRT-PCR) test in laboratory examination of respiratory specimens.

Respiratory Specimen Screening

To determine the infection and clarify the diagnosis, a respiratory specimen screening regimen was implemented, including collection of sequential throat swabs from all close contacts. The first throat swab was collected as soon as the person was identified as a close contact by the trace back investigation. Subsequent throat swabs were collected during medical observation.

All specimens were placed in sterile viral transport medium for 2009 H1N1 virus testing following a standard protocol. RNA was extracted and tested by rRT-PCR with pandemic 2009 H1N1-specific primers and probes following the WHO protocol. These assays were performed at biosafety level (BSL) two facilities in Sichuan Centers for Disease Control and Prevention.

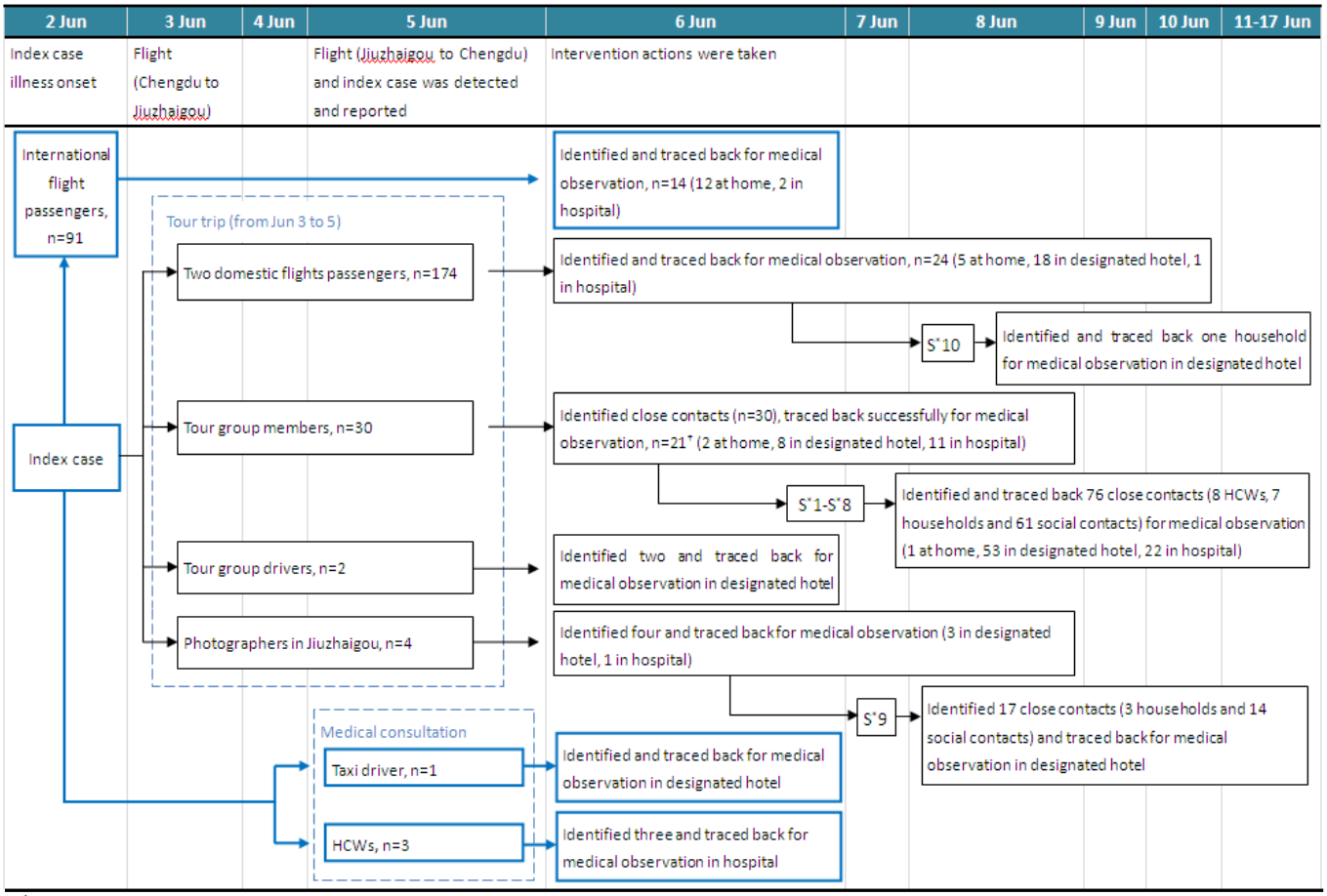
Statistical Analysis

Median and range values were used for continuous variables and medians were compared between the three close contact groups with the Wilcoxon rank sum test. Positive proportion and 95% confidence intervals were calculated according to the binomial distribution. Frequencies and percentages for each of the three close contact groups were calculated and compared using the Chi-square test; Fisher's exact test was employed when cells had less-than-five frequency. All statistical tests were two-sided with a significance level set at 0.05.

