Novel Influenza A (H1N1) Outbreak at the U.S. Air Force Academy

Epidemiology and Viral Shedding Duration

Catherine Takacs Witkop, MD, MPH, Mark R. Duffy, DVM, MPH, Elizabeth A. Macias, PhD, Thomas F. Gibbons, PhD, James D. Escobar, MPH, Kristen N. Burwell, MPH, Kenneth K. Knight, MD, MPH

Background: The U.S. Air Force Academy is an undergraduate institution that educates and trains cadets for military service. Following the arrival of 1376 basic cadet trainees in June 2009, surveillance revealed an increase in cadets presenting with respiratory illness. Specimens from ill cadets tested positive for novel influenza A (H1N1 [nH1N1])–specific ribonucleic acid (RNA) by real-time reverse transcriptase–polymerase chain reaction.

Purpose: The outbreak epidemiology, control measures, and nH1N1 shedding duration are described.

Methods: Case patients were identified through retrospective and prospective surveillance. Symptoms, signs, and illness duration were documented. Nasal-wash specimens were tested for nH1N1-specific RNA. Serial samples from a subset of 53 patients were assessed for presence of viable virus by viral culture.

Results: A total of 134 confirmed and 33 suspected cases of nH1N1 infection were identified with onset date June 25–July 24, 2009. Median age of case patients was 18 years (range, 17–24 years). Fever, cough, and sore throat were the most commonly reported symptoms. The incidence rate among basic cadet trainees during the outbreak period was 11%. Twenty-nine percent (31/106) of samples from patients with temperature <100°F and 19% (11/58) of samples from patients reporting no symptoms for ≥24 hours contained viable nH1N1 virus. Of 29 samples obtained 7 days from illness onset, seven (24%) contained viable nH1N1 virus.

Conclusions: In the nH1N1 outbreak under study, the number of cases peaked 48 hours after a social event and rapidly declined thereafter. Almost one quarter of samples obtained 7 days from illness onset contained viable nH1N1 virus. These data may be useful for future investigations and in scenario planning.

(Am J Prev Med 2009;xx(x):xx) Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine

Background

In April 2009, Department of Defense–affiliated laboratories in San Diego and San Antonio recovered unsubtypeable influenza A virus from patient samples. The viral specimens were transported to the CDC influenza laboratory, where both viral samples were determined to be a novel influenza A virus of swine origin (nH1N1), consistent with virus isolated from patients in a Mexico influenza outbreak that began in March 2009.[1] Previous novel influenza strains required 6 months or longer to establish worldwide distribution; however, the nH1N1 virus strain established worldwide distribution within 6 weeks.[2] On June 11, 2009, the WHO[3] raised the influenza pandemic alert status to Level 6 in response to established global human-to-human transmission. By July 2009, more than 40,000 nH1N1 cases had been confirmed, and 263 deaths in the U.S. were attributed to the nH1N1 virus.[4]

Characterizing virus–host interactions and the epidemiology of nH1N1 is important in both assumptions made during planning and in defining effective control measures. Studies[5,6] of seasonal influenza suggest that viral shedding occurs for as long as 7 days after symptom onset. No similar studies on shedding of nH1N1 have been published.[7] In addition, there are no published studies of the epidemiology of nH1N1 infection among military training populations or institutions of higher education. With the 2009 influenza season upon us, characterization of the epide-

From the U.S Air Force Academy (Witkop, Knight), Colorado Springs, Colorado; and the U.S. Air Force School of Aerospace Medicine Epidemiology Consult Service (Duffy, Macias, Gibbons, Escobar, Burwell), Brooks City Base, Texas

Address correspondence and reprint requests to: Catherine Takacs Witkop, MD, MPH, 10 AMDS/SGPF, 2355 Faculty Drive, Room 2N286, U.S. Air Force Academy, Colorado Springs CO 80840. E-mail: katika@aya.yale.edu.

0749-3797/09/$–see front matter
doi:10.1016/j.amepre.2009.10.005

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
2009		**00-00-2009 to 00-00-2009**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Novel Influenza A (H1N1) Outbreak at the U.S. Air Force Academy. Epidemiology and Viral Shedding Duration	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **U.S. Air Force Academy,10 AMDS/SGPF,2355 Faculty Drive,Colorado Springs,CO,80840**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**	**Same as Report (SAR)**	**6**	

miology and duration of shedding for the nH1N1 virus is critical.

