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MAJOR ARTICLE

Exposure to Influenza Virus Aerosols During Routine Patient Care

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Background. Defining dispersal of influenza virus via aerosol is essential for the development of prevention measures.

Methods. During the 2010–2011 influenza season, subjects with influenza-like illness were enrolled in an emergency department and throughout a tertiary care hospital, nasopharyngeal swab specimens were obtained, and symptom severity, treatment, and medical history were recorded. Quantitative impaction air samples were taken not ≤0.305 m (1 foot), 0.914 m (3 feet), and 1.829 m (6 feet) from the patient's head during routine care. Influenza virus was detected by rapid test and polymerase chain reaction.

Results. Sixty-one of 94 subjects (65%) tested positive for influenza virus. Twenty-six patients (43%) released influenza virus into room air, with 5 (19%) emitting up to 32 times more virus than others. Emitters surpassed the airborne 50% human infectious dose of influenza virus at all sample locations. Healthcare professionals (HCPs) were exposed to mainly small influenza virus particles (diameter, <4.7 μm), with concentrations decreasing with increasing distance from the patient's head ($P < .05$). Influenza virus release was associated with high viral loads in nasopharyngeal samples (shedding), coughing, and sneezing ($P < .05$). Patients who reported severe illness and major interference with daily life also emitted more influenza virus ($P < .05$).

Conclusions. HCPs within 1.829 m of patients with influenza could be exposed to infectious doses of influenza virus, primarily in small-particle aerosols. This finding questions the current paradigm of localized droplet transmission during non–aerosol-generating procedures.

Keywords. Influenza; aerosol; exposure; infection control; routine care; healthcare providers.

Millions have lost their lives to influenza in pandemics, and epidemics of varying severity occur worldwide each year [1]. Strategies to prevent and control the often explosive outbreaks are limited to vaccination and treatment, if available, or to isolation and barrier precautions [2, 3]. Vaccination is considered the most important preventive measure, but there is a recognized need for additional control measures [4]. To ensure that the most effective control strategies are implemented, there must be a broader understanding of how and by whom influenza virus is transmitted [5–9].

Influenza virus can be transmitted by air [6–9]. Breathing, talking, coughing, and sneezing release influenza virus into air, with sizes ranging from submicron particles (during breathing) to large droplets (during coughing/sneezing) [6, 9–11]. The Centers for Disease Control and Prevention (CDC), the Institute of Medicine, the European Centre for Disease Control and Control, and the World Health Organization (WHO) have expressed lack of knowledge and the urgent need for research in influenza virus transmission routes. CDC and WHO state that influenza virus transmission primarily occurs by large-particle respiratory droplets traveling within a short distance of the source and that such particles are blocked during encounters between patients and healthcare professionals (HCPs) by face masks worn by HCPs [2–4, 12, 13]. Only during aerosol-generating procedures such as

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bronchoscopy are fit-tested respirators required. Deposition of influenza virus into the lungs (as small particles) or upper respiratory tract (as large droplets) may alter infection risk and illness severity [8, 14, 15].

Although influenza virus RNA has been detected in the air of pediatric departments and general emergency departments (EDs), no direct association with patients or healthcare activities has been determined [16, 17]. Carriage of influenza virus in the nasopharynx (shedding) has been linked to age and acute/chronic health conditions. However, it remains unclear whether shedding or other patient factors promote the release of influenza virus into the air [18–20]. The existence of superspreaders—patients infecting numerous contacts—has also been suggested [21, 22].

With the threat of pandemic influenza and uncertainty regarding efficacy of barrier precautions, the CDC's National Institute of Occupational Safety and Health and the Institute of Medicine have given priority to the development of methods to determine human influenza virus transmission routes [2, 4]. This study examines the spatial distribution of influenza virus aerosols generated by symptomatic patients in a healthcare setting and identifies clinical features associated with high levels of influenza virus release.

METHODS

Participants and Recruitment

During the influenza 2010–2011 influenza season, a convenience sample of 94 patients >2 years of age admitted to the ED (52 patients) or an inpatient care unit (42 patients) of Wake Forest Baptist Medical Center (WFBMC) were screened for influenza-like illness (ILI). ILI was defined as documented fever (temperature, ≥37.8°C) or patient-reported fever in the past 12 hours, cough/sore throat, and suspected influenza [2]. Demographic characteristics, medical and vaccination history, and treatments were recorded. Informed consent or assent was obtained from participants. The study was approved by the Institutional Review Board of WFBMC.

