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Detection of Avian Influenza A(H7N2) Virus Infection Among Animal Shelter Workers Using a Novel Serological Approach—New York City, 2016–2017

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Abstract

Background.—In 2016, an influenza A(H7N2) virus outbreak occurred in cats in New York City's municipal animal shelters. One human infection was initially detected.

Methods.—We conducted a serological survey using a novel approach to rule out cross-reactive antibodies to other seasonal influenza viruses to determine whether additional A(H7N2) human infections had occurred and to assess exposure risk.

Results.—Of 121 shelter workers, one had serological evidence of A(H7N2) infection, corresponding to a seroprevalence of 0.8% (95% confidence interval, .02%–4.5%). Five persons exhibited low positive titers to A(H7N2) virus, indicating possible infection; however, we could not exclude cross-reactive antibody responses to seasonal influenza viruses. The remaining 115 persons were seronegative. The seropositive person reported multiple direct cat exposures without using personal protective equipment and mild illness with subjective fever, runny nose, and sore throat.

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Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copy-edited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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Conclusions.—We identified a second case of A(H7N2) infection from this outbreak, providing further evidence of cat-to-human transmission of A(H7N2) virus.

Keywords

influenza; H7N2; outbreak; zoonotic; serology; human infection

The first reported outbreak of low pathogenic avian influenza (LPAI) A(H7N2) virus among cats was detected in 3 facilities of the municipal animal shelter system in New York City (NYC), New York, in 2016 [1]. Influenza A(H7N2) virus was identified on 14 December 2016 from tissue specimens collected from a cat euthanized for severe pneumonia. The cat had been admitted to the Manhattan facility on 12 November and fell ill within 2 days. Widespread transmission of influenza A(H7N2) virus occurred among cats in the Manhattan facility followed by the Brooklyn and Staten Island facilities. On 29 December 2016, cats from the 3 shelters were relocated to a temporary quarantine facility. By the end of the outbreak, approximately 500 cats had tested positive for influenza A(H7N2) virus; most developed mild to moderate illness [2, 3]. Influenza A(H7N2) had never before been reported in cats, raising concern of the potential role of felines as a source of infection to humans as shelter workers had been exposed to sick cats for several weeks [1, 3].

Because the risk to humans was unknown, the NYC Department of Health and Mental Hygiene conducted case finding during 17–19 December. Shelter employees were screened and tested for influenza A by real-time reverse-transcription polymerase chain reaction (RT-PCR), regardless of symptoms, and exposed persons (eg, persons who adopted cats from or volunteered at the Manhattan facility) meeting symptom criteria were also tested [1]. RT-PCR testing and genetic sequencing confirmed influenza A(H7N2) virus infection in 1 person during the outbreak. This was the first documented case of cat-to-human transmission of influenza A(H7N2) virus [1, 4].

The unrecognized and ongoing exposure to infected cats from mid-November to late December 2016 made it possible that additional human infections had occurred. It was no longer possible to detect acute viral infections using molecular methods such as RT-PCR, leaving serology as the only option available to detect infections occurring before the outbreak's identification, or those that went undetected or were not detected because of suboptimal timing of specimen collection. Establishing whether an infection with a novel influenza virus occurred poses unique laboratory challenges due to the lack of criteria for serological confirmation for H7 viruses and the potential for antibody cross-reactivity between novel and seasonal influenza viruses. We conducted a serological survey, using a novel approach to discriminate cross-reactive seasonal influenza virus antibodies from influenza A(H7N2) antibodies in single serum, to determine whether additional influenza A(H7N2) human infections had occurred among shelter workers before outbreak identification and to assess occupational exposure risk.

METHODS

Serological Survey Among Animal Shelter Workers

We administered a cross-sectional serological survey to staff from the Manhattan and Brooklyn shelters during 25 January–8 February 2017. Because of the timeframe and the small number of quarantined cats (~4%) that originated from the Staten Island facility, we did not recruit participants at this facility. Eligible participants included shelter employees and volunteers, regardless of whether they worked with infected cats, from 12 November 2016, the date the first cat with RT-PCR–confirmed influenza A(H7N2) virus was admitted to the Manhattan facility, to 29 December 2016, the date when cats were moved to the temporary quarantine facility [1].

We developed a questionnaire to capture participant demographics and activities that might have placed them at risk for infection, including cat and environmental exposures, job duties and practices, and personal protective equipment (PPE) use before and after outbreak identification. Participants were also asked to report any history of illness from 12 November 2016 to the interview date, healthcare utilization, seasonal influenza vaccination, and chronic medical conditions.