In July 2009, the U.S. Air Force Academy (USAFA) experienced an outbreak of nH1N1 illness. An investigation was initiated to (1) describe the outbreak epidemiology, (2) define and implement control measures to limit transmission, and (3) determine the duration of viral shedding from patients in the outbreak.

Methods

Setting

The USAFA, located west of Colorado Springs CO is a 4-year academic undergraduate institution that educates and trains cadets for active-duty military service as officers. Incoming students are known as basic cadet trainees (BCTs) during the summer prior to the commencement of the first academic year. BCTs are organized into squadrons of 135–140 individuals. On June 25, a total of 1376 BCTs arrived at the USAFA to begin a 6-week military training program. On July 6, active surveillance of diagnostic codes for respiratory illnesses demonstrated an increase in the number of visits for respiratory complaints that surpassed levels from the two previous years. By July 7, two cadets evaluated at outside facilities were identified as positive for influenza A by rapid antigen test.

Because of a strong suspicion that the responsible virus was nH1N1, identification, treatment, and containment efforts were begun immediately. Moreover, the USAFA does not use rapid antigen testing because of its modest sensitivity. Instead, nasal-wash specimens were collected from patients with influenza like illness (ILI) by saline wash (2–4 mL) of the nasopharynx repeated through each nostril.[8] ILI was initially defined as having an oral temperature ≥100.5°F and respiratory symptoms. Specimens were transported to the U.S. Air Force School of Aerospace Medicine (USAFSAM) epidemiology laboratory, Brooks City Base TX (near San Antonio), and tested for the presence of nH1N1-specific ribonucleic acid (RNA) by real-time reverse transcriptase–polymerase chain reaction (rRT-PCR).[1] All specimens were tested for influenza A; influenza B; respiratory syncytial virus; parainfluenza 1, 2, and 3; and adenovirus. However, only nH1N1 was identified during the outbreak period.

Beginning on July 7, all cadets meeting the ILI case definition were sent to a separate dorm area to convalesce until they were 7 days from symptom onset and were symptom free for 24 hours. On July 10, an additional dorm area was designated for those presenting with similar respiratory complaints but with a temperature of 99.0°F to 100.4°F. Patients in this group also remained isolated for 7 days and until 24 hours after symptom resolution, but they were separated from those with temperatures ≥100.5°F. The separation of this group, in addition to preventing potential transmission, allowed characterization of the spectrum of disease. Interim analysis of data revealed that approximately 50% of individuals with highest recorded temperatures between 100.0°F and 100.4°F were positive for nH1N1, with a lower incidence of positive nH1N1 results in those with temperatures <100.0°F. These findings led to a change in the criterion for isolation in the second area to having a temperature in the range of 100.0°F to 100.4°F.

On July 10, the USAFSAM epidemiology laboratory reported that of the first 18 nasal washes tested for the presence of nH1N1 by rRT-PCR, 15 (83%) yielded positive results. By this time, 88 BCTs were already in the separated dorm area.

Case Definition and Finding

A **confirmed** nH1N1 case patient was defined as a BCT, a cadet involved with BCT training, or a preparatory (prep) school student with symptom onset from June 25 to July 24, 2009, who had a nasal-wash specimen with nH1N1 virus identified by rRT-PCR. A **suspected** case patient also belonged to the groups mentioned above and presented with respiratory complaint onset from June 25 to July 24, 2009; had a highest recorded temperature of ≥100.5°F; and had no nasal wash obtained.

Electronic medical records were reviewed to retrospectively identify cases with dates of onset between June 25 and July 6. Case patients presenting for medical care starting on July 6 through July 24 were prospectively identified. Demographic and clinical data from confirmed and suspect patients were obtained from electronic medical records and from a standard influenza surveillance questionnaire. The 10th Medical Group pharmacy supplied information related to oseltamivir prescription.

Additional Outbreak Control Measures

Patients were prescribed oseltamivir at the treating physician's discretion, but were generally given 75 mg of oseltamivir two times daily for 5 days if the patients indicated onset of symptoms no more than 72 hours prior to presentation. Upper-class cadets ensured meal delivery to patient rooms. Healthcare providers made daily rounds of the separated dorm and approved release to the BCT population when a cadet had reached the end of the 7-day exclusion period and had been asymptomatic for ≥24 hours.