Setting

WFBMC is an 885-bed tertiary care teaching hospital. There are approximately 36 000 inpatient admissions and >89 000 ED visits annually involving pediatric and adult patients. During the study season, 247 influenza virus–positive patients were identified (115 inpatients, 67 clinic patients, and 65 ED patients). A mandatory vaccination policy for all HCPs was in place. Air sampling was conducted in patient rooms under turbulent airflows (6 total air changes/hour specified) at a room temperature of approximately 20°C and relative humidity of 40%. Air was filtered by end filters compliant with standard 52.2-2007 of the American National Standards Institute and American Society of Heating, Refrigerating, and Air-Conditioning Engineers, with a minimum efficiency reporting value of 15 [23].

Nasopharyngeal Swab Specimens and Air Sampling

Nasopharyngeal swab specimens were obtained from each subject. Samples were used for bedside rapid testing (BinaxNOW Influenza A&B, Inverness Medical Professional Diagnostics, Princeton, NJ) and inoculation into Becton Dickinson Universal Viral Transport System (BD Diagnostics, Franklin Lakes, NJ) for real-time reverse transcription polymerase chain reaction (rRT-PCR) analysis. Air samples were not obtained from participants negative for influenza virus by rapid testing.

The airborne dispersal pattern of influenza virus was assessed in a 20-minute run by three 6-stage Andersen air samplers (AS) placed facing the participant at head level at distances of ≤0.305 m, 0.914 m, and 1.829 m [24]. Particles carrying influenza virus were collected in Hanks balanced salt solution for rRT-PCR testing as described previously [25]. Participants were laying in bed during air sampling but were free to move their heads. They were asked to remove any equipment (eg, face or oxygen masks), with prior approval from their HCPs. None of the following aerosol-generating procedures were performed during air sampling: bronchoscopy, sputum induction, intubation and extubation, autopsies, cardiopulmonary resuscitation, and open suctioning of airways [2].

Measures of Illness

A self-administered questionnaire collected disease symptoms present at admission, using a Likert scale, and the duration of illness (Table 1). Severity of illness and interference with daily life by ILI were reported by participants, using a 100-mm visual analog scale [26]. Throughout air sampling, patients' coughs and sneezes were counted and assessed for severity (mild, moderate, or severe) by study personnel and were defined by the sum of the products of frequency and severity.

rRT-PCR Analysis

Aliquots of 140 μL of each nasopharyngeal swab specimen and AS stage were put into lysis buffer (AVL buffer, Qiagen, Valencia, CA) for RNA extraction and archiving at −80°C. Viral RNA from each aliquot was extracted with the Qiagen QIAamp Viral RNA mini spin kit, and rRT-PCR was performed to detect influenza A and B viruses (positive crossing threshold of <40 cycles). rRT-PCR analysis protocols and probe and primer sequences were provided by the CDC (Influenza Division, Virus Surveillance and Diagnostics Branch). Fluorogenic probes and primers were synthesized to CDC specifications by Biosearch Technologies (Novato, CA). Human RNase P gene RNA was detected in parallel for each specimen as an internal control procedure for human subject specimen adequacy.