Serum Collection, Serological Analyses, and Disposition

A single blood specimen was collected from each participant by venipuncture at the time of interview. Serum specimens were processed at the NYC Public Health Laboratory and shipped to the Influenza Division, US Centers for Disease Control and Prevention (CDC) for serological analyses.

All sera were tested against the influenza A(H7N2) virus isolated from the confirmed human case from the same outbreak (A/New York/108/2016) by both a modified hemagglutination inhibition (HI) assay using horse erythrocytes [5] and a microneutralization (MN) assay [6], as previously described. A (H1N1)pdm09 virus, A/California/07/2009, was also used in the MN assay. All serum specimens with MN titer ≥40 or HI titer ≥40 to A/New York/108/2016 virus underwent further testing by serum adsorption with influenza A(H7N2) (A/New York/108/2016), circulating A(H3N2) (A/Hong Kong/4801/2014), and A(H1N1)pdm09 (A/Michigan/45/2015) viruses. Preabsorbed and postadsorbed sera were tested by MN and recombinant H7 (rH7)– and recombinant H3 (rH3)–specific immunoglobulin M (IgM) and immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) to exclude the possibility of antibody cross-reactivity between H7 and seasonal influenza A viruses that participants might have been exposed to previously. We calculated geometric mean titers (GMTs) of replicates. Details of experimental procedures are further described in the Supplementary Materials.

We defined seropositive as any sera with MN titers ≥40 and HI titers ≥40 with no cross-reactivity to seasonal viruses by MN-and rH7-specific ELISAs. This positivity threshold is consistent with World Health Organization (WHO) criteria for serological confirmation of A(H5N1) infection in a single serum specimen collected at day 14 or later after symptom onset (defined as MN titers ≥80 using a starting dilution of 1:20 and a positive result using a second serological assay) [7]; there are no formal criteria for H7 viruses. We utilized serum

adsorption techniques to differentiate cross-reactive antibodies from H7-specific antibody responses. Participants with a single serum specimen that did not consistently reach diagnostic thresholds (both MN titer ≥40 and HI titer ≥40) or contain cross-reactive antibodies with seasonal viruses were considered indeterminate, indicating possible infection. Participants with MN titers <40 and HI titers <40 were seronegative.

Statistical Analysis

We used SAS 9.2 (SAS Institute) to analyze survey data. We compared epidemiologic characteristics of participants by serostatus. Seroprevalence and exact 95% confidence intervals (CIs) were calculated. Suspected cases of influenza A(H7N2) virus infection were defined as reports of conjunctivitis [8, 9] or ≥2 symptoms of sore throat, subjective fever, muscle aches, or cough, with onset ≤10 days after exposure to a shelter cat [1]. “Direct or close contact” was defined as working with cats by performing ≥1 of the following activities: feeding, holding, handling, restraining, playing with, petting, cleaning, bathing, grooming, medicating, performing or assisting with medical procedures, swabbing sick cats for oropharyngeal aspirates, cleaning medical or surgical areas, and cleaning kennels and cages. “Indirect contact” was defined as visiting or walking through a room housing cats. “No contact” was defined as having never performed any direct or indirect activities with cats while working.

Ethics Statement

This activity was conducted as part of a public health response to an outbreak investigation and was not considered to be human subjects research in accordance with federal human subject protection regulations. We obtained written informed consent from all participants.

RESULTS

Animal Shelter Worker Characteristics

Ninety-five of 219 (43%) employees and 26 of 383 (7%) volunteers at the shelters during the exposure period participated in the investigation (overall response rate, 20%) (Table 1). The median age was 31 years (interquartile range [IQR], 27–46 years), 69% were female, and 57% were white. Employees worked a median of 40 hours per week (IQR, 38–40); volunteers worked a median of 4 hours per week (IQR, 2–6). Median duration from last shelter cat exposure to serum collection was 36 days (range, 27–73 days). Of 121 persons, 99 (82%) had direct or close contact with cats, and 17 (14%) had indirect contact with cats. Thirty-eight persons (31%) were considered at increased risk for developing influenza-related complications, including 8 persons aged ≥65 years, and 30 persons <65 years who had reported ≥1 underlying medical condition [10]. Fifty-eight participants (48%) reported receiving the 2016–2017 influenza vaccine.