Results

This is the first known outbreak of 2009 H1N1 in China among tourist group[6]. From 6 to 8 Jun 2009, a total of 172 close contacts were identified. Among them, 163 (95%) were successfully traced back for medical observation by 17 Jun 2009 (Figure 1 and table 1).

During the medical observation, 11 contacts developed symptoms and were classified as suspected case-patients; 10 of the 11 (91%) were confirmed as secondary cases. The remaining one suspected case-patient was a 26-year-old woman who was a friend of secondary case 6 and joined the same tour group with the index case.



* S denotes secondary case.

† Nine of 21 (43%) tour group members were not successfully contacted and placed under medical observation before returning home, because these nine tour group members left Chengdu on the same day that the index case was detected. As for their destinations, two went to Liaoning Province, two to Chongqing municipality, two to Xinjiang Province, two to Hubei Province and one to Singapore. We contacted local health authorities to follow up their health status. Of these nine tourists outside Sichuan, eight were placed under medical observation at home or in a designated hotel for seven days at once by provincial CDCs in Mainland China, and no one developed symptoms during medical observation. However, the person who returned to Singapore could not be traced back. Sichuan CDC notified the diplomatic affairs agency so that Singapore could implement close contact tracing and medical observation.

Figure 1. Flow chart of close contact tracing and components of a 2009 H1N1 tour group outbreak in China, 2009

During the medical observation, being without fever, she began to cough on the second day after her last exposure. Three throat swabs were collected from her; one each on the second, fourth and fifth day after her last exposure. She was excluded from 2009 H1N1 virus infection because all swabs were tested negative.

Of the 163 close contacts who were successfully traced back and kept under medical observation, 122 (75%) close contacts had at least one throat swab collected, with mean of two days after last exposures (range 1-8).

A total of 181 swabs were collected and numbers of swabs collected from day 1 to 8 after last exposure were 32 (18%), 46 (25%), 21 (12%), 23 (13%), 25 (14%), 7 (4%), 23 (13%) and 4 (2%). Among these 122 close contacts, 34 (28%) and 10 (8%) had two or three sequential swabs, respectively. The reasons for not collecting swab or second swab were either the contact refused or attempt to contact was failed.

A total of 17 swabs collected from 10 secondary cases whom were symptomatic contacts (suspected case-patient) positive with 2009 H1N1 virus. Asymptomatic cases were not tested positive of 2009 H1N1 virus. Positive proportions among group-1 HCW, group-2 tour group and household, and group-3 passengers and social close contacts were none of 11 (0.0), 8 of 41 (0.20) and 2 of 120 (0.02), respectively (Table 1).

All of the 17 swabs collected from day 1 to 5 after last exposure were 6 (35%), 2 (12%), 5 (29%), 3 (18%) and 1 (6%). Positive proportion by days of swab collection after last exposure showed a high ratio on day 1 (0.19), before sharply decreased to a valley on day 2 (0.04) and surged to a peak on day 3 (0.24). After day 3, it was declined to zero from day 6 and onwards (Figure 2).

Table 1. Comparison of interventions and respiratory specimen screening among three close contacts groups in a 2009 H1N1 tour group outbreak in China, 2009

Intervention and respiratory specimen screening	Total (N=172)	HCW (N=11)	Tour group and household (N=41)	Passengers and social contacts (N=120)	P-value
Proportion of close contacts successfully traced back, n (%)	163 (95)	11 (100)	32 (78)	120 (100)	**<0.001** *
Medical observation					
At home (%)	20 (12)	0 (0)	2 (6)	18 (15)	
At designated hotel (%)	103 (63)	1 (9)	15 (47)	87 (73)	
In hospital (%)	40 (25)	10 (91)	15 (47)	15 (12)	**<0.001** *
Centralized management (%)	143 (88)	11 (100)	30 (94)	102 (85)	0.182 *
Symptomatic close contact (%)	11 (7)	0 (0)	9 (28)	2 (2)	**<0.001** *
Swab collection from contacts under medical observation	122 (75)	6† (55)	21‡ (66)	95§ (79)	**0.013** *
Only one swab (%)	78 (64)	6 (100)	7 (33)	65 (68)	
Two swabs (%)	34 (28)	0 (0)	5 (24)	29 (31)	
Three swabs (%)	10 (8)	0 (0)	9 (43)	1 (1)	
Two or more swabs collection (%)	44 (36)	0 (0)	14 (67)	30 (32)	**<0.001** *
Days from last exposure to first swab collection, media (IQR)	2 (1, 8)	1 (1, 3)	1 (1, 2)	2 (1, 8)	**<0.001**¤
Days from last exposure to second swab collection, media (IQR)	5 (2, 7)	NA¶¶	3 (2, 6)	5 (3, 7)	0.132¤
Days from last exposure to third swab collection, media (IQR)	4 (3, 7)	NA¶¶	4 (3, 7)	6	0.400¤
Positive with 2009 H1N1 virus, n (%)	10 (8)	0 (0)	8 (38)	2 (2)	**<0.001** *