Table 1. Participant Characteristics

Characteristic	Influenza Virus–Positive Subjects				Influenza Virus–Negative Subjects		
	Total	Emitters	Nonemitters	P^a		P^b	OR (95% CI)[c]
Sex							
Male	32 (52.5)	17 (65.4)	15 (42.9)	0.12	22 (66.7)	.20	…
Female	29 (47.5)	9 (34.6)	20 (57.1)		11 (33.3)		…
Race/ethnicity							
White	30 (49.2)	12 (46.2)	18 (51.4)	0.66	20 (60.6)	.32	…
Black	4 (6.6)	1 (3.85)	3 (8.6)		0		…
Other	27 (44.3)	13 (50)	14 (40)		13 (39.4)		…
Hispanic	6 (9.8)	3 (11.5)	3 (8.6)	1.00	2 (6.1)	.71	…
Non-Hispanic	55 (90.2)	23 (88.5)	32 (91.4)		31 (93.9)		…
Age, y							
Mean (SD)	31.2 (22.5)	29.7 (22.7)	32.3 (22.7)	0.55	22.4 (21.1)	.03	…
<18	24 (39.3)	11 (42.3)	13 (37.1)	0.79	16 (50)	.38	…
≥18	37 (60.7)	15 (57.7)	22 (62.9)		16 (50)		…
Patient status at enrollment							
Inpatient	35 (57.4)	13 (50)	22 (62.9)	0.43	7 (21.2)	.001	5.0 (1.9–13.3)
ED patient	26 (42.6)	13 (50)	13 (37.1)		26 (78.8)		…
Treatment							
Antivirals[d]							
Yes	29 (47.5)	14 (53.9)	15 (42.9)	0.44	3 (9.1)	<.001	9.1 (2.5–32.9)
No	32 (52.5)	12 (46.1)	20 (57.1)		30 (90.9)		…
Antibiotics							
Yes	12 (19.7)	5 (19.2)	7 (20.0)	1.00	10 (30.3)	.35	…
No	48 (78.7)	21 (80.8)	27 (77.1)		22 (66.7)		…
Unknown	1 (1.6)	0	1 (2.9)		1 (3.0)		…
Radiography performed							
Yes	32 (52.5)	10 (38.5)	22 (62.9)	0.07	12 (36.4)	.19	…
No	29 (47.5)	16 (61.5)	13 (37.1)		21 (63.6)		…
Medical history							
Transplant							
Yes	5 (8.2)	3 (11.5)	2 (5.7)	0.64	2 (6.1)	1.00	…
No	56 (91.8)	23 (88.5)	33 (94.3)		31 (93.9)		…
Cancer							
Yes	7 (11.5)	3 (11.5)	4 (11.4)	1.00	1 (3.0)	.25	…
No	54 (88.5)	23 (88.5)	31 (88.6)		32 (97.0)		…
Diabetes mellitus							
Yes	8 (13.1)	5 (19.2)	33 (94.3)	0.27	1 (3.0)	.15	…
No	53 (86.9)	21 (80.8)	2 (5.7)		32 (97.0)		…
Splenectomy							
Yes	4 (6.6)	1 (3.8)	3 (8.6)	0.63	1 (3.0)	.65	…
No	57 (93.4)	25 (96.2)	32 (91.4)		32 (97.0)		…
Cardiovascular disease							
Yes	14 (22.9)	5 (19.2)	9 (25.7)	0.76	2 (6.1)	.05	…
No	47 (77.1)	21 (80.8)	26 (74.3)		31 (93.9)		…
HIV positive							
Yes	0	0	0		1 (3.0)	.35	…
No	61	26	35		32 (97.0)		…
Kidney disease							
Yes	3 (4.9)	1 (3.8)	2 (5.7)	1.00	1 (3.0)	1.00	…
No	58 (95.1)	25 (96.2)	33 (94.3)		32 (97.0)		…

Table 1 continued.

Characteristic	Influenza Virus–Positive Subjects				Influenza Virus–Negative Subjects		
	Total	Emitters	Nonemitters	P^a		P^b	OR (95% CI)[c]
Liver disease							
Yes	1 (1.6)	0	1 (2.9)	1.00	1 (3.0)	1.00	…
No	60 (98.4)	26 (100)	34 (97.1)		32 (97.0)		…
Sickle cell disease							
Yes	2 (3.3)	0	2 (5.7)	0.50	2 (6.1)	.61	…
No	59 (96.7)	26 (100)	33 (94.3)		31 (93.9)		…
Asthma							
Yes	12 (19.7)	8 (30.8)	4 (11.4)	0.10	2 (6.1)	.13	…
No	49 (80.3)	18 (69.2)	31 (88.6)		31 (93.9)		…
Seizure history							
Yes	2 (3.3)	2 (7.7)	0	0.18	0	.54	…
No	59 (96.7)	24 (92.3)	35		33		…
Developmental delay							
Yes	1 (1.6)	1 (3.8)	0	0.43	1 (3.0)	1.00	…
No	60 (98.4)	25 (96.2)	35		32 (97.0)		…
Neurological conditions							
Yes	3 (4.9)	2 (7.7)	1 (2.9)	0.57	1 (3.0)	1.00	…
No	58 (95.1)	24 (92.3)	34 (97.1)		32 (97.0)		…
Vaccination status							
Seasonal influenza vaccine							
Yes	19 (31.1)	10 (38.5)	9 (25.7)	0.40	8 (24.2)	.63	…
No	42 (68.9)	16 (61.5)	26 (74.3)		25 (75.8)		…
Pneumococcal vaccine							
Yes	6 (9.8)	2 (7.7)	4 (11.4)	1.00	1 (3.0)	.42	…
No	55 (90.2)	24 (92.3)	31 (88.6)		32 (97.0)		…

Data are no. (%) of subjects, unless otherwise indicated.

Abbreviations: CI, confidence interval; ED, emergency department; HIV, human immunodeficiency virus; OR, odds ratio.

[a] Emitters vs nonemitters.