Serological Detection of Influenza A(H7N2)–Specific Antibodies

Compared with antibody titers to seasonal A(H1N1) virus, most participants had low or undetectable antibody titers to influenza A(H7N2) virus (Figure 1). Among all participants, the GMT to influenza A(H7N2) virus was 7.2 (95% CI, 6.4–8.1) by MN, and 6.0 (95% CI,

5.6–6.4) by HI, compared with MN GMT of 115 to a seasonal A(H1N1) virus (95% CI, 85.6–154.6) that they may have been exposed to through past vaccination or infection.

Of 121 participants, 6 (5%) had MN titers ≥40 to the A/NewYork/108/2016 A(H7N2) virus isolated from the human case in this same outbreak. One of 6 participants also had an HI titer ≥40 to this virus. The antibody specificity of these persons was further determined by antibody adsorption of the sera with influenza A(H7N2), A(H3N2), and A(H1N1) viruses or phosphate-buffered saline controls. One participant met seropositivity criteria for influenza A(H7N2) virus infection; this person's specimen was collected 39 days from last shelter cat exposure (Table 2, subject 1). This person had an MN titer of 80 and an HI titer of 40 to influenza A(H7N2) virus. Post–serum adsorption, influenza A(H7N2) neutralizing antibody titers were removed by adsorption with influenza A(H7N2) virus but not by seasonal viruses, suggesting that antibody responses were specific to A/New York/108/2016 influenza A(H7N2) virus (Table 2). Further analysis with rH7-specific IgG and IgM ELISA suggested that this person mounted primarily influenza A(H7N2)–specific IgG responses, with no influenza A(H7N2) IgM antibodies and low preexisting H3N2 MN antibodies (Table 2 and Figure 2).

Sera from 5 of 6 participants (Table 2, subjects 2–6) did not consistently achieve diagnostic thresholds to influenza A(H7N2) on the basis of initial screening criteria of MN tiers ≥40 and HI titers ≥40 (Table 2). Furthermore, following serum adsorption with A(H3N2) virus, all 5 participants demonstrated reduced influenza A(H7N2) MN titers or rH7-specific IgG and IgM titers as a result of cross-reactive antibodies to seasonal influenza viruses and were considered indeterminate for influenza A(H7N2) infection. The remaining 115 participants were seronegative against influenza A(H7N2) virus (HI <40 and MN <40). Median duration from last shelter cat exposure to serum collection was 36 days (range, 27–73 days) among seronegative participants compared with 31.5 days (range, 28–42 days) among participants with positive and indeterminate serology results ($P = .4$, Wilcoxon rank-sum test). The overall seroprevalence of influenza A(H7N2) infection in this cohort was 1 of 121 (0.8%; 95% CI, .02%–4.5%).

Clinical and Occupational Characteristics of Participants With Positive and Indeterminate Serology Results

All 6 participants with positive and indeterminate serology results had direct cat exposure during the exposure period. The influenza A(H7N2)–seropositive participant was an animal shelter employee. This person had no known preexisting medical conditions, and reported mild illness characterized by subjective fever, runny nose, and sore throat that did not require medical attention. Symptoms began on 12 December 2016 and resolved within 5 days without antiviral treatment. They reported multiple direct cat exposures, including swabbing sick cats for oropharyngeal aspirates without a gown, mask, respirator, or face shield before becoming aware of the outbreak. One of 5 persons with indeterminate laboratory results reported ≥2 symptoms (sore throat, subjective fever, and cough) of suspected influenza A(H7N2) virus infection ≤10 days after exposure to shelter cats. None reported conjunctivitis or sought medical care. All reported direct cat exposures, and none reported using a mask, eye protection, or respirators before becoming aware of the outbreak (Table

3). Thirty of 115 (26%) seronegative persons reported symptoms, most commonly runny nose, cough, and sore throat, followed by headache and subjective fever. Eight persons reported conjunctival symptoms. Seven persons sought care. Only one person was tested for influenza and tested negative. Ninety-three of 115 seronegative persons (81%) reported having direct contact with cats, including holding, petting, playing or socializing, feeding, restraining and handling, and cleaning kennels and cages. Three seronegative employees also reported swabbing sick cats. Because only 1 human infection was identified, we did not have sufficient data to analyze risk factors for human influenza A(H7N2) virus infection.