Healthcare providers and staff caring for patients with respiratory illness were offered oseltamivir prophylaxis and advised to wear a protective mask while in the same room as the patient exhibiting respiratory symptoms. Healthcare providers and technicians were fitted for and provided N95 masks. Technicians collecting nasal-wash samples wore a mask, a gown, gloves, and eye protection.

Screening events were conducted during the outbreak period. On July 13, BCTs marched to a location 3 miles north of the main campus to participate in 12 days of field-training activities. BCTs had their temperature measured with a paper oral thermometer (Tempadot) approximately 1 hour after arrival, and those with a temperature ≥99.6°F were referred for physician evaluation. On July 15, a cohort of 239 students arrived at the USAFA to start a 1-year prep school course. The prep school students were screened for temperature ≥99.6°F on arrival and were screened again on July 19. Students meeting the screening criteria were referred to a physician for evaluation.

The third screening event occurred on August 1 after the remainder of the student body (>3000 cadets) returned to campus. Upon arriving on campus, each cadet completed a screening questionnaire (*Do you feel like you have a fever or have you had a fever in the past 5 days?* and *Do you have a cough or sore throat?*). A cadet answering *yes* to both questions required immediate evaluation by a provider. All cadets were given an

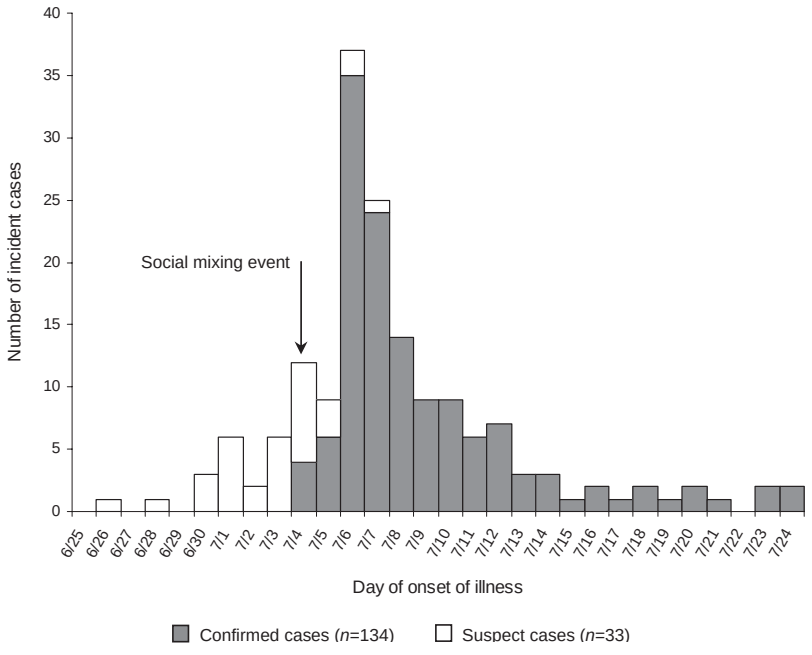

Figure 1. Confirmed (rRT-PCR positive) and suspect (respiratory complaint, temperature ≥100.5°F, and no specimen obtained) cases of novel influenza A (H1N1) virus infection at the U.S. Air Force Academy, by date of illness onset, from June 25 through July 24, 2009

education sheet on H1N1 that listed recommendations on when to seek care.

Public health personnel initiated an intense infection control and education campaign within the first 24 hours of detecting the outbreak. Mass briefings were conducted on proper cough and hand hygiene, and educational materials were provided for the base newspaper, incoming upper-class cadets, and parents of cadets. Cadets and USAFA personnel also received e-mails detailing the current situation and recommendations for prevention of transmission. Hand sanitizers were placed throughout the dorms and at the entrances to the dining facility.