[b] All influenza virus–positive subjects vs influenza-negative subjects.

[c] Reported for statistically significant differences between all influenza virus–positive subjects and influenza-negative subjects.

[d] Oseltamavir.

Quantitative rRT-PCR analysis was performed to determine the influenza virus copy number in nasopharyngeal swab and air specimen, as described previously [25]. Briefly, primer sequences for the influenza virus M gene amplification target were used. Synthesized DNA vectors (GeneArt, Invitrogen, Grand Island, NY) containing target influenza A and B virus M gene regions encoded in plasmid vector were used to create standard curves to quantify viral RNA in patient samples. All rRT-PCR reactions were setup and run using a 96-well format and an Eppendorf epMotion 5070 robot with MasterCycler ep Realplex 2 instrument (Eppendorf, Hauppauge, NY). PCR product was detected using the QuantiTech SYBR Green rRT-PCR Kit (catalog number 204 243, Qiagen). The average number of influenza virus RNA copies per rRT-PCR assay of nasopharyngeal swab and AS specimens was calculated.

The viral load was expressed in copies per human respiratory minute volume (10 L/min) to reflect inhalation exposure by an active adult HCP. To allow comparison of rRT-PCR results to the airborne 50% human infectious dose (HID_{50}), a ratio range of 150 to 650 RNA copies to 1 median tissue culture infective dose ($TCID_{50}$) was used [8, 27]. With HID_{50} values ranging from 0.6 to 3.0 $TCID_{50}$, RNA influenza virus copies span from 90 to 1950 copies 14].

Statistical Analysis

Subject characteristics, influenza virus types, viral load, and symptoms were described by influenza virus test result (positive vs negative) and emitter status (emitter, superemitter, and nonemitter). We defined emitters as subjects surrounded by influenza virus aerosols, including superemitters, who

Table 2. Comparison of Influenza Virus Types, Nasopharyngeal Viral Load, and Symptoms Among Emitters and Nonemitters of Influenza Virus via Air

Characteristic	Influenza Virus–Positive Subjects		P^a	OR (95% CI)[b]
	Emitters	Nonemitters		
Influenza A virus infection	13 (50)	18 (51.4)	1.00	…
Influenza B virus infection	13 (50)	17 (48.6)		…
Nasopharyngeal VL, no. of copies, mean (SD)	2 539 979 (7 433 480)	885 242 (4 190 682)	.01	1.38 (1.07–1.76)[c]
Symptoms at admission				
Sneezing			.29	
Absent	1 (3.9)	1 (2.9)		…
Mild/moderate	25 (96.2)	29 (82.9)		…
Severe	0	5 (14.3)		…
Runny nose			.64	
Absent	2 (7.7)	1 (2.9)		…
Mild/moderate	21 (80.8)	31 (88.6)		…
Severe	3 (11.5)	3 (8.6)		…
Congestion				
Absent	0	3 (8.6)	.38	…
Mild/moderate	25 (96.2)	31 (88.6)		…
Severe	1 (3.9)	1 (2.9)		
Sore throat				
Absent	9 (34.6)	8 (22.9)	.64	…
Mild/moderate	10 (38.5)	17 (48.6)		…
Severe	7 (26.9)	10 (28.6)		…
Cough				
Absent	0	0	.38	…
Mild/moderate	8 (30.8)	7 (20.0)		…
Severe	18 (69.2)	28 (80.0)		…
Malaise			.09	
Absent	0	0		…
Mild/moderate	11 (42.3)	7 (20.0)		…
Severe	15 (57.7)	28 (80.0)		…
Chills			.03	
Absent	5 (19.2)	0		…
Mild/moderate	11 (42.3)	20 (57.1)		…
Severe	10 (38.5)	15 (42.9)		…
Headache			.72	
Absent	3 (11.5)	2 (5.7)		…
Mild/moderate	17 (65.4)	23 (65.7)		…
Severe	6 (23.1)	10 (28.6)		…
Symptoms during air sampling				
Coughing			.64	
Absent	2 (7.7)	6 (17.1)		…
Mild/moderate	18 (69.2)	21 (60)		…
Severe	6 (23.1)	6 (17.1)		…
Sneezing			.24	
Absent	15 (57.7)	25 (71.4)		…
Mild/moderate	9 (34.6)	10 (28.6)		…
Severe	2 (7.7)	0		…
Severity of illness scale, mean (SD)				
All patients	77.7 (13.6)	76.3 (14.7)	.85	…
Inpatient (n = 35)	79.6 (12.3)	83.9 (9.0)	.31	…
ED patients (n = 26)	75.8 (15.0)	63.5 (13.6)	.05	1.06 (1.00–1.13)

Table 2 continued.