DISCUSSION

Avian influenza virus infections in cats are rare and no serologic criteria for single serum exist to confirm influenza A(H7N2) virus infection. We designed a novel diagnostic approach to detect antibodies against the influenza A(H7N2) virus and exclude cross-reactivity between H7 and other seasonal influenza virus antibodies using MN, HI, and strain-specific IgM and IgG ELISA using single serum specimens collected during an outbreak among cats in NYC animal shelters. We identified 1 animal shelter employee with serological evidence of influenza A(H7N2) infection, bringing the total to 2 confirmed human infections during this outbreak. Excluding the first case diagnosed by RT-PCR with negative acute-phase serum, the seroprevalence of confirmed human infections in this cohort was 1 of 121 (0.8%). Although 5 additional employees had low positive titers to influenza A(H7N2) virus, we could not exclude possible influenza A(H7N2) infection because of cross-reactive antibody responses from exposure to seasonal H1 and H3 influenza viruses.

Serology allowed us to confirm a subclinical, mild infection that would otherwise have gone undetected. False-negative RT-PCR results from nasopharyngeal swab specimens could have resulted from suboptimal specimen collection, suboptimal timing of collection relative to symptom onset, or an infection with insufficient viral shedding. Paired serum collection is normally recommended for influenza serology to capture antibody changes before and after infection. However, during this outbreak, collection of paired serum specimens with optimal timing was not feasible. We demonstrated the value of serology to detect novel influenza virus infections following an outbreak, even when limited by single serum collection. In contrast to seasonal influenza viruses like (A)H1N1 where populations have complex preexisting immunity, human infection with A(H7) virus is uncommon and the population has a naive immune background to influenza A(H7N2) virus. Thus, an elevated antibody titer specific to influenza A(H7N2) virus could be indicative of infection.

No confirmatory serology criteria exist for H7 viruses. Our approach is in accordance with WHO criteria for detecting human infections with influenza A(H5N1) virus. Both H5 and H7 viruses have low preexisting titers in the population, thus allowing for the detection of infection using single serum [7]. Because this outbreak was concurrent with seasonal influenza virus transmissions and shared epitopes between influenza viruses can cause cross-reactive antibody responses [11], we also incorporated serum adsorption assays to differentiate antibody responses to influenza A(H7N2) from 2 circulating seasonal influenza A viruses. This approach is supported by the literature; in a review weighing serological evidence of human exposure to animal influenza viruses, studies that addressed antibody

cross-reactivity received higher grade scores [12]. We found a reduction in influenza A(H7N2) neutralizing antibody titers postadsorption with A(H3N2) virus when sera were adsorbed with purified whole viruses, suggesting that antibodies to influenza A(H7N2) were recognizing shared epitopes between influenza A(H7N2) and A(H3N2) viruses. We also evaluated the rH7-specific IgG and IgM responses in all 6 persons with MN ≥40. While IgM is an immune marker for acute primary infection, IgG subtype antibodies are more abundant following influenza infection, despite slower kinetics than IgM antibodies [13]. The seropositive participant clearly had influenza A(H7N2)–specific neutralizing antibodies. The lack of rH7-specific IgM and the abundance of rH7-specific IgG in the serum are consistent with the duration from last shelter cat exposure to serum collection on day 39. The 5 additional persons exhibited low positive influenza A(H7N2) antibodies, indicating possible infection; however, the influenza A(H7N2) antibody titers from sera collected from these participants did not consistently achieve diagnostic thresholds by both MN and HI, and cross-reactivity of seasonal influenza virus antibodies could not be excluded. Although the antibody titers to influenza A(H7N2) virus are low in this population, as detected by MN and HI assays, all 6 persons with seropositive and indeterminate titers, as well as some seronegative participants (data not shown), had high rH7 IgG titers. This could be because of the shared binding epitopes on the stem and the head of the hemagglutinin glycoprotein between influenza A(H7N2) and seasonal viruses [14].

This is only the fourth person in the United States to be infected with influenza A(H7N2) virus and the only serologically confirmed human infection known to be associated with exposure to cats. Of 2 previously documented human influenza A(H7N2) infections in the northeastern United States within the LPAI lineage, one was an immunocompromised person living in New York in 2003; the source of the infection was not determined [8, 15, 16]. The other was a serologically confirmed influenza A(H7N2) human infection among 80 government workers involved in culling activities during a 2002 influenza A(H7N2) outbreak among turkeys and chickens in Virginia [17]. Low seroprevalence of influenza A(H7N2) virus antibodies among animal shelter workers in our study is consistent with reports from serosurveys after other outbreaks of A(H7) virus infections. With the exception of influenza A(H7N9) viruses in China, outbreaks among poultry of both low and highly pathogenic influenza A(H7) viruses have rarely resulted in cases of human infection [8] commonly associated with mild respiratory illness or ocular disease, typically conjunctivitis [15, 18, 19]. During 2003, in an LPAI A(H7N3) outbreak in Italy, anti-H7 antibodies were detected in 3.8% of poultry workers [20].

