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Exhaled Air Dispersion Distances During Noninvasive Ventilation via Different Respironics Face Masks

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Background: As part of our influenza pandemic preparedness, we studied the exhaled air dispersion distances and directions through two different face masks (Respironics; Murrysville, PA) attached to a human-patient simulator (HPS) during noninvasive positive-pressure ventilation (NPPV) in an isolation room with pressure of -5 Pa.

Methods: The HPS was positioned at 45° on the bed and programmed to mimic mild lung injury (oxygen consumption, 300 mL/min; lung compliance, 35 mL/cm H_2O). Airflow was marked with intrapulmonary smoke for visualization. Inspiratory positive airway pressure (IPAP) started at 10 cm H_2O and gradually increased to 18 cm H_2O , whereas expiratory pressure was maintained at 4 cm H_2O . A leakage jet plume was revealed by a laser light sheet, and images were captured by high definition video. Normalized exhaled air concentration in the plume was estimated from the light scattered by the smoke particles.

Findings: As IPAP increased from 10 to 18 cm H_2O , the exhaled air of a low normalized concentration through the ComfortFull 2 mask (Respironics) increased from 0.65 to 0.85 m at a direction perpendicular to the head of the HPS along the median sagittal plane. When the IPAP of 10 cm H_2O was applied via the Image 3 mask (Respironics) connected to the whisper swivel, the exhaled air dispersed to 0.95 m toward the end of the bed along the median sagittal plane, whereas higher IPAP resulted in wider spread of a higher concentration of smoke.

Conclusions: Substantial exposure to exhaled air occurs within a 1-m region, from patients receiving NPPV via the ComfortFull 2 mask and the Image 3 mask, with more diffuse leakage from the latter, especially at higher IPAP. (CHEST 2009; 136:998–1005)

Abbreviations: EPAP = expiratory positive airway pressure; HPS = human-patient simulator; IPAP = inspiratory positive airway pressure; NPPV = noninvasive positive-pressure ventilation; SARS = severe acute respiratory syndrome

Human cases of the highly pathogenic avian influenza A/H5N1 were first documented¹ in Hong Kong in 1997. The continued circulation of the H5N1 virus in migratory birds and the widespread occurrence of the H5N1 avian influenza infection in poultry and birds in several continents have increa-

sed the risk of human exposure to avian influenza.² Respiratory failure is the major complication in

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patients hospitalized with influenza A/H5N1 infection, and many patients progress rapidly to ARDS

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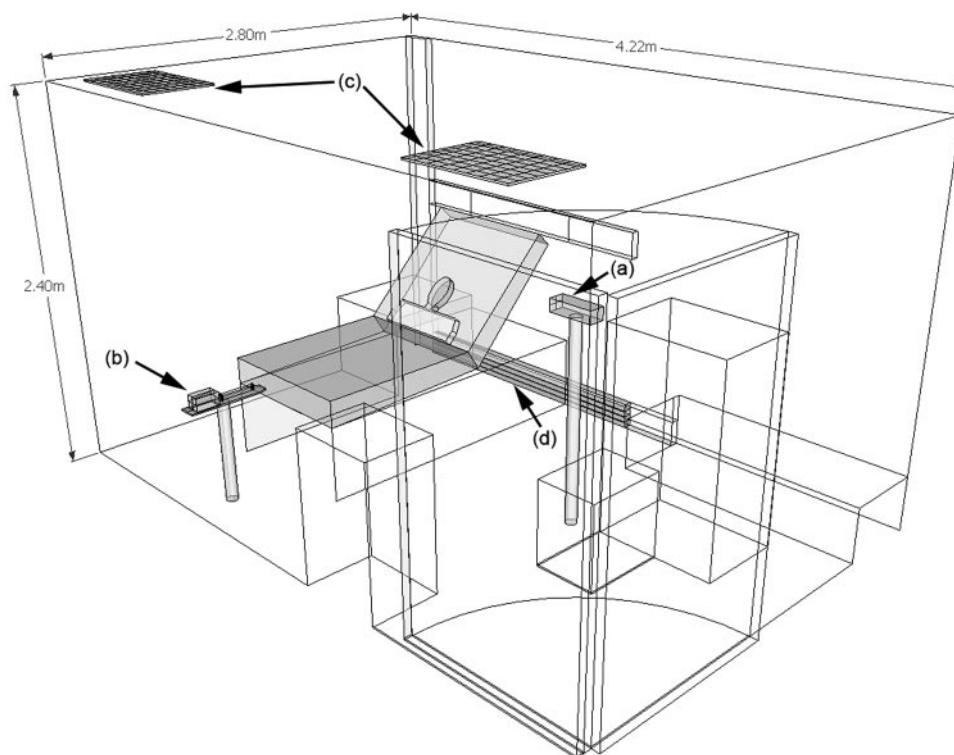