Characteristic	Influenza Virus–Positive Subjects			
	Emitters	Nonemitters	P^a	OR (95% CI)[b]
Interference with life scale, mean (SD)				
All patients	87.7 (11.2)	85.9 (15.2)	.69	…
Inpatient (n = 35)	89.2 (11.9)	93.2 (8.9)	.37	…
ED patients (n = 26)	86.2 (10.6)	73.5 (15.7)	.02	1.13 (1.01–1.27)
Total symptom score,[d] mean (SD)				
All patients	16.5 (4.1)	17.5 (3.3)	.42	…
Inpatient (n = 35)	16.2 (3.7)	18.0 (3.4)	.15	…
ED patients (n = 26)	16.8 (4.5)	16.5 (2.9)	.74	…
Days sick, mean (SD)				
All patients	3.3 (1.3)	3.9 (1.6)	.15	…
Inpatients (n = 35)	3.5 (1.5)	4.4 (1.6)	.17	…
ED patients (n = 26)	3.2 (1.1)	3.1 (1.1)	.96	…

Data are no. (%) of subjects, unless otherwise indicated.

Abbreviations: CI, confidence interval; ED, emergency department; OR, odds ratio; VL, viral load.

[a] Emitters vs nonemitters.

[b] Reported for statistically significant differences between emitters and nonemitters.

[c] For every 10-fold increase in $\log_{10}$-transformed nasal viral load, there was a 38% greater risk of being an emitter.

[d] Defined as the sum of individual symptom scores (0–5) reported at admission, excluding fever.

exceeded average influenza virus aerosol concentrations by multiple times, and nonemitters, who had no influenza virus detectable in aerosol. Frequencies and percentages were calculated for categorical variables, and statistical significance was assessed using χ^2 and Fisher exact tests. For continuous variables, means and SDs were calculated, and statistical significance was assessed using *t* tests and Wilcoxon rank sum tests, depending on the data distribution. To assess the spatial distribution of influenza virus aerosols on the basis of rRT-PCR-based count, a generalized estimating equation model for Poisson distribution with the log link function was used. Significance was set at an α level of .05. All analyses were performed using SAS 9.2 (Cary, NC).

RESULTS

Influenza Virus Positivity, Patient Characteristics, and Symptoms

Ninety-four patients with ILI symptoms were enrolled. Sixty-one (65%) tested positive for influenza virus, with 31 carrying influenza A virus and 30 carrying influenza B virus. Thirty-five subjects underwent air sampling as inpatients, and 26 underwent air sampling in the ED. Aerosolized influenza virus was detected in 26 subjects (43%; 13 inpatients and 13 ED patients). Results of rapid testing matched rRT-PCR results of nasopharyngeal and air samples. Twenty-four patients were <18 years of age (11 emitters and 13 nonemitters), and 37 were ≥18 years of age (15 emitters and 22 nonemitters). More specific age cohorts were as follows: 2–6 years, 4 emitters and 3 nonemitters; 7–12 years, 5 and 7, respectively; 13–17 years, 2 and 3, respectively; 18–24 years, 1 and 3, respectively; 25–30 years, 2 and 3, respectively; 21–36 years, 0 and 1, respectively; 37–42 years, 4 and 3, respectively; 43–48 years, 3 and 1, respectively; 49–54 years, 2 and 4, respectively; 55–60 years, 2 and 3, respectively; and ≥61 years, 1 and 4, respectively.

Patient characteristics are summarized in Table 1. Influenza virus–negative patients were younger, less likely to receive antiviral therapy, and more likely to be enrolled in the ED, compared with influenza virus–positive patients. Comparison of emitters with nonemitters showed no significant differences.

Table 2 compares influenza virus–specific variables and symptoms during air sampling. Emitters carried higher nasopharyngeal viral loads than nonemitters. Coughing and sneezing during air sampling was associated with increased influenza virus release into room air only among patients with increased nasopharyngeal viral load. Emitters (both ED patients and inpatients) were less likely to have chills and reported higher severity of illness and interference with daily lives than nonemitters (ED patients only). Five of the 26 emitters (19%) released, on average, 32 times more influenza virus into room air (Figure 1); all other characteristics or symptoms were statistically similar. Three ED patients were admitted to the hospital with sickle cell syndrome (1 case), sickle cell syndrome and asthma (1 case), or foot injury (1 case); none were emitters.