In this study, the course of illness in the seropositive person was mild, characterized by sore throat, myalgia, and cough [1]. This observation is consistent with reports of other North American lineage viruses [8, 15, 21]. Infection with this virus also manifests as a mild respiratory illness in animal models [22].

Both persons with documented influenza A(H7N2) infection from this outbreak, including the previously identified human index case, had close, prolonged, direct contact with sick cats and their respiratory secretions, in the absence of respiratory or facial PPE [1]. Although occupational activities that involve direct contact with respiratory secretions likely confer a higher risk of transmission, we were unable to characterize the risk associated with

particular exposures. There was evidence of widespread contamination of the quarantine facility that temporarily housed the 500 cats, suggesting exposure could have occurred even among staff with no direct cat contact [23]. Among this cohort, many persons were exposed to ill cats without PPE; antibodies to influenza A(H7N2) were not detected for most persons. Although we could not characterize the risk associated with specific exposures, the correct use of PPE while performing potentially high-risk behaviors might reduce the risk for infection from novel influenza viruses and should be emphasized. In addition, CDC guidelines recommend that antiviral treatment with oseltamivir, zanamivir, or peramivir should be promptly administered among persons suspected of novel influenza virus infection [24].

Although the seroprevalence of influenza A(H7N2) virus infection was low during this outbreak, our findings provide evidence for transmissibility of influenza viruses from cats to humans. This cross-species circulation of a novel influenza A(H7N2) virus in a new mammalian host that happens to be a companion animal is important to understand; as influenza A(H7N2) viruses evolve, the transmissibility or pathogenicity of this virus might increase, posing a greater public health concern. The influenza A(H7N2) virus isolated from the index case displayed genetic features associated with improved infectivity and adaptation in mammals, similar to previous LPAI A(H7N2) viruses characterized in the United States [25]. Any H7 virus that acquires the potential to efficiently transmit among humans could, if introduced into a naive population, cause a pandemic. Designing studies to prospectively collect data from paired sera during the acute and convalescent stages of illness is key to better understand the immune response to influenza A(H7N2) virus infection in humans and the potential risk posed to exposed persons.

We were limited by the availability of single serum collection postexposure due to timing of the serosurvey. Ideally, collection of acute and convalescent sera would enable direct detection of influenza A(H7N2) antibody rise following infection. We could not obtain convalescent sera on the RT-PCR–confirmed index case from this outbreak to validate our assay. Second, participants could have been previously exposed to many seasonal influenza viruses. We only used the most contemporary circulating seasonal viruses in the adsorption assays to rule out cross-reactivity. Third, despite extensive efforts to recruit shelter staff to participate, the overall response rate was low, especially among volunteers. Fourth, because the study occurred well after the outbreak began, the questionnaire involved a recall period of several weeks with questions regarding cat exposures and clinical illness during the influenza season. Also, because there were insufficient positives and most participants were exposed to cats, we could not conduct a meaningful analysis of risk factors for human influenza A(H7N2) virus infection due to transmission from infected cats. Finally, although the outbreak investigation eventually identified an influenza A(H7N2) specimen collected on 26 October 2016 from a cat in the Manhattan facility, we used 12 November as the exposure start date to coincide with initial RT-PCR testing of staff conducted in December. It is unlikely that we would have identified additional staff.

Our study provides further evidence of cat-to-human transmission of influenza A(H7N2) viruses. Transmission of this virus is a rare event, even among persons with extensive exposure. Continued monitoring of rare avian influenza viruses, such as influenza A(H7N2),

at the animal–human interface remains crucial to assess the public health risk of these strains. Serological assays using single serum specimens can help to identify additional infections to novel influenza viruses that may have otherwise been missed by molecular methods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments.

