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Letter to the Editor

Airborne transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): What is the implication of hospital infection control?

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To the Editor—Airborne transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), has been increasingly recognized in the indoor air environment,[1] especially in poorly ventilated premises.[2] In the recent update of a scientific brief by Centers for Disease Control and Prevention, the modes of SARS-CoV-2 transmission include inhalation of very fine respiratory droplets and aerosol particles, deposition of virus on exposed mucous membranes, and touching mucous membranes with soiled hands contaminated with virus.[3] A nosocomial outbreak of COVID-19 was possibly attributed to airborne transmission in an old-fashioned general ward with low ceiling height, despite 6 air changes per hour (ACH).[4] To establish the role of airborne transmission of SARS-CoV-2 in the healthcare setting, it is important to demonstrate the presence of SARS-CoV-2 RNA and (preferably) viable virus in the air sample. However, this requires a challenging experiment. In the previous reports of air sampling in the clinical areas, findings have been inconsistent.[5] This inconsistency is not unexpected because air samplers with different mechanisms of sample collection (eg, solid impactors, liquid impactors, filters, and other sampling methods) were used. In addition, the testing protocols were different in terms of the relative position between patients and air samplers, number of patients in the room or ward, volume of air collected per sample, and the ACH in the patient care areas. Patient factors of transmission include the severity of clinical symptoms, the presence of aerosol-generating procedure (AGP), viral load of clinical specimens, and whether the patient wore a surgical mask during sample collection. Current literature reporting the detection of SARS-CoV-2 RNA in the air in the healthcare setting is summarized in Supplementary Table 1 (online). Most of these studies do not mention the patient's viral load or whether the patient wore a surgical mask during sample collection.

To demonstrate the SARS-CoV-2 RNA viral load correlation between air and clinical samples, we performed air sampling in the airborne infection isolation room (AIIR; 16 m^2 and 12 ACH) where a single asymptomatic COVID-19 patient was cared for from June 11 to June 17, 2021. This patient was transferred to this hospital and had SARS-CoV-2 (PANGO lineage B.1.525). No AGP was performed during air sample collection. We collected the air sample using the AerosolSense Sampler (Thermo Fisher Scientific, Waltham, MA),[6] which is ~35.5 cm in 3 dimensions and weighs 11.8 kg. It was placed 1 m from the patient's head. A single-use sampling cartridge containing 2.5 cm collection substrates was installed into the sampler. The air sample was collected through an omnidirectional inlet and was directed toward the collection substrate through an accelerating slit impactor at a flow rate of 200 L per minute. Particles were trapped on the collection substrate as the air moved around the collection area. After the sampling cycles of 2, 4, and 8 hours with patient with and without surgical masks, the sample cartridges were removed and sent to microbiology laboratory within 30 minutes. The collection substrates were then immersed into 1.5 mL viral transport medium and 250 μL medium for total nucleic acid extraction using the eMAG extraction system (bioMérieux, Marcy-l'Etoile, France) following the manufacturer's instructions. Quantification of SARS-CoV-2 RNA in the air samples was performed using the ultra-sensitive reverse-transcriptase droplet digital polymerase chain reaction (RT-ddPCR) with the QX200 Droplet Digital PCR System (Bio-Rad Life Science, Hercules, CA) as previously described.[7] The nasopharyngeal swabs were subjected to the same laboratory processing protocol. The viral loads of the air and clinical samples are summarized in Table 1.