FIGURE 1. The room dimension and equipment layout inside the negative-pressure isolation room. The camera (arrow a) and the laser device (arrow b) were positioned along the coronal plane on the left side of the patient and along the sagittal plane of the patient at the end of the bed, respectively. Two fresh air diffusers, serving as air inlets, were mounted on the ceiling (arrow c). The negative pressure of the isolation room was provided by the air exhausts positioned at the bottom of the bed (arrow d).

and multiorgan failure, requiring intensive care support.^{2–4} Noninvasive positive-pressure ventilation (NPPV) may play a limited supportive role for early ARDS/acute lung injury as a bridge to invasive mechanical ventilation in an influenza pandemic, although it is contraindicated in critically ill patients with multiorgan failure and hemodynamic instability.^{5,6}

However, as influenza virus may be contained in fine particles generated during tidal breathing,⁷ the application of NPPV may further disperse potentially infected aerosols and contribute to nosocomial transmission of influenza. We have previously reported⁸ that exhaled air particles could be dispersed up to a radial distance of 0.5 m from patients receiving NPPV using the Ultra Mirage mask (ResMed; Bella Vista, NSW, Australia). This current study aimed to examine the directions and dispersion distances of exhaled air during application of NPPV via other commonly used face masks. Knowledge about the directions and extent of exhaled air leakage in different masks is essential for the development of preventive measures to reduce the risk of nosocomial transmission during application of NPPV to these high risk patients in an influenza pandemic.

MATERIALS AND METHODS

The experiments were conducted in one of 36 double-door, negative-pressure (-5 Pa) isolation rooms specifically constructed on the top floor of the hospital after the major outbreak of severe acute respiratory syndrome (SARS) to facilitate the management of patients with highly infectious diseases.⁹ The isolation room measured $2.8 \times 4.22 \times 2.4$ m (Fig 1). The experimental design and method of data analysis have been described in detail in our previous studies^{8,10–12} on exhaled air dispersion related to the application of NPPV, simple oxygen mask, and jet nebulizer.

NPPV and Lung Model

We studied the deliberate leakage from the exhalation ports of ComfortFull 2 (Fig 2A) and Image 3 (Fig 2B) masks (Respironics; Murrysville, PA), firmly attached to a high fidelity human-patient simulator (HPS) [HPS 6.1; Medical Education Technologies Inc; Sarasota, FL]. The HPS represented a 70-kg adult man sitting on a 45° inclined hospital bed. It was programmed to breathe spontaneously to mimic mild lung injury. The lung compliance was set as 35 mL/cm H_2O , and the oxygen consumption was set as 300 mL/min. Tidal volume and respiratory rate were regulated so that a respiratory exchange ratio of 0.8 was maintained during measurements. Typically, this was achieved with a tidal volume of 300 mL and a respiratory rate of 25 breaths/min.^{13,14}

The HPS contains a realistic airway and a lung model that undergoes gas exchange by removing oxygen and adding carbon dioxide to the system simultaneously. The lung compliance and