Duration of nH1N1 Shedding

Patients transferred to the separate dorm were requested to provide a nasal-wash sample approximately every 48 to 72 hours until release. Samples were collected by medical technicians according to standard protocol,[8] and specimens were shipped on ice the following day to the USAFSAM epidemiology laboratory. Temperature and presence or absence of symptoms were documented for each cadet at every sample collection, and the date of symptom resolution was noted for each cadet. To determine presence of viable virus, specimens were inoculated onto primary monkey kidney cells.[9] Shell vials were stained at 24–48 hours for respiratory viruses, including influenza A. Tubes were incubated at 35°C for 10 days and assessed for cytopathic effect followed by immunofluorescent staining for influenza A. Cultures negative at 10 days were tested by hemadsorption to rule out influenza virus growth. Viable virus shedding was defined as culture-positive results at any time (24–48-hour shell vial or 10-day tissue culture).

Statistical Analysis

Data were accumulated in a spreadsheet program and analyzed using SPSS, version 14.0, and Epi Info 3.3.2. For descriptive results, categorical variables were given as proportions and continuous variables were described by the median or mean and range.

Results

Descriptive Epidemiology

There were 134 confirmed and 33 suspected nH1N1 cases identified for a total of 167 incident cases. Onset dates ranged from June 26 to July 24, 2009. Case counts peaked on July 6, with 37 case patients reporting symptom onset, and the counts declined over the remainder of the outbreak period (Figure 1). The peak occurred approximately 48 hours after a 4th of July event where >1300 BCTs socialized with members of other squadrons. Among the 134 confirmed cases, 115 (86%) were BCTs; ten (7%) were prep school students; and nine (7%) were upper-class cadets.

Of the 115 confirmed cases among BCTs, 20% (23) were women compared to 21% women in the total BCT population. The median age of case patients among BCTs was 18 years (range 17–24 years), consistent with the median age of BCTs. The most frequently reported signs and symptoms included cough, chills, sore throat, headache, and fatigue (Table 1). Among 86 confirmed

Table 1. Clinical characteristics of 86 patients with complete clinical information and confirmed nH1N1 infection

Sign or symptom	No. of patients (%)
Documented fever ≥100°F	81 (94)
Cough	80 (93)
Fatigue	74 (86)
Sore throat	74 (86)
Headache	72 (84)
Chills	70 (81)
Body ache	54 (63)
Rhinorrhea	41 (49)
Sinus congestion	38 (44)
Chest pain	25 (29)
Stiffness	24 (28)
Dyspnea	22 (25)
Diarrhea	8 (9)
Vomiting	8 (9)
Conjunctivitis	6 (7)
Earache	6 (7)

Table 2. Outbreak period incidence (attack rate) of nH1N1 infection by squadron among basic cadet trainees

Squadron	Confirmed[a] and suspected cases	Squadron population	Attack rate (per 100)
A	10	132	7.6
B	24	134	17.9
C	9	133	6.8
D	16	131	12.2
E	10	138	7.2
F	18	137	13.1
G	20	130	15.3
H	14	138	10.1
I	15	136	11.0
J	12	137	8.8
Total	148	1346	11.0

[a]Real-time reverse transcriptase–polymerase chain reaction positive

patients with complete clinical information, the highest recorded temperature for each patient ranged from 98.4°F to 104.6°F, with a mean of 101.3°F. Among a group of 53 BCTs with confirmed nH1N1 infection and for whom date of symptom resolution was recorded, the mean duration of symptoms was 5.6 days (range, 1–12 days). Disease severity was moderate to mild, and no deaths or hospitalizations were attributed to nH1N1 during the outbreak period. Among these 53 BCTs, 40 received oseltamivir treatment, and their mean duration of illness was 5.8 days (95% CI=4.9, 6.7 days; range, 1–12 days) compared to a mean of 5.0 days (95% CI=4.0, 6.0 days; range 3–8 days; p=0.36) in the 13 who did not receive oseltamivir treatment. The primary difference between these two groups was that they presented either in the first 48 hours of their symptoms or later than that.

Outbreak period incidence rates (attack rates) for confirmed and suspected cases among the ten training squadrons ranged from 6.8/100 BCTs to 17.9/100 BCTs (Table 2). The overall attack rate for confirmed and suspected cases among BCTs was 11.0/100 BCTs.

Outbreak Control Measures

A total of 228 cadets (213 BCTs) were placed in separated dorm areas during the outbreak period. The July 15 screening of approximately 1250 BCTs who completed the march to field training resulted in referral of eight (<1%) BCTs to a physician for further evaluation; four were diagnosed with ILI and sent to the separate dorm. There were no confirmed or suspect cases among healthcare personnel.

