

# Supplemental treatment of air in airborne infection isolation rooms using high-throughput in-room air decontamination units

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**Background:** Evidence has recently emerged indicating that in addition to large airborne droplets, fine aerosol particles can be an important mode of influenza transmission that may have been hitherto underestimated. Furthermore, recent performance studies evaluating airborne infection isolation (AII) rooms designed to house infectious patients have revealed major discrepancies between what is prescribed and what is actually measured.

**Methods:** We conducted an experimental study to investigate the use of high-throughput in-room air decontamination units for supplemental protection against airborne contamination in areas that host infectious patients. The study included both intrinsic performance tests of the air-decontamination unit against biological aerosols of particular epidemiologic interest and field tests in a hospital AII room under different ventilation scenarios.

**Results:** The unit tested efficiently eradicated airborne H5N2 influenza and *Mycobacterium bovis* (a 4- to 5-log single-pass reduction) and, when implemented with a room extractor, reduced the peak contamination levels by a factor of 5, with decontamination rates at least 33% faster than those achieved with the extractor alone.

**Conclusion:** High-throughput in-room air treatment units can provide supplemental control of airborne pathogen levels in patient isolation rooms.

**Key Words:** Airborne transmission; air purification; protective environments; influenza transmission.

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Recent evidence concerning the airborne transmission of influenza viruses suggests that in addition to short-range contact arising from large airborne droplets (eg, >5-10  $\mu\text{m}$ ) expelled from human coughs and sneezes, smaller fine particles and droplet nuclei (<5  $\mu\text{m}$ ) that travel over large distances may be an effective contamination source as well.<sup>1-5</sup> Specifically, Fabian et al<sup>1</sup> detected RNA from influenza A and B viruses in the exhaled breath of infected patients, with the vast majority of exhaled particles <1  $\mu\text{m}$  in diameter. Using

a guinea pig model, Mubareka et al<sup>2</sup> demonstrated the efficient aerosol transmission of influenza A over long ranges, >1 m from the source. Recent studies on airborne transmission among ferrets (which are considered a good model for testing vaccines or drugs against any new flu strains in lieu of a pandemic) have reported similar findings.<sup>3,4</sup> These findings and the recent review by Tellier<sup>5</sup> indicate that the relative importance of influenza transmission from small airborne particles, which can remain airborne for more than 60 minutes, may be underestimated, and that precautionary measures to address this risk should be considered.

There is clear evidence demonstrating a definitive association between the transmission of airborne infections and the ventilation of buildings.<sup>6</sup> As such, current guidelines for airborne environmental infection control in health care facilities issued by the Centers for Disease Control and Prevention (CDC) call for housing patients infected with organisms spread via airborne droplet nuclei in specialized care environments known as airborne infection isolation (AII) rooms.<sup>7</sup> Owing to the recognized importance of airborne transmission of tuberculosis, similar guidelines also have been issued for patients with suspected or confirmed *Mycobacterium tuberculosis* infection.<sup>8</sup> These isolation rooms should receive numerous air changes per hour

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Conflict of interest: Nicolas Laudinet is a microbiologist employed by AirInSpace.

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(ACH) and have a negative pressure of at least 2.5 Pa, such that the airflow is directed from the peripheral adjacent space into the room. Air within these rooms is preferably exhausted outside, but may be recirculated provided that it is first filtered through high-efficiency particulate air (HEPA) filters (eg, >99.97% filtration efficiency for all particles  $\geq 0.3 \mu\text{m}$ ). Furthermore, the use of personal respiratory protection is indicated for all persons entering these rooms.