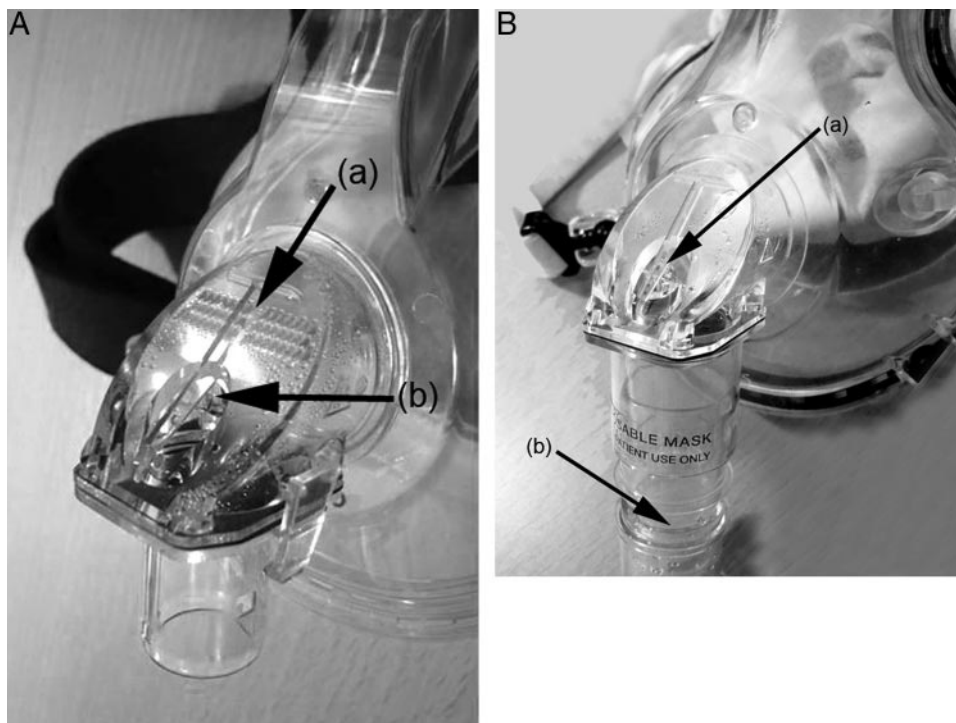


FIGURE 2. A: a ComfortFull 2 full face mask with three pairs of exhalation diffusers (arrow a) for quiet exhalation and an entrainment valve (arrow b) that provides quick access to room air if the pressure falls below 3 cm H₂O. B: an Image 3 full face mask, with an entrainment valve (arrow a) that provides quick access to room air if the pressure falls below 3 cm H₂O connected to a Whisper Swivel exhalation port (arrow b).

airway resistance also responds in a realistic manner to relevant respiratory challenges. In addition, the HPS produces an airflow pattern that is close to the *in vivo* situation and has been applied in previous studies^{15–19} to simulate human respiration.

NPPV was applied using a bilevel positive airway pressure device (VPAP III ST; ResMed) via each mask. The inspiratory positive airway pressure (IPAP) was initially set at 10 cm H₂O and gradually increased to 18 cm H₂O. The expiratory positive airway pressure (EPAP) was maintained at 4 cm H₂O throughout the study.⁸

Flow Visualization

The visualization of airflow around each NPPV face mask was facilitated by marking the air with smoke particles (M-6000 smoke generator, N19; DS Electronics; Sydney, NSW, Australia), as in our previous studies.^{8,10–12} The oil-based smoke particles, measuring < 1 μm in diameter, are known to follow the airflow pattern precisely with negligible slip.²⁰ The smoke was introduced continuously to the right main bronchus of the HPS. It mixed with alveolar gas and then exhaled through the airway. Sections through the leakage jet plume were then revealed by a thin laser light sheet (green, 532-nm wavelength, continuous-wave mode) created by a diode-pumped solid stated laser (OEM UGH-800 mW; Lambdapro Technologies; Beijing, People's Republic of China) with custom cylindrical optics for two-dimensional laser light sheet generation.^{8,10–12}

The light sheet was initially positioned in the median sagittal plane of the HPS and was subsequently shifted to the paramedian sagittal planes. This allowed us to investigate the regions directly above and lateral to the mask and the HPS.^{8,10–12}

All leakage jet plume images revealed by the laser light sheet were captured by the high-definition video camera (Sony high-definition digital video camcorder, HDR-SR8E ClearVid complementary metal oxide semiconductor sensor; Sony; Tokyo, Japan [with Vario-Sonnar T* Lens; Carl Zeiss; Jena, Germany]) with an optical resolution of 1,440 × 1,080 pixels per video frame. Normalized smoke concentration in the plume was estimated from the light intensity scattered by smoke particles.^{8,10–12}

Image Analysis

We estimated normalized smoke concentration in the mask leakage air from the light scattered by the particles. The analysis was based on scattered light intensity being proportional to particle concentration under the special conditions of constant intensity laser light sheet illumination and monodisperse, small (submicromolar) particles.²⁰ In short, the thin laser light sheet of near constant intensity illuminated smoke particle markers in the mask airflow leakage. Smoke particles scattered laser light perpendicular to the light sheet, and the data were collected and integrated by the video camera element and lens.^{8,10–12}

Image Capture and Frame Extraction

The motion video of at least 20 breathing cycles for each NPPV setting was captured, and individual frames were extracted as gray-scale bitmaps for intensity analysis. Frames were extracted at times initiated from the beginning of each inspiration to generate an ensemble average for the corresponding instant of the respiratory cycle.^{8,10–12} The time at which the normalized

concentration contours spread over the widest region from the NPPV mask was chosen for the ensemble average to estimate the greatest dispersion distance. This was found to be approximately at the mid-respiratory cycle.⁸

Intensity Averaging and Concentration Normalization

All gray-scale frames were read into a program specifically developed for this study (MathCad 8.0; MathSoft Inc; Cambridge, MA)²¹ along with background intensity images taken with the laser switched off. The background intensity image was subtracted from each frame pixel by pixel to remove any stray background light, and the pixel intensity values were averaged over all frames to determine the ensemble-averaged intensity. The resulting image was the total intensity of light scattered perpendicular to the light sheet by the smoke particles and was directly proportional to smoke concentration under the conditions mentioned above. The image was normalized against the highest intensity found within the leakage jet plume to generate normalized particle concentration contours.^{8,10–12}

As the smoke particles marked air that originated from the airways of the HPS before leaking from the mask, the concentration contours effectively represent the probability of encountering air around the patient that has come from within the mask and/or the respiratory system of the patient. The normalized concentration contours are made up of data collected from at least 20 breaths. A contour value of 1 indicates a region that consists entirely of air exhaled by the patient, where there is a very high chance of exposure to the exhaled air, such as at the mask exhaust vents. A value near 0 indicates no measurable air leakage in the region and a small chance of exposure to the exhaled air.^{8,10–12} The study received nonionizing radiation and biological/chemical safety approval by the Chinese University of Hong Kong.