* Frequencies were compared among three groups using Chi-square test; Fisher's exact test employed once the cells had expected count less than 5.

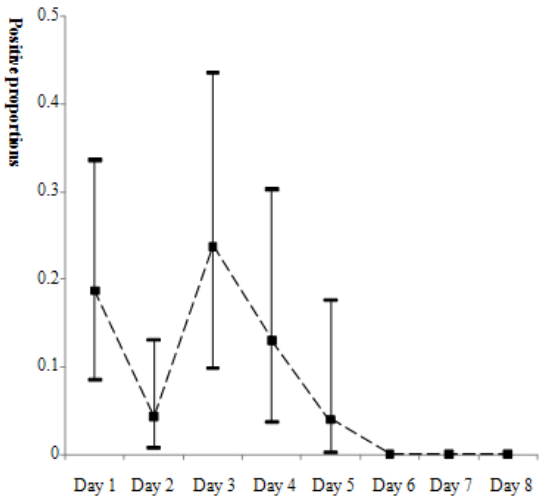
† Only six HCWs had swabs collected for rRT-PCR testing. The remaining five HCWs acute-phrase sera collected and tested negative by HI assay.

‡ Five tour group members and six household close contacts of secondary case-patients refused to have swabs collected.

§ 25 social close contacts, including six co-workers, five bus or taxi drivers and 14 roommates, refused to have swabs collected.

¤ Medians were compared among three groups with the Wilcoxon rank sum test.

¶¶ NA denotes not available.



Error bars indicate 95% confidence intervals.

Figure 2. Positive proportions of swabs collected from 122 close contacts in a tour group outbreak of 2009 H1N1 in China, 2009

Discussion

The tour group members came from various provinces throughout China with potential to spread the disease widely and quickly upon their return after the short tour. This was a special and extraordinary risk to accelerate the disease spread. To achieve the optimal control of 2009 H1N1 during this outbreak in the tour group just as the disease was making a debut in China, tracing back the close contacts and placing them under centralized medical observation was one of the effective interventions since the tour group could play a critical role in spreading such a communicable disease. The urgent need for strict interventions with this tour group was considered to be crucial and technically valuable in order to establish a detailed disease transmission model during the early stage of the 2009 H1N1 pandemic.

In addition to tracing back the close contacts and managing them, other interventions were also necessary and complement each other, such as enhanced surveillance, border entry screening, vaccination campaign and chemoprophylaxis with antivirals. Each intervention had advantages and

disadvantages. In enhanced surveillance, more case-patients might be detected, but the number of investigated cases would be probably increased, including those were not actually infected, resulting in a lower specificity and burdensome to health workers because of a broad surveillance case definition. In this outbreak of 2009 H1N1 in China, due to low risk for seasonal influenza infection among the close contacts and absence of effective vaccine for 2009 H1N1 virus with inadequate stockpile of effective antiviral drugs, only non-pharmaceutical control measures were used, such as hand hygiene, social distancing, risk communication, and travel screening and restrictions.

Respiratory specimen screening was one of the exceptional actions taken to control this outbreak. Sequential specimen collection could clarify the diagnosis of close contacts in time, validate effectiveness of interventions and provide information on virus shedding. In this outbreak, 10 secondary cases were confirmed among close contacts of the index case while there was no infected case among close contacts of secondary cases. No infection had been identified among asymptomatic cases in this outbreak which was differed from seasonal influenza's asymptomatic infection rate of about 33%[11].

The positive proportion was remarkably high on day 1 and day 3, and decreased to zero on day 6. This pattern was consistent with and elaborated more details to previous reports, which showed most patients shed virus from one day before onset of symptoms through five to seven days after or until symptoms resolve[2,12].