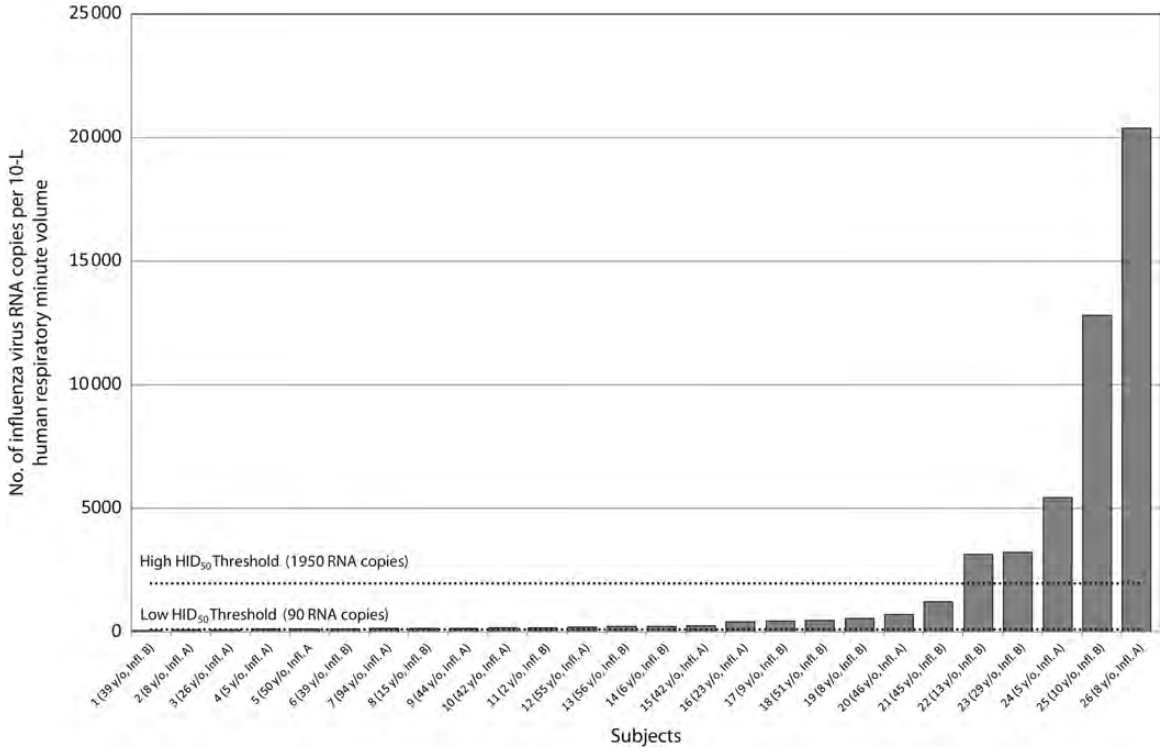

Figure 1. Total aerosol concentrations of influenza virus emitted by individual subjects over 20 minutes. In the *x*-axis, patient age and influenza virus type are shown in parentheses. Abbreviations: HID_{50}, 50% human infectious dose; Infl., influenza; y/o, years old.

Aerosol Dispersal Patterns

Figure 2 displays the spatial distribution of influenza virus–containing aerosol particles in patient rooms, by particle size (ie, <4.7 μm and ≥4.7 μm). With increasing distance from the patient's head (from 0.305 m to 1.829 m), the viral load decreased significantly and the number of small particles increased significantly, relative to the number of large particles. No differences between influenza virus types, emitters and superemitters, and patient location were detected.

DISCUSSION

Protecting HCPs against influenza virus requires a clear understanding of how this virus is aerosolized and by whom it is emitted [4]. Our study focused on the presence of influenza virus in aerosols in the vicinity of symptomatic patients during routine care. Twenty six of 61 influenza virus–infected patients released influenza virus into room air. We found infectious amounts of virus up to 6 feet from patients during non–aerosol-generating patient-care activities, predominantly in small particles (diameter, <4.7 μm). High nasopharyngeal viral load, severity of illness, and impact on daily life were linked to dispersal. Five of the 26 emitters released influenza virus in exceptionally high concentrations.

The spatial distribution pattern of influenza virus in patient rooms revealed high influenza virus concentrations within 0.914 m of the patient's head, dropping significantly by 1.829 m. Previous studies found influenza virus RNA in the air of ED settings [16, 17]. Tseng et al detected influenza A virus in a pediatric ED [16], whereas Lindsley et al found mostly small particles containing influenza A virus in a general ED [17]. However, both studies assessed the general viral air load independent of patients or care activities. We established that HCPs could be exposed to airborne influenza virus at a distance of up to 1.829 m (6 feet) from a patient with symptomatic influenza virus infection.