RESULTS

The results are presented with reference to the median sagittal plane.

NPPV Applied via the ComfortFull 2 Mask

The first scenario was conducted with the bilevel positive airway pressure device (VPAP III ST; ResMed) set at IPAP of 10 cm H₂O and an EPAP of 4 cm H₂O. The normalized concentration contours of air leakage distribution around the patient and mask in the median sagittal plane are shown in Figure 3A and B. We observed a vertical, cone-shaped leakage plume from the mask exhalation diffuser that propagated well above and almost perpendicular to the patient. The maximum dispersion distance of smoke particles, defined as the boundary with a region encountering < 5% normalized concentration of exhaled air (light blue contour smoke concentration scale), was 0.65 m, whereas that of a high concentration (containing > 75% normalized concentration of exhaled air, red zone and above) was 0.36 m. There was no significant room contamination by exhaled air (as reflected by the blue background in the isolation room) other than the exhalation jet plume.

As IPAP increased from 10 to 14 cm H₂O, the maximum exhaled dispersion distance of the low-concentration exhaled air was similar at 0.65 m, but that of high-concentration exhaled air increased to 0.40 m, with contamination of the isolation room, with some exhaled air concentration outside the exhalation jet plume (Fig 3C). When IPAP was increased to 18 cm H₂O, the dispersion distance of low-concentration exhaled air was 0.85 m, whereas that of high-concentration exhaled air increased to 0.51 m along the median sagittal plane (Fig 3D). More background contamination of the isolation room by smoke particles was noted at higher IPAP, due to interaction between the downstream ceiling-mounted ventilation vent and the upstream exhaled air from the HPS.

NPPV Applied via the Image 3 Mask Connected to the Whisper Swivel

The Image 3 mask required an additional exhalation device (Whisper Swivel; Respironics) to prevent carbon dioxide rebreathing. The exhaled air leakage was much more diffuse than that of the ComfortFull 2 mask because of the downstream leakage of exhaled air through the Whisper Swivel exhalation port. At IPAP of 10 cm H₂O, the maximum dispersion distance of low-concentration exhaled air (light blue zone on smoke concentration scale) was 0.95 m toward the end of the bed, whereas that of medium-concentration exhaled air (containing > 50% of normalized concentration of exhaled air, green zone and above) was about 0.6 m along the median sagittal plane (Fig 4A). As IPAP increased from 10 to 14 cm H₂O, the exhaled air of medium concentration increased to 0.95 m toward the end of the bed along the median sagittal plane of the HPS (Fig 4B).

When IPAP was increased to 18 cm H₂O, the exhaled air of low concentration dispersed diffusely to fill up most of the isolation room (*ie*, beyond 0.95 m, as captured by the camera), whereas exhaled air of a medium concentration, occupying wider airspace, was noted to spread 0.8 m toward the end of the bed, with the accumulation of a high concentration of exhaled air (red zone on scale) within 0.34 m from the center of the mask, along the median sagittal plane of the HPS (Fig 4C).

DISCUSSION

As there is no reliable and safe marker that can be introduced into human lungs for experimental purposes, we have studied the maximum distribution of exhaled air, marked by very fine smoke particles, from the HPS during the application of NPPV using two different face masks. In this study, we have