Although the CDC's recommendations for hospital AII rooms have been in place for several years, recent performance assessments have shown large discrepancies between what is recommended and what is actually observed in the field.<sup>9-14</sup> For instance, Saravia et al<sup>9</sup> found that of the approximately 500 AII rooms that they evaluated, only 32% met the negative pressure requirement, 49% did not achieve adequate ACH, and nearly 10% had final filters that did not attain a 90% measured efficiency rating. Moreover, 9% of the AII rooms were actually operating under positive pressure. Other studies have reported that up to 45% of the negative-pressure AII rooms investigated were actually positively pressured relative to surrounding areas.<sup>14,15</sup>

Bringing health care establishments into compliance with CDC recommendations is important, but will be a costly and time-consuming endeavor. Furthermore, in some cases renovations to existing heating, ventilating, and air-conditioning (HVAC) systems are not feasible due to engineering constraints. Auxiliary means of improving air quality without the need to modify a building's HVAC system can be accomplished using so-called "portable air cleaners." The CDC has recognized these portable air cleaners as a supplemental means of increasing the number of air changes per hour (ACH) in controlled environments.<sup>7</sup> Small devices that do not deliver sufficiently high throughputs have been shown to be ineffective, thus the CDC only recommends using industrial-grade units capable of HEPA filtration rates in the range of 300-800 ft<sup>3</sup>/min.<sup>7</sup> The fundamental criteria needed to achieve effective air cleaning from such auxiliary devices were recently reviewed by Shaughnessy and Sextro.<sup>16</sup>

One relatively inexpensive and readily implemented measure to gain added protection from airborne contamination risk is the use of personal respiratory protection.<sup>5</sup> Indeed, recent pandemic flu threats have rightly led authorities to embrace this strategy, with recommendations that health care workers (HCWs) wear N95 respirators in critical hospital settings.<sup>17</sup> However, N95-classified face masks do not provide complete protection, and a good face seal, which is often difficult to achieve, is required for their proper function. In addition, some studies have indicated that these respirators might not provide the expected protection level against bacteria and virus, and that

respirators with the same rating manufactured by different companies have different filtration efficiencies for the most penetrative particles (0.1-0.3  $\mu\text{m}$ ).<sup>18-20</sup>

The foregoing factors led us to consider supplemental, rapid, and cost-effective measures that can be taken to lower the risk of infection from infectious patients via the airborne route. Our objective was to evaluate the use of auxiliary means that allow a hospital to quickly lower airborne contamination levels in critical areas without the need to modify the building's HVAC system. For this, we chose to investigate the use of a high-throughput in-room air decontamination unit in conjunction with a standard AII room operated with and without negative pressure. Our work involved laboratory bench tests to ensure that the air decontamination unit used was indeed capable of eradicating relevant airborne pathogens (ie, influenza virus and *M tuberculosis*) and field tests using a surrogate airborne pathogen (*Serratia marcescens*) to evaluate air decontamination kinetics and levels under different room ventilation scenarios.

## MATERIALS AND METHODS

The viral model used in this study was the H5N2 avian flu strain (A/Finch/England/2051/91 H5N2). This strain is not known to be pathogenic to humans and serves as a surrogate model for the lethal H5N1 avian and H1N1 swine influenza viruses. Handling and storage of the virus was carried out in the BSL-3 laboratory facilities at the Laboratoire de Virologie and Pathogénèse Virale, Lyon, France. Standard cell inoculation procedures were used to determine the infectivity of the viral samples obtained. Infectivity was conveniently determined by infecting a particular cell line with increasing dilutions of the virus material and determining the highest dilution producing a cytopathic effect in 50% of the inoculated cells. The 50% endpoint dilution, here expressed as a tissue culture infections dose (TCID<sub>50</sub>) of 50/mL, was then calculated using the Reed-Muench method.<sup>21</sup> Serial dilutions of 10<sup>-1</sup> to 10<sup>-7</sup> of the viral samples were prepared, from which 50  $\mu\text{L}$  of each dilution was inoculated in 96-well microplates containing 200  $\mu\text{L}$  of Madin-Darby canine kidney (MDCK) epithelial cells. This inoculation was repeated 10 times for each dilution. After a 24-hour postinfection period, the medium was changed (eagle minimum essential medium [EMEM] supplemented with 2 mM glutamine, 200 U Peni/Strepto, and 1 mg/mL trypsin). After a 96-hour postinfection period, an infectious dose of virus was confirmed using hemagglutination of chicken red blood cells (0.5%). The final titration limit was determined according to the Reed-Muench calculation. For aerosol generation, 20 mL of 1  $\times$  10<sup>7</sup> TCID<sub>50</sub> H5N2 avian flu virus was used.

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