Duration of nH1N1 Shedding

A total of 159 serial nasal-wash specimens were collected from 53 cadets. The proportion of samples containing viable nH1N1 virus was highest in those obtained on Days 1–3 from symptom onset and declined with each proceeding day, beginning on Day 2. Among 29 samples obtained 7 days from symptom onset, seven (24%) contained viable nH1N1 virus (Table 3). Among 106 samples obtained from patients with a temperature <100°F at the time of sample collection, 31 (29%) contained viable nH1N1 virus, and 11 (19%) of 58 samples obtained from patients who had been symptom free for ≥24 hours at the time of collection contained viable nH1N1 virus.

Conclusion

On June 25, an incoming class of BCTs reported to the USAFA originating from all 50 states and 11 foreign countries. In July, the BCT class experienced a novel H1N1 outbreak representing one of the largest recognized nH1N1 clusters at a U.S. college to date. The outbreak period incidence rate (attack rate) of confirmed and suspected cases among the BCT class was 11/100 BCTs.

No deaths or hospitalizations were associated with this outbreak. BCTs undergo extensive medical screening prior to acceptance to the USAFA (e.g., asthma is a disqualifying medical condition). Therefore, mild disease severity and lack of adverse outcomes during this outbreak may be attributable to the stringent physical requirements for acceptance at the USAFA. The mean duration of illness, however, was greater than 5 days, and a small subset of cadets was subsequently diagnosed with bronchitis and pneumonia. Furthermore, college student populations with more heterogeneous health conditions could experience more severe disease, including possible mortality in those with major underlying medical conditions.

Table 3. Proportion of nasal-wash samples with viable nH1N1 by temperature, symptoms, and days from symptom onset

	Samples collected (*n*)	Culture positive (*n*)	Proportion culture positive (%)
Temperature ≥100°F	53	46	87
Temperature <100°F	106	31	29
<24 hours symptom free or symptomatic	101	61	60
≥24 hours symptom free	58	11	19
Day from symptom onset (including day of symptom onset)			
1st (day of symptom onset)	7	6	86
2nd	21	20	95
3rd	23	20	87
4th	10	7	70
5th	22	9	41
6th	11	4	36
7th	29	7	24
8th	16	2	13
9th	13	1	8
10th–14th	20	0	0

Individuals experiencing nH1N1 disease may shed virus up to 24 hours prior to onset of symptoms[10]; therefore, it is possible that nH1N1 was introduced by one or more BCTs or trainers before being aware of illness themselves. A retrospective records review identified low levels of patients presenting with ILI in BCTs prior to a 4th of July event where BCTs socialized with members of other squadrons. On July 6, cadet clinic personnel recognized an increase in BCTs presenting for medical care. The number of BCTs presenting for care increased during the next 2 days and peaked when 130 presented with complaints of respiratory symptoms on July 8. A surveillance system that used coding data was in place at the USAFA; this system can compare daily visits for respiratory illnesses with historical data from the previous 2 years. Such surveillance, if not already in place at colleges and universities, can be a useful tool for early detection of an outbreak.

The outbreak, as defined by date of symptom onset, peaked on July 6, when 37 confirmed and suspect case patients reported onset. Onset date counts of confirmed and suspect cases declined during the next 14 days. The outbreak was likely propagated by the mixing event on July 4. The interval between the mixing event and peak reported symptom onset is consistent with reported incubation periods for nH1N1, ranging from 1 to 5 days.[10] In addition, all ten BCT squadrons experienced nH1N1 transmission in a short time period, suggesting that the outbreak was initially propagated by a single event.

The rapid peak of the outbreak and subsequent decline indicate the effectiveness of response and mitigation efforts enacted immediately on outbreak recognition. Communication was critical during the outbreak. Timely risk communication allowed for isolation of sick BCTs within 24 hours of identification of the first suspected cases.

Other interventions that potentially contributed to the relatively rapid containment of this large outbreak included a public health campaign that began within 48 hours of the first suspected cases. This effort involved e-mails to students, staff, and other military personnel and publication of an article in the base newspaper to educate the population about nH1N1 and how to reduce transmission. It also included increased distribution of hand sanitizers to students and placement of hand sanitizers throughout the dorms and the dining facility. Real-time use of data from this population to make interim changes to the screening and management of the cadet population probably contributed to containment as well. Infection control among healthcare workers also potentially limited virus transmission and further spread as no nH1N1 transmission was recognized among them. There was no significant difference in duration of illness between those treated and those not treated with oseltamivir; furthermore, treatment selection bias may have played a role in the small difference that was seen.