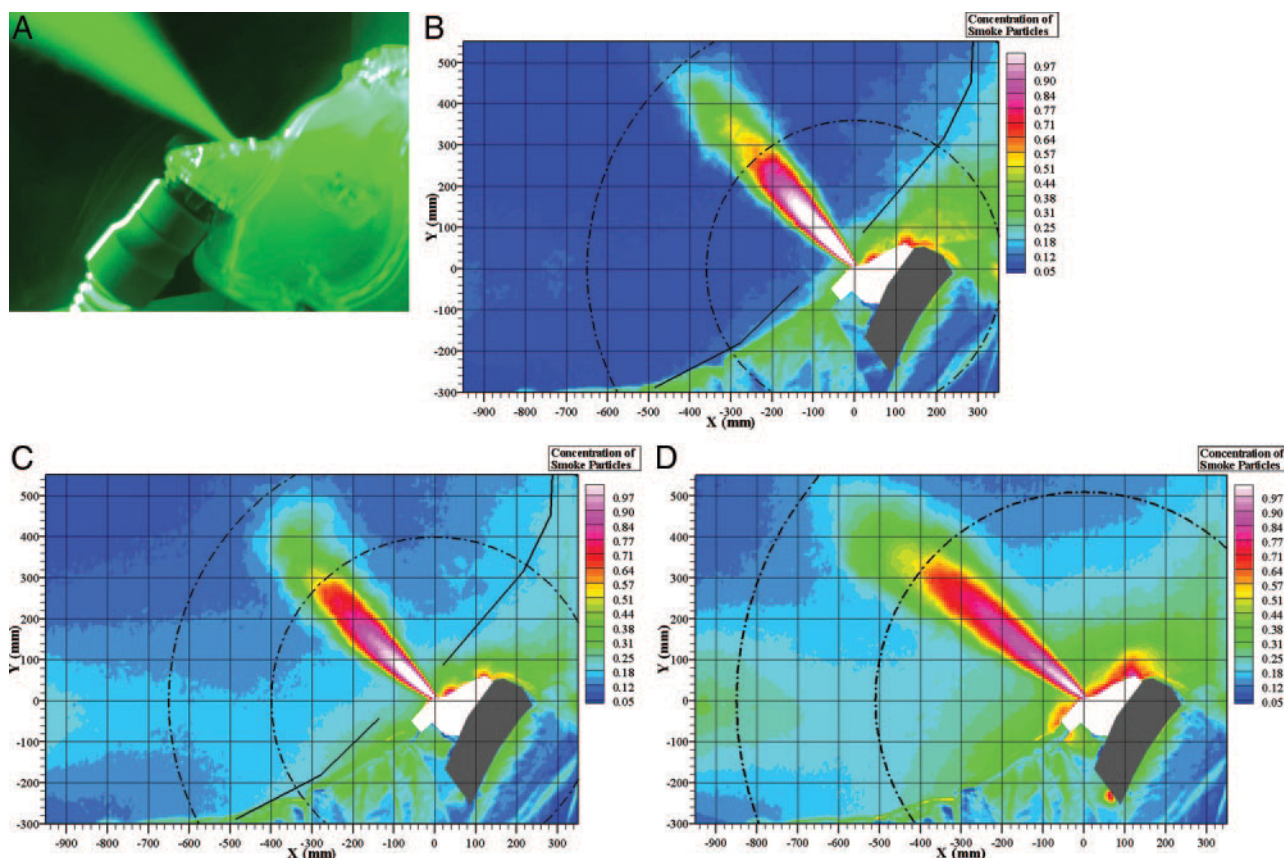


FIGURE 3. A: the ComfortFull 2 mask was attached to a high-fidelity HPS. The photograph was taken with the room light switched off and revealed exhaled smoke dispersion through the exhalation diffuser of the mask attached to the HPS. B: B to D refer to data related to the ComfortFull 2 mask. The x-axis represents the distance from the center of the mask along the median sagittal plane, whereas the y-axis represents the vertical distance from the center of the mask. Normalized concentration in the plume was estimated by computer analysis from the light scattered by smoke particles. Shown at IPAP of 10 cm H₂O and EPAP of 4 cm H₂O. The white color code and the red color code represented regions consisting of 100% and 70%, respectively, of exhaled air, whereas the background of the isolation room (deep blue code) was essentially free of exhaled air. C: at IPAP of 14 cm H₂O. D: at IPAP of increased to 18 cm H₂O.

shown that the dispersion distances of a low normalized concentration of exhaled air through the ComfortFull 2 mask exhalation diffuser increased from 0.65 to 0.85 m at a direction perpendicular to the head of the HPS along the sagittal plane when IPAP was increased from 10 to 18 cm H₂O, respectively, with more background contamination of the isolation room at higher IPAP. In contrast, even when a low IPAP of 10 cm H₂O was applied to the HPS via the Image 3 mask with the Whisper Swivel exhalation port, the exhaled air leaked far more diffusely than via the ComfortFull 2 mask, dispersing a low normalized concentration of 0.95 m along the median sagittal plane of the HPS, whereas a higher IPAP resulted in a wider spread of a higher normalized concentration of smoke around the HPS in the isolation room with negative pressure.

NPPV is effective in the treatment of patients with respiratory failure due to COPD, acute cardiogenic pulmonary edema, and pneumonia in immunocom-

promised patients, but the evidence supporting its use in patients with pneumonia is still limited.²² Moreover, there is a potential risk when applying NPPV in patients hospitalized with viral pneumonia. In this regard, the deliberate leakage via the exhalation ports may generate droplet nuclei and disperse infective aerosols through evaporation of water content of respiratory droplets and resulting in a superspreading event.²³ Nonetheless, NPPV has been applied to a small number of human H5N1 infections without causing any nosocomial outbreak, although the patients eventually died of multiorgan failure despite invasive mechanical ventilatory support.^{24,25} There were also anecdotal reports^{26,27} that NPPV applied using a single circuit was effective in treating respiratory failure due to SARS and might reduce the need for intubation. However, a case-control study²⁸ involving 124 medical wards in 26 hospitals in Guangzhou and Hong Kong has identified SARS patients requiring oxygen therapy and NPPV as independent risk factors for superspread-