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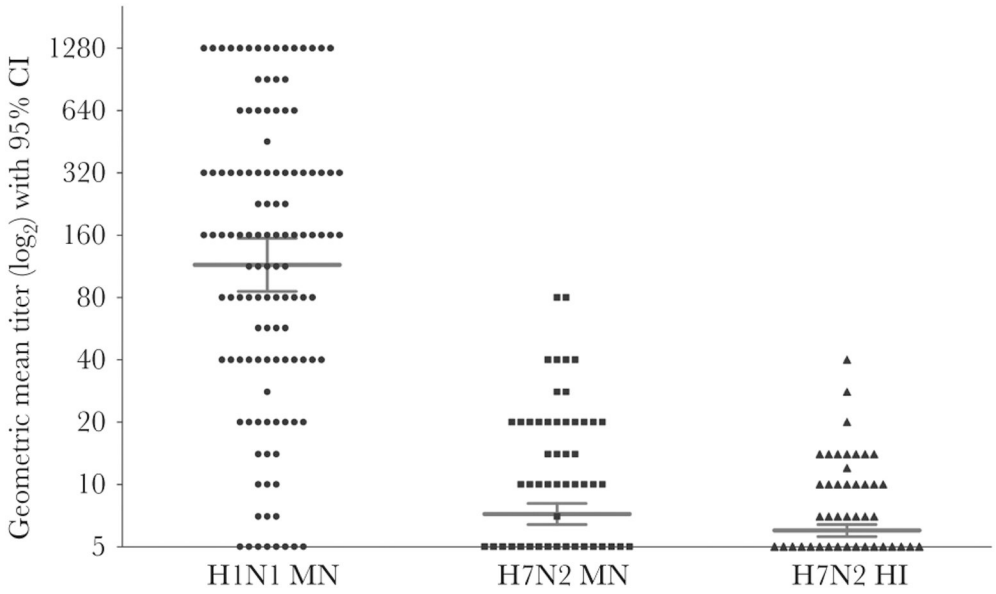

Figure 1.

Distributions of microneutralization (MN) and hemagglutination inhibition (HI) geometric mean titers against influenza A(H7N2) and A(H1N1) viruses among animal shelter workers. Single serum collected from 121 workers during 25 January–8 February 2017 were examined by MN and HI assays for antibody activity against influenza A(H7N2) (A/New York/108/2016) virus. Serum was also examined by MN assays for antibody activity against influenza A(H1N1)pdm09 (A/Michigan/45/2015) virus. Abbreviations: CI, confidence interval; HI, hemagglutination inhibition; MN, microneutralization.

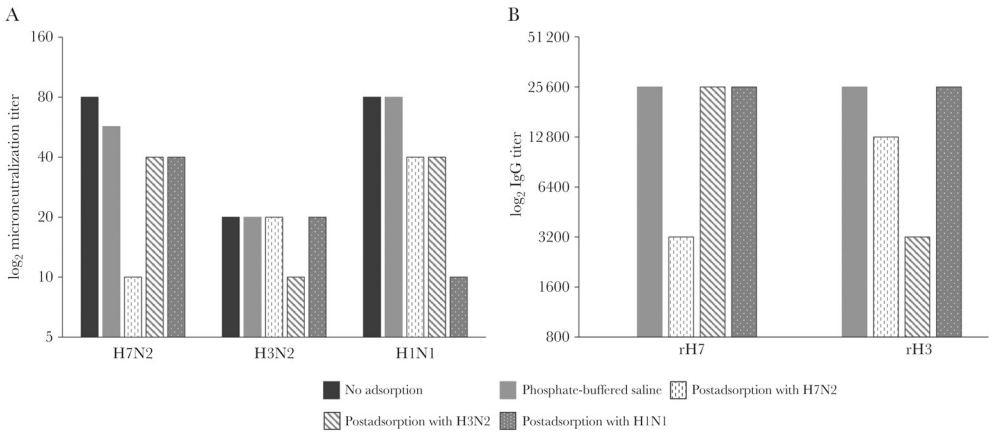

Figure 2.

Antibody serum adsorption profile of an influenza A(H7N2)–seropositive case (n = 1) with influenza A(H7N2) (A/NewYork/108/2016) virus, circulating A(H3N2) (A/HongKong/4801/2014) virus, and A(H1N1)pdm09 (A/Michigan/45/2015) virus by microneutralization assay (*A*), and recombinant H7– and recombinant H3–specific immunoglobulin G enzyme-linked immunosorbent assay (*B*). Abbreviation: IgG, immunoglobulin G.

Table 1.

Epidemiologic Characteristics of 121 Animal Shelter Employees and Volunteers With Possible Risk of Influenza A(H7N2) Infection in New York City, 2016