Our findings have implications for hospital infection control. In contrast to our previous report of undetectable SARS-CoV-2 RNA in 1,000 L air samples,[8] the SARS-CoV-2 RNA was detected at a concentration of 0.009 copies/L in the room of a COVID-19 patient who was not wearing surgical mask, with a moderate level of viral load (6,828,801 copies/mL) in the nasopharyngeal swab sample when 96,000 L air was collected over 8 hours. SARS-CoV-2 RNA was also detected (0.005 copies/L) in another 8-hour air sample from the room of this COVID-19 patient who was wearing a surgical mask. It appears that a low quantity of SARS-CoV-2 RNA can be detected in air, even in an AIIR with 12 ACH, when a large volume of air is collected for a prolonged period. If the experiment is performed in a general ward with 6

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Table 1. SARS-CoV-2 RNA Viral Load Correlation Between Clinical and Air Samples in Airborne Infection Isolation Room Where A Single Asymptomatic COVID-19 Patient Received Care[a]

Sample No. [b]	Wearing Surgical Mask During Air Sampling [c]	Duration/Total Volume of Air Collection [d]	Viral Load of NPS (Copies per mL) [e, f]	Viral Load of Air Sample (Copies per Sample) [f]	Viral Load of Air Sample (Copies per L of Air)
1	No	2 h/24,000 L	355,692	ND	. . .
2	Yes	2 h/24,000 L	355,692	ND	. . .
3	No	4 h/48,000 L	14,140	ND	. . .
4	Yes	4 h/48,000 L	14,140	ND	. . .
5	No	8 h/96,000 L	6,828,801	774	0.009
6	Yes	8 h/96,000 L	974	497	0.005

Note. ND, not detected; NPS, nasopharyngeal swab; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]No aerosol-generating procedure was performed during the air sample collection.
[b]The air samples were collected during the daytime. To explore the presence of SARS-CoV-2 RNA in the air, the first sample (sample 5) was collected for 8 h in the airborne infection isolation room where patient not wearing surgical mask. Subsequently, we collected air samples at 2-h and 4-h intervals near the same patient wearing and not wearing a surgical mask, followed by the last air sample (ie, sample 6, 8 hours wearing surgical mask).
[c]The COVID-19 patient wore American Society of Testing and Materials level 1 standard surgical masks during air sampling.
[d]AerosolSense Sampler (Thermo Fisher Scientific, Waltham, MA) was used. The airflow rate was 200 L per minute.
[e]The viral load of NPS was collected on the same day as the air sampling.
[f]Specific primer/probe set targeting the SARS-CoV-2 N2 gene and the human housekeeping gene RNase P gene were assessed for use in RT-ddPCR. The following cycling conditions were used: 50°C (60 min), 95°C (10 min), 40 cycles of 94°C (30 s) and 60°C (1 min), 98°C (10 min), 4°C (30 min), 4°C (∞). Data analysis was performed by using the QuantaSoft Analysis Pro Sofware (Bio-Rad Life Science, Hercules, CA).

ACH, a higher quantity of SARS-CoV-2 RNA may be detected in the air. Therefore, inhalation of SARS-CoV-2 by patients may be possible if there is an unrecognized COVID-19 case in the same cubicle.[4] In such a case, a portable high-efficiency particulate filter may be installed, especially in an old-fashioned ward with suboptimal ventilation. In addition to the recommendation that healthcare workers (HCWs) wear surgical respirators during AGPs, we also suggest universal masking of patients and HCWs to reduce the risk of nosocomial transmission of SARS-CoV-2 in the healthcare setting.[9] These measures should be followed until herd immunity of COVID-19 through mass vaccination has been achieved.

Similar to the healthcare system in other developed areas, in Hong Kong we manage COVID-19 patients in hospital AIIRs with 12 ACH or in community treatment facilities with air ventilation of 80 L per second per person.[10] Full personal protective equipment, including surgical respirator, cap, face shield, gown, and gloves, is mandated when caring for COVID-19 patients. The risk of inhalation of SARS-CoV-2 by HCWs in hospital AIIRs or community treatment facilities is extremely low. However, transmission of SARS-CoV-2 is not only limited to the airborne route. Infection control professionals should update HCWs with new scientific evidence while enforcing hand hygiene, standard precautions, contact precautions, and droplet precautions to prevent nosocomial outbreaks of COVID-19.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2021.318

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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