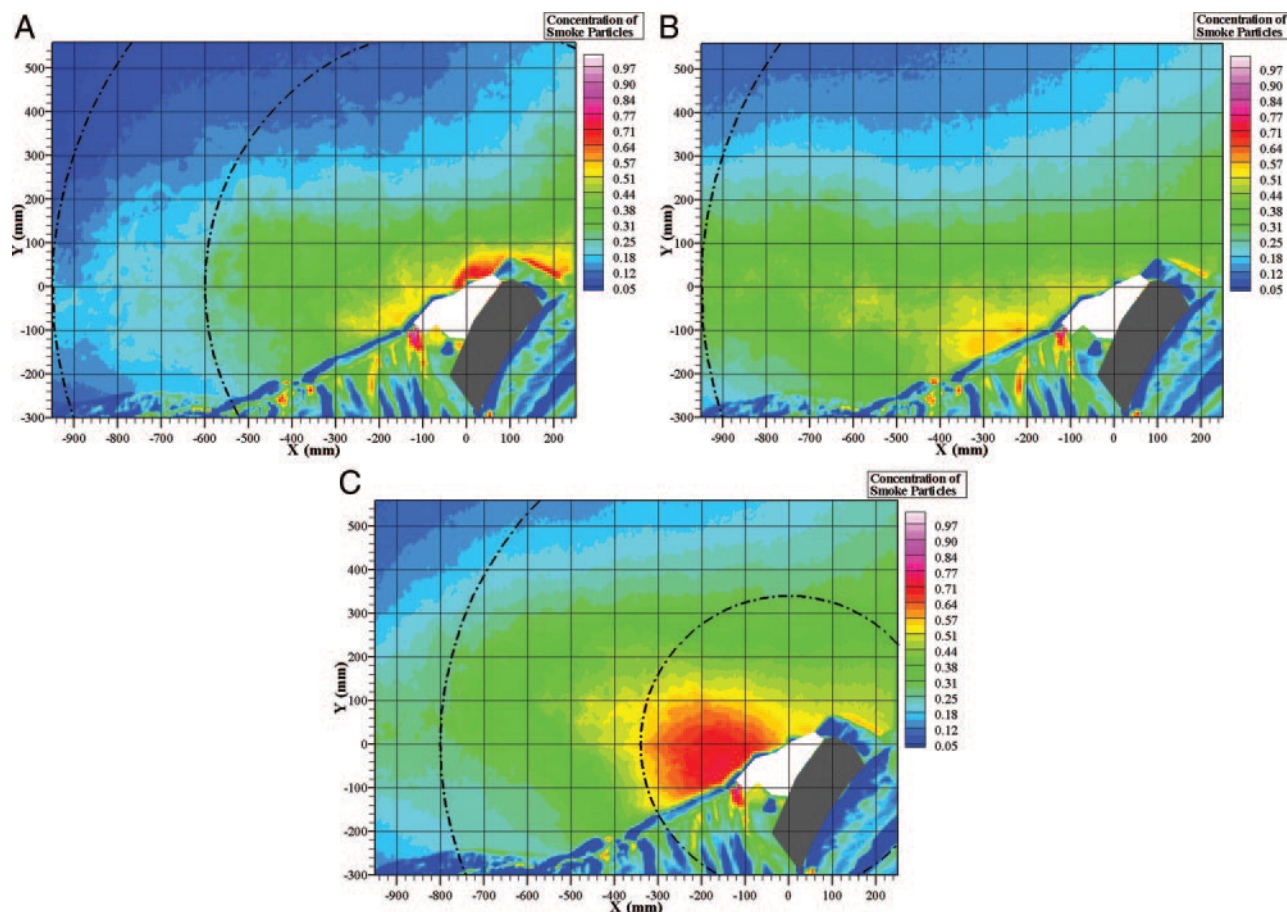


FIGURE 4. Data related to the Image 3 full face mask. A: at IPAP of 10 cm H₂O. B: at IPAP of 10 to 14 cm H₂O. C: at IPAP of 18 cm H₂O.

ing nosocomial outbreaks of SARS. Similarly, a systematic review²⁹ has shown a strong association between ventilation, air movements in buildings, and the airborne transmission of infectious diseases such as measles, tuberculosis, chickenpox, influenza, smallpox, and SARS.

The use of a jet nebulizer for the administration of aerosolized albuterol in an index patient on a crowded medical ward probably enhanced the spread of SARS, leading to a major nosocomial outbreak in our hospital in 2003.^{9,30} We have recently shown¹² that the maximum dispersion distance of exhaled air through the side vent of the jet nebulizer, driven by 6 L/min air, was about 0.8 m lateral to the HPS. We have previously shown^{8,11} that the maximum exhaled air distances from patients receiving oxygen via a Hudson mask and during NPPV via the Ultra Mirage mask (ResMed) were 0.4 and 0.5 m, respectively, when the HPS was programmed at very mild lung injury (Fig 5).