The USAFA outbreak provided a unique opportunity to gain valuable information about the natural behavior of the nH1N1 virus. Findings from serial nasal washes indicated viable virus shedding on Day 7 from symptom onset among approximately one quarter of confirmed cases. Furthermore, being afebrile and asymptomatic did not guarantee that the patient was no longer shedding viable nH1N1 virus; in fact, 19% of those who reported being symptom free for more than 24 hours were still found to shed viable virus. Quantitative analyses of culture results obtained in this study were felt to be inappropriate because of the potential for variability in specimen-collection techniques among staff, in specimen-handling procedures, and in transit times to the diagnostic laboratory. The lack of quantitative analyses is a limitation of this study. Detection of virus by culture may not necessarily indicate that transmission is still possible. Recommended avenues for future investigation include detailed quantitative analyses of viral titer during the follow-up period and the identification of specific symptoms associated with viable viral shedding and viral titer.

Novel H1N1 is now endemic in all 50 U.S. states. University- and college-based outbreaks of H1N1 have already occurred and more can be expected as students gather from diverse geographic areas, reside in dorm settings, and attend mass gatherings such as football games, pep rallies, and student assemblies. The combination of aggressive separation of ill BCTs, public health education, and prompt implementation of healthcare infection control practices limited the duration and scope of the nH1N1 infection at the USAFA. Comprehensive plans and rapid implementation are critical. Isolation procedures implemented at the USAFA may not be practical in other university settings; however, preparedness planning, public health education activities, and healthcare infection control practices implemented at the USAFA can be adopted in other university settings.

We would like to thank the members of the USAFSAM Epidemiology Lab and Consult Services and the 10th Medical Group for their outstanding support in this investigation. Specifically we would like to thank Col (Dr.) Paul Sjoberg, Lt Col (Dr.) Victor MacIntosh, Genny Maupin, and Alicia Guerrero from the Epidemiology Consult Service and Madison Green and providers and medical technicians from the 10th Medical Group. We would also like to thank Dr. Gregory Poland for his review of an earlier version of the manuscript.

The views expressed are those of the authors and do not necessarily represent the views of the U.S. Air Force or the U.S. Department of Defense.

No financial disclosures were reported by the authors of this paper.

References

1. Dawood FS, Jain S, Finelli L, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009;360:2605–15.
2. WHO. Pandemic (H1N1) 2009 briefing note 3 (revised). Changes in reporting requirements for pandemic (H1N1)2009 virus infection. www.who.int/csr/disease/swineflu/notes/h1n1_surveillance_20090710/en/index.html.
3. Pandemic alert Level 6: scientific criteria for an influenza pandemic fulfilled. Euro Surveill 2009;14:19237.
4. CDC. 2009 H1N1 Flu (Swine Flu). www.cdc.gov/h1n1flu/.
5. Sato M, Hosoya M, Kato K, Suzuki H. Viral shedding in children with influenza virus infections treated with neuraminidase inhibitors. Pediatr Infect Dis J 2005;24:931–2.
6. Lee N, Chan PK, Hui DS, et al. Viral loads and duration of viral shedding in adult patients hospitalized with influenza. J Infect Dis 2009;200:492–500.
7. CDC. Interim guidance on specimen collection, processing, and testing for patients with suspected swine-origin influenza A (H1N1) virus infection. www.cdc.gov/h1n1flu/specimencollection.htm.
8. Canas LC, Lohman K, Pavlin JA, et al. The Department of Defense laboratory-based global influenza surveillance system. Mil Med 2000;165(7S 2):52–6.
9. Robinson CC. Respiratory viruses. In: Specter S, Hodinka RL, Young SA, Wiedbrauk DL, eds. Virology manual. 4th ed. Washington DC: ASM Press, 2009:203–48.
10. Thacker E, Janke B. Swine influenza virus: zoonotic potential and vaccination strategies for the control of avian and swine influenzas. J Infect Dis 2008;197(1S):S19–24.