The size of airborne particles determines how influenza virus is transmitted. Large particles (diameter, ≥20 μm) have limited travel distance, while smaller particles (diameter, <5 μm) stay airborne longer and spread widely [6, 11, 28]. We found that up to 89% of influenza virus–carrying particles were <4.7 μm in diameter. Notably, no aerosol-generating procedures were undertaken during air sampling [2]. The predominance of small particles has been reported previously, with influenza virus detected in the exhaled breath of 4 of 12 subjects (33%) breathing normally [27]. Although the majority of particles (>87%) were <1 μm in diameter, the sizes containing virus were not identified. The effect of coughing was

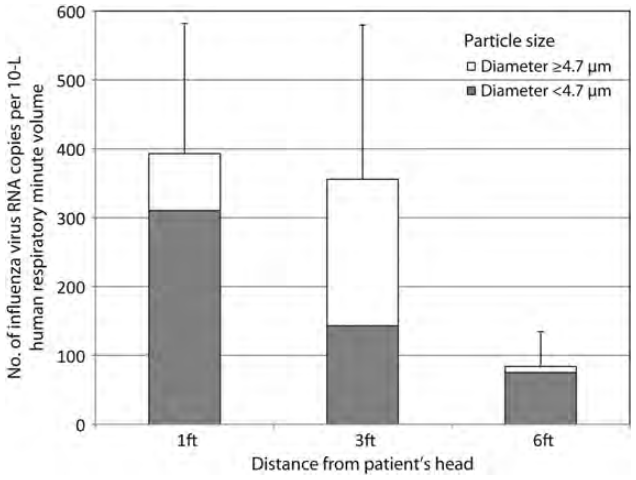

Figure 2. Spatial distribution of the average aerosol concentrations of influenza virus, measured over 20 minutes, in patient rooms. The number of emitters exceeding the low HID_{50} (defined as >90 RNA copies) was 13 (50%) at ≤0.305 m, 11 (42%) at 0.914 m, and 9 (35%) at 1.829 m. The number of emitters exceeding the high HID_{50} (defined as >1950 RNA copies) was 3 (12%) at ≤0.305 m, 2 (8%) at 0.914 m, and 1 (4%) at 1.829 m. The same emitter can exceed the HID_{50} at >1 distance.

studied in 47 influenza virus–positive patients [29]. Thirty-eight (81%) released influenza virus, with 65% of RNA contained in particles <4 μm in diameter. The published data and our findings indicate that small particles carry the majority of influenza virus other than virus released during aerosol-generating procedures [17, 27, 29]. We consider it unlikely that, during routine care, influenza virus is transmitted solely by droplet-sized particles.

To date all influenza virus aerosol studies, including ours, have used RT-PCR to detect influenza virus, because of the difficulties working with low concentrations of particles and the insensitivity of cell cultures [8]. Infectivity of an airborne virus is difficult to assess by rRT-PCR when the targets of measurement are fragments of the viral genetic code, compared with a functioning virus [8]. However, estimates of the decay of influenza virus aerosols can be used to establish the infectious dosage contained in virus RNA. Previous studies have calculated a ratio of 150–650 RNA copies to 1 $TCID_{50}$ [8]. Alford et al reported an influenza virus HID_{50} of 0.6–3 $TCID_{50}$, translating into RNA load of 90–1950 copies [14]. In our study, the lower HID_{50} of 90 was achieved by all emitters, whereas 5 patients surpassed the higher dose of 1950 copies. The air viral load is given as a total over 20 minutes. However, subjects may release influenza virus in bursts by sneezing or coughing, creating peak concentrations of influenza virus within minutes if not seconds. Therefore, with a 6-foot (1.829 m) zone, HCPs can be exposed to concentrations of influenza virus that are sufficient to cause infection.

Identification of emitters may improve understanding of influenza virus transmission. Patients can carry influenza virus in their respiratory tract from days to months, a phenomenon commonly described as shedding [18–20]. In our study, shedding was linked to virus emission. Patients had a 38% greater tendency of releasing influenza virus with every 10-fold increase of the respiratory viral load. Shedding has been associated with specific patient characteristics and symptoms: younger age, days sick, impaired immune system, severity of illness, and fever [18–20]. For dispersal, however, age, days sick, immune defects, or other chronic conditions were not related. Fever was one of the screening criteria of ILI and could not be used for analysis. The age-effect difference may be explained by young patients shedding more virus than adults but emitting similar amounts, because of a lower respiratory volume. While chronic conditions did not impact dispersal, acute symptoms did: higher severity of illness and greater impact on daily life were associated with increased influenza virus release. The latter symptoms were reported by ED patients but not by inpatients, pointing to a different health perception between the groups at enrollment, with symptom acuity leading patients to visit the ED. It should be noted that the visual analog scale used for the severity measures has been shown to allow a more precise documentation of the patients' health status than the Likert scale used to document symptoms on admission [26]. The 2 indicators, severity of illness and impact on daily life, may be considered to identify emitters in the ED.