This study showed that the maximum exhaled air dispersion distance from the ComfortFull 2 mask was 0.95 m at a predictable direction from the

exhalation diffuser perpendicular to the HPS, but leakage though the Image 3 mask, connected to the Whisper Swivel exhalation port, was far more extensive and diffuse. The Whisper Swivel is an efficient exhalation device to prevent carbon dioxide re-breathing, but it would not be advisable to use such an exhalation port in managing patients with febrile respiratory illness of unknown etiology, especially in the setting of an influenza pandemic with high human-to-human transmission potential for fear of causing major nosocomial infection. It is also important to avoid the use of higher IPAP, which could lead to wider distribution of exhaled air and substantial room contamination as demonstrated in this study. The World Health Organization interim guidelines on the prevention and control of acute respiratory diseases in health care has included NPPV among those aerosol-generating procedures in which there is a possibility of an increased risk of respiratory pathogen transmission. In addition to maintaining contact, droplet, and standard precautions among the health-care workers when providing routine care to such patients, the World Health

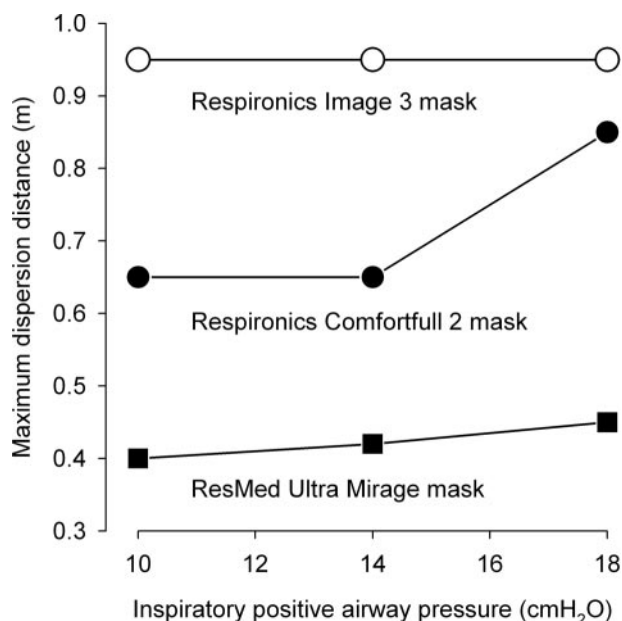


FIGURE 5. Maximum exhaled air dispersion distances during the application of NPPV to the HPS via different face masks. In the study of the ResMed Ultra Mirage mask,⁸ tidal volume was set at 500 mL, and a respiratory rate of 14 breaths/min was used to represent a patient with very mild lung injury. For the study of Respiration masks, tidal volume was set as 300 mL, and a respiratory rate of 25 breaths/min was used to represent a patient with mild lung injury.^{13,14} EPAP was maintained at 4 cm H₂O throughout the studies.

Organization recommends³¹ full personal protection equipment for the health-care workers covering the torso, arms, eyes, nose, and mouth, and this should include a long-sleeved gown, single-use gloves, eye protection, and a N95 mask or the equivalent as the minimum level of respiratory protection. NPPV should be provided in an adequately ventilated single room, and the addition of an expiratory port with a bacterial/viral filter can reduce aerosol emission.³¹

Our study was limited by the use of smoke particles as markers for exhaled air. The inertia and weight of larger droplets in an air droplet two-phase flow would certainly cause them to have less horizontal dispersion than the continuous air carrier phase in which they travel due to increased inertia and drag. However, the evaporation of water content in some droplets during NPPV may produce droplet nuclei suspended in air, whereas the larger droplets will fall to the ground in a trajectory pathway.²⁵ As the smoke particles in this study mark the continuous air phase, our data contours are referring to exhaled air. Our results would therefore represent the “upper bound” estimates for the dispersion of droplets, which would be expected to follow a shorter trajectory than the air jet due to gravitational effects but not fully reflect the risk of droplet transmis-

sion.^{8,10–12} Similarly, we would expect a higher concentration of droplets closer to the floor than that estimated by our contours because of the shorter trajectory of the droplets.

In summary, substantial exposure to exhaled air occurs within 1 m from patients receiving NPPV in an isolation room with negative pressure via the ComfortFull 2 mask and the Image 3 mask connected to the Whisper Swivel exhalation port, with far more extensive leakage and room contamination via the latter device, especially at higher IPAP. Health-care workers should take adequate precautions when providing NPPV support to patients with pneumonia of unknown etiology complicated by respiratory failure.