Characteristic	No. (%)
Median age, y (IQR)	31 (27–46)
Median hours worked per week (IQR)	40 (20–40)
Median days from last exposure to sera collection (IQR)	36 (29–42)
Worker type	
Employee	95 (78.5)
Volunteer	26 (21.5)
Sex	
Female	84 (69.4)
Male	37 (30.6)
Race	
White	69 (57.0)
Black	19 (15.7)
Other	18 (14.9)
Asian	8 (6.6)
Multiracial	7 (5.8)
Ethnicity	
Not Hispanic or Latino	91 (75.2)
Hispanic or Latino	30 (24.8)
Shelter worked in	
Manhattan only	53 (43.8)
Brooklyn only	41 (33.9)
Worked at >1 shelter[a]	27 (22.3)
Worked in temporary quarantine facility[b]	31 (25.6)
Underlying medical condition(s)	64 (52.9)
High-risk status[c]	38 (31.4)
Vaccinated for 2016–2017 seasonal influenza	58 (47.9)
Vaccinated before November 2016	17 (14.1)
Type of exposure to cats	
Direct contact[d]	99 (81.8)
Indirect contact[e]	17 (14.0)
No contact[f]	5 (4.1)

Data are presented as No. (%) unless otherwise indicated.

Abbreviation: IQR, interquartile range.

[a]A total of 19 participants reported working at both the Manhattan and the Brooklyn animal shelters; of those, 6 reported working in at least one other animal shelter. The other 8 persons reported working in at least one other animal shelter in addition to the Manhattan or Brooklyn animal shelters.

[b] On 29 December 2016, the American Society for the Prevention of Cruelty to Animals established a temporary quarantine facility to allow affected shelters to sanitize facilities and resume normal operations and to provide a space to move exposed or ill cats until the outbreak was over.

[c] Defined as persons at higher risk for influenza complications, including persons aged ≥65 years, women who are pregnant, persons with documented chronic health conditions (per the Advisory Committee on Immunization Practices), and Native Americans, Alaska Natives, and Native Hawaiians.

[d] Defined as performing ≥1 of the following activities at every shift, or at some but not all shifts: holding, petting, playing or socializing, cleaning, bathing, and grooming, restraining and handling, administering medications, performing or assisting with medical procedures, swabbing sick cats for oropharyngeal aspirates, feeding, cleaning kennels and cages, and cleaning medical or surgical areas.

[e] Defined as visiting or walking through a room where cats were housed at every shift or some but not all shifts.

[f] Defined as never performing any direct or indirect activities with cats while working.

Table 2.

Serological Responses of Shelter Workers With Initial Screen of Microneutralization Titers ≥40 or Hemagglutination Inhibition Titers ≥40 to Influenza A(H7N2) Virus

		Subject No.					
Characteristic		**1**	**2**	**3**	**4**	**5**	**6**
Days from seasonal vaccination to serum collection		NA	40	41	NA	NA	NA
Days from last day of exposure to sera collection		39	21	28	28	28	42
H7N2 HI titer		40	14	14	14	5	5
H7N2 MN titer		80	40	40	40	40	80
H7N2 MN titers postadsorption with	PBS only	57	40	20	40	20	28
	H7N2	10	10	10	10	10	10
	H3N2	40	20	10	10	10	28
	H1N1	40	28	20	40	14	28
rH7 IgM titers postadsorption with	PBS only	<[a]	800	<[a]	800	1600	800
	H7N2	<[a]	<[a]	<[a]	<[a]	<[a]	<[a]
	H3N2	<[a]	<[a]	<[a]	<[a]	800	<[a]
	H1N1	<[a]	<[a]	<[a]	<[a]	800	<[a]
rH7 IgG titers postadsorption with	PBS only	25 600	25 600	12 800	25 600	12 800	12 800
	H7N2	3200	1600	800	800	800	1600
	H3N2	25 600	6400	6400	12 800	3200	6400
	H1N1	25 600	12 800	6400	12 800	6400	6400
H3N2 MN titer		20	80	14	28	10	320
H1N1 MN titer		80	320	320	40	40	113

Titers are geometric mean titers of at least 2 replicates.

Abbreviations: HI, hemagglutination inhibition; IgG, immunoglobulin G; IgM, immunoglobulin M; MN, microneutralization; NA, no seasonal influenza vaccination; PBS, phosphate-buffered saline.

[a]<100 (predilution).

Table 3.