Failing either to find contacts to engage in interview or to provide swabs lessened the potential effectiveness of this implementation strategy of close contact tracing and timely respiratory specimen collection. As for response to this outbreak, nine tourists were not contacted successfully and 35 contacts refused to have respiratory swabs collected. This hindered the power of our observation on identification of 2009 H1N1 virus among asymptomatic close contacts.

In conclusion, a tour group represents a special circumstance with a high potential to spread disease further and quickly. Group members from many different places gather for a few days and then return home. If an emergent or re-emergent disease occurs in any tour group, immediate and effective actions are necessary to prevent the spread of disease, including comprehensive close contact tracing and medical observation of all contacts.

Timely respiratory specimen collection and testing can accommodate early detection of asymptomatic cases and provide more information for better understanding of the disease. However, well-designed studies to evaluate this further are needed to provide more supporting evidences.

Acknowledgements

We thank the Sichuan Provincial and Chengdu Prefecture Center for Disease Control and Prevention for assistance in coordinating field investigation, specimen collection, laboratory testing and provision of logistics support, and the Health Bureau in Sichuan Province, Chengdu City and Ministry of Health in China for generously facilitating this study. We also thank Jeffery McFarland (Center for Disease Control and Prevention, United States), Chuleeporn Jiraphongsa (Field Epidemiological Training Program, Thailand) and Huai Yang (China-U.S. Collaborative Program on Emerging and Re-emerging Infectious Diseases) for review of manuscript and technical support.

Suggested Citation

Zhou L, Feng YX, Zhang WD, Yu HJ. Interventions and respiratory specimen screening of close contacts to control an outbreak of pandemic influenza A (H1N1) virus in a tour group, China, 2009. OSIR. 2010 Sep;3(2):6-11.
<http://www.osirjournal.net/issue.php?id=20>.

References

1. WHO. Pandemic (H1N1) 2009 - update 100. 2010 May 14 [cited 19 May 2010]. <http://www.who.int/csr/don/2010_05_14/en/index.html>.
2. Zimmer S, Burke D. Historical perspective - emergence of influenza A (H1N1) viruses. N Engl J Med. 2009;361:279-85.
3. Jordan HT, Mosquera MC, Nair H, France AM, Swine Flu Investigation Team, EIS officers. Swine-origin influenza A (H1N1) virus infections in a school-New York City, April 2009. MMWR 2009;58:1-3.
4. Cutler J, Schleihauf E, Hatchette TF, Billard B, Gaynor WC, Davidson R, et al. Investigation of the first cases of human-to-human infection with the new swine-origin influenza A (H1N1) virus in Canada. CMAJ. 2009;181:159-163. Epub 2009 Jul 20.

5. Bin C, Xingwang L, Yuelong S, Nan J, Shijun C, Xiayuan X, et al. National influenza A pandemic (H1N1) 2009 clinical investigation group. Clinical and epidemiologic characteristics of 3 early cases of influenza A pandemic (H1N1) 2009 virus, People's Republic of China. Emerg Infect Dis. 2009;15:1418-1422.
6. Han K, Zhu X, He F, Liu L, Zhang L, Ma H, et al. Lack of airborne transmission during outbreak of pandemic (H1N1) 2009 among tour group members, China, June 2009. Emerg Infect Dis. 2009 Oct;15(10):1578-81.
7. Ministry of Health of China. Diagnostic and treatment protocol of pandemic 2009 H1N1. 2009 Oct 13 [cited 22 Jan 2010]. <http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohyzs/s3586/200910/43111.htm>.
8. Centers for Disease Control and Prevention. Interim guidance for clinicians on identifying and caring for patients with swine-origin influenza A (H1N1) virus infection. 2009 [cited 6 Jul 2009]. <http://www.cdc.gov/h1n1flu/identifyingpatients.htm>.
9. World Health Organization. WHO technical advice for case management of influenza A (H1N1) in air transport. 2009 May 13 [cited 6 Jul 2009]. <http://www.who.int/ihr/travel/A(H1N1)_air_transport_guidance.pdf>.
10. Centers for Disease Control and Prevention. Interim guidance for infection control for care of patients with confirmed or suspected novel influenza A (H1N1) virus infection in a healthcare setting. 2009 [cited 6 Jul 2009]. <http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm>.
11. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A (H1N1)v without travel history in a school in the Toulouse District, France, June 2009. Euro Surveill 2009;14(27).
12. Carrat F, Vergu E, Ferguson NM, Lemaitre M, Cauchemez S, Leach S, et al. Timelines of infection and disease in human influenza: a review of volunteer challenge studies. Am J Epidemiol 2008;167:775-85.