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REFERENCES

- 1 Yuen KY, Chan PK, Peiris M, et al. Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* 1998; 351:467–471
- 2 Abdel-Ghaffar AN, Chotpitayasunondh T, Gao Z, et al. Writing committee of the second World Health Organization consultation on clinical aspects of human infection with avian influenza A (H5N1) virus: update on avian influenza A (H5N1) virus infection in humans. *N Engl J Med* 2008; 358:261–273
- 3 Arabi Y, Gomersall CD, Ahmed QA, et al. The critically ill avian influenza A (H5N1) patient. *Crit Care Med* 2007; 35:1397–1403
- 4 Hui DS. Review of clinical symptoms and spectrum in humans with influenza A/H5N1 infection. *Respirology* 2008; 13(suppl):S10–S13
- 5 Hui DS. Influenza A/H5N1 infection: other treatment options and issues. *Respirology* 2008; 13(suppl): S22–S26
- 6 Clinical management of human infection with avian influenza A (H5N1) virus. World Health Organization updated advice 15 Aug 2007. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/clinicalmanage07/en/. Accessed August 24, 2009
- 7 Fabian P, McDevitt JJ, DeHaan WH, et al. Influenza virus in human exhaled breath: an observational study. *PLoS One* 2008; 3:e2691
- 8 Hui DS, Hall SD, Chan MT, et al. Non-invasive positive pressure ventilation: an experimental model to assess air and particle dispersion. *Chest* 2006; 130:730–740
- 9 Lee N, Hui DS, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003; 348:1986–1994
- 10 Hui DS, Ip M, Tang JW, et al. Airflows around oxygen masks: a potential source of infection? *Chest* 2006; 130:822–826

- 11 Hui DS, Hall SD, Chan MTV, et al. Exhaled air dispersion during oxygen delivery via a simple oxygen mask. *Chest* 2007; 132:540–546
- 12 Hui DS, Chow BK, Hall SD, et al. Exhaled air and aerosolized droplet dispersion during application of a jet nebulizer. *Chest* 2009; 135:648–654
- 13 Kuhlen R, Max M, Dembinski R, et al. Breathing pattern and workload during automatic tube compensation, pressure support and T-piece trials in weaning patients. *Eur J Anaesthesiol* 2003; 20:10–16
- 14 Light RB. Pulmonary pathophysiology of pneumococcal pneumonia. *Semin Respir Infect* 1999; 14:218–226
- 15 Good ML. Patient simulation for training basic and advanced clinical skills. *Med Educ* 2003; 37(suppl):14–21
- 16 Meka VV, van Oostrom JH. Bellows-less lung system for the human patient simulator. *Med Biol Eng Comput* 2004; 42:413–418
- 17 So CY, Gomersall CD, Chui PT, et al. Performance of an oxygen delivery device for weaning potentially infectious critically ill patients. *Anaesthesia* 2004; 59:710–714
- 18 Goodwin JA, van Meurs WL, Sa Couto CD, et al. A model for educational simulation of infant cardiovascular physiology. *Anesth Analg* 2004; 99:1655–1664
- 19 Lampotang S, Lizdas DE, Gravenstein N, et al. An audible indication of exhalation increases delivered tidal volume during bag valve mask ventilation of a patient simulator. *Anesth Analg* 2006; 102:168–171
- 20 Soo SL. Fluid dynamics of multiphase systems. Toronto, ON, Canada: Blaisdell Publishing Company, 1967
- 21 Mathcad 8.0 for Windows user's guide. Cambridge, MA: MathSoft Inc, 2000
- 22 Ambrosino N, Vaghegghini G. Noninvasive positive pressure ventilation in the acute care setting; where are we? *Eur Respir J* 2008; 31:874–886
- 23 Tang JW, Li Y, Eames I, et al. Factors involved in the aerosol transmission of infection and control of ventilation in health-care premises. *J Hosp Infect* 2006; 64:100–114
- 24 Tran TH, Nguyen TL, Nguyen TD, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. *N Engl J Med* 2004; 350:1179–1188
- 25 Peiris JS, Yu WC, Leung CW, et al. Re-emergence of fatal human influenza A subtype H5N1 disease. *Lancet* 2004; 363:617–6195
- 26 Han F, Jiang YY, Zheng JH, et al. Noninvasive positive pressure ventilation treatment for acute respiratory failure in SARS. *Sleep Breath* 2004; 8:97–106
- 27 Cheung TM, Yam LY, So LK, et al. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. *Chest* 2004; 126:845–850
- 28 Yu IT, Xie ZH, Tsoi KK, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not in others? *Clin Infect Dis* 2007; 44:1017–1025
- 29 Li Y, Leung GM, Tang JW, et al. Role of ventilation in airborne transmission of infectious agents in the built environment: a multidisciplinary systematic review. *Indoor Air* 2007; 17:2–18
- 30 Wong RS, Hui DS. Index patient and SARS outbreak in Hong Kong. *Emerg Infect Dis* 2004; 10:339–341
- 31 World Health Organization. Infection and control of epidemic and pandemic-prone acute respiratory diseases in health care: World Health Organization interim guidelines. Available at: http://www.who.int/csr/resources/publications/WHO_CD_EPR_2007_6/en/. Accessed August 24, 2009