Coughing and sneezing represent a mechanical component for emission [6, 10, 11, 27, 29]. We found that patients carrying high concentrations of influenza virus also released the virus more frequently into air while coughing or sneezing. This interaction points to a multifactorial process including physiological parameters, such as shedding, and mechanical aspects, such as sneezing and coughing, in releasing influenza virus.

Not all patients emitted influenza virus in a similar fashion. While the majority of symptomatic subjects released <1300 RNA copies, 5 subjects produced significantly higher levels of influenza virus RNA (up to 20 400 copies). Interestingly, the percentage of superemitters (19%) fits the proposed 20/80 rule, suggesting that roughly 20% of the most infectious individuals are responsible for 80% of infections [21]. Although this rule has not proven for influenza virus transmission, the concept of heterogeneity in infectiousness should be considered because it has been demonstrated in severe acute respiratory syndrome [21, 22]. Targeting superemitters to control transmission may also be a more effective and efficient alternative to the broad approach that targets all patients with influenza [22]. However, our limited sample did not allow us to identify specific symptoms or characteristics for superemitters. More data regarding person-to-person virus transmission are necessary before the role of superemitters can be established.

This study has limitations. We used PCR methods to detect genetic evidence of influenza virus in aerosol particles, rather than cell culture to analyze virion growth, making it impossible to distinguish viable from nonviable virus. Furthermore, our study addresses exposure to influenza virus aerosol rather than transmission to persons susceptible to influenza virus infection. The cross-sectional design provides only a snapshot of the emission dynamics of influenza virus, making generalizations of the dispersal routes over illness progression difficult. Participants were recruited from a convenience sample of ED and inpatients, using CDC ILI criteria and a rapid influenza virus test as screening tools. This excluded asymptomatic emitters and possibly favored more severely sick patients carrying high amounts of influenza virus in their respiratory tract [30]. AS have been successfully used to collect virus aerosols but fail to differentiate among larger particle sizes (diameter, >7 μm) [31]. Sampling was performed in real-life environments that did not allow for control of air changes, flow patterns, and other characteristics that may influence virus detection. Influenza virus aerosols may have been generated by infected individuals other than the participants. However, the influenza virus types isolated from swab specimens were also found in the air surrounding the individuals, vaccination was mandatory for all HCPs, and shedding was associated with influenza virus emission, making outside contamination less likely. Determining an infectious dose for influenza virus is hampered by the scarcity of human exposure studies, with the uncertainty of this estimate revealed by the width of the range of potentially infectious dosages identified in the literature.

The current paradigm is that influenza virus transmission primarily occurs by large particles traveling only 1 m (3.3 feet) (according to the WHO) or 1.829 m (6 feet) (according to the CDC) from the source [2, 3, 13]. While transmission via small-particle aerosols (ie, airborne transmission) or indirect contact transmission cannot be ruled out, the recommendations focus on droplet and standard precautions, with special instructions for aerosol-generating procedures. Droplet precautions require a facemask (eg, surgical mask), while fitted respirators (N95) are recommended for aerosol-generating procedures [2, 13]. We found that patients produced mostly small influenza virus–carrying particles during routine, non–aerosol-generating care activities. HCPs could be exposed to infectious doses of influenza virus at a distance of up to 1.829 m (6 feet) from patients, with small particles potentially exceeding the suggested exposure zones [2, 3]. This raises concerns regarding the adequacy of protection afforded to HCPs by the current recommendations during routine care [2, 3, 13].

In summary, frequent release of small particles at distances of up to 1.829 m from the patient's head during routine non–aerosol-generating activities may warrant a reevaluation of the current recommendations [2, 3, 13]. Characteristics of emitters, including severity of illness and impact of illness on daily life, should be further evaluated as screening tools. The detection of superemitters suggests that infectiousness may vary among patients with influenza. Our study offers new evidence of the natural emission of influenza virus and may provide a better understanding of how to best protect HCPs during routine care activities.

Notes

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