Demographic and Exposure Characteristics Among Animal Shelter Workers and Volunteers by Serostatus

Characteristic	Seronegative[a] No. (%) (n = 115)	Seropositive 1	Indeterminate 2	3	4	5	6
Employment characteristics							
Worker type: employee (vs volunteer)	89 (77.4)	Employee	Employee	Employee	Employee	Employee	Employee
Hours worked or volunteered per week: median (min, max)	40 (1,60)	40	40	40	37.5	40	40
Shelter location: worked at Manhattan only	50 (43.5)	Brooklyn	Manhattan	Manhattan	Manhattan	Brooklyn	Brooklyn
Worked at >1 shelter	27 (23.5)	No	No	No	No	No	No
Worked in temporary quarantine facility[b]	29 (25.2)	No	Yes	No	No	Yes	No
Medical history							
High-risk status[c]	37 (32.2)	No	Yes	No	No	No	No
Received any 2016–2017 seasonal flu vaccine	56 (48.7)	No	Yes	Yes	No	No	No
Vaccinated before November 2016	17 (14.8)	No	No	No	No	No	No
Self-reported symptoms during 12 November 2016–8 January 2017[d]							
Fever measured with thermometer	5 (4.3)	−	−	−	−	−	−
Felt feverish	22 (19.1)	+	+	−	−	−	−
Cough	42 (36.5)	−	+	+	+	−	−
Muscle aches	12 (10.4)	−	−	−	−	−	−
Sore throat	26 (22.6)	+	+	−	−	−	−
Itchy eyes, redness, or drainage	8 (70)	−	−	−	−	−	−
Any ≥2 symptoms or conjunctivitis[e]	30 (26.1)	+	+	−	−	−	−
Influenza-like illness[f]	27 (23.5)	+	+	−	−	−	−
Direct exposures to cats							
Holding, petting, playing, or socializing	90 (78.3)	+	+	+	+	+	+
Cleaning, bathing, and grooming	30 (26.1)	+	−	+	−	+	−
Restraining and handling	74 (64.4)	+	−	+	+	+	+
Administering medications	18 (15.7)	−	−	+	−	−	−
Performing or assisting with medical or surgical procedures	21 (18.3)	−	−	+	+	−	−

Characteristic	Seronegative[a] No. (%) (n = 115)	Seropositive 1	Indeterminate 2	3	4	5	6
Swabbing sick cats for oropharyngeal aspirates	3 (2.61)	+	−	−	−	−	−
Feeding	77 (67.0)	+	+	+	+	+	+
Cleaning kennels and cages	64 (55.7)	+	−	+	+	+	−
Cleaning medical or surgical areas	23 (20.0)	−	−	+	−	−	−
Indirect exposures to cats							
Visited or walked through a room where cats were housed	110 (95.7)	+	+	+	+	+	+
PPE use at all times when working with cats, before outbreak awareness among those with direct exposures to cats							
Gown or Tyvek suit	5/93 (5.4)	−	−	−	−	−	−
Eye protection (goggles, full face shield)	1/93 (1.1)	−	−	−	−	−	−
Surgical mask	2/93 (2.2)	−	−	−	−	−	−
N95 respirator	0/93 (0)	−	−	−	−	−	−
Single or double gloves	57/93 (61.3)	+	+	+	+	−	−
Handwashing after removing gloves	39/92 (42.4)	−	−	−	+	−	+
Shoe covers	3/93 (3.2)	−	−	−	−	−	−
PPE use at all times after outbreak awareness among those with direct exposure to cats who reported working with cats after becoming aware of outbreak[g]							
Gown or Tyvek suit	36/60 (60.0)	+	+	+	+	+	NA
Eye protection (goggles, full face shield)	23/60 (38.3)	−	+	+	+	−	NA
Surgical mask	34/60 (56.7)	−	+	+	+	+	NA
N95 respirator	0/60 (0)	−	−	−	−	−	NA
Single or double gloves	54/60 (90.0)	+	+	+	+	+	NA
Handwashing after removing gloves	47/60 (78.3)	−	+	+	+	−	NA
Shoe covers	43/60 (71.7)	+	+	+	+	+	NA

[a]Data are No. (%) unless otherwise indicated.

Abbreviations: +, characteristic present; −, characteristic absent; NA, not applicable; PPE, personal protective equipment.

[b]On 29 December 2016, the American Society for the Prevention of Cruelty to Animals established a temporary quarantine facility to allow affected shelters to sanitize facilities and resume normal operations and to provide a space to move exposed or ill cats until the outbreak was over.

[c] Defined as those aged ≥65 years, women who are pregnant, persons with documented chronic health conditions per the Advisory Committee on Immunization Practices, Native Americans, Alaska Natives, and Native Hawaiians.

[d] Defined as ≤10 days after the last possible date of exposure (29 December 2016) to shelter cats.

[e] Defined as ≥2 symptoms (sore throat, fever, cough, muscle aches) or conjunctivitis.

[f] Defined as fever and cough or sore throat.

[g] Administrative controls and PPE recommendations were made as of 15 December 2016 and 20 December 2016 for the Manhattan and Brooklyn shelters, respectively.