Infection control in mass respiratory failure: Preparing to respond to H1N1

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The first hints of a global public health crisis emerged with the identification of a new strain of H1N1 influenza A in March and April 2009 in Mexico City. By June 11, the World Health Organization had declared the outbreak of 2009 H1N1 a global pandemic. Now, with the continued growing presence of 2009 H1N1 on the global scene, much attention has been focused on the key role of personal protective equipment in healthcare infection control. Much less emphasis has been placed on specific interventions that may minimize the increased infectious risk commonly associated with critical care delivery. Given the frequency of high-risk respiratory procedures such as intubation and delivery of aerosolized medications in the ICU, the delivery of critical care presents unique infection control challenges and unique opportunities to augment usual infection control practice with specific source-control efforts. Here, we summarize data regarding risks to critical care healthcare workers from previous respiratory virus outbreaks, discuss findings from the early 2009 H1N1 experience that suggest reasons for increased concern for those delivering critical care, and review best available evidence regarding strategies for source control in respiratory and critical care delivery. (Crit Care Med 2010; 38[Suppl.]:S000–S000)

KEY WORDS: H1N1 influenza A virus; infection control; respiratory virus; pandemic; healthcare worker

The first hints of a global public health crisis emerged with the identification of a new strain of H1N1 influenza A in March and April 2009 in Mexico City, and a report from San Diego, California, of a novel influenza A virus capable of person-to-person transmission. The first US patient infection with what is now called 2009 H1N1 influenza was confirmed by the US Centers for Disease Control and Prevention laboratories on April 15. By June 11, the outbreak of 2009 H1N1 was declared a pandemic by the World Health Organization (1–5). Now, as the autumn 2009 respiratory virus season descends on the northern hemisphere and clusters of severe illness associated with H1N1 are increasingly reported, disaster preparedness planning has taken on a new urgency.

With the continued growing presence of 2009 H1N1 on the global scene, many questions remain about how hospitals can best prepare to protect their staff and prevent healthcare-associated infections in their facilities. Will adequate amounts of effective vaccine be ready in time? What types of precautions are necessary to protect workers and other patients, and in what situations are increased levels of precautions appropriate? What gaps remain in our infection control knowledge and how can we position ourselves as a healthcare community to address them? All of these questions are important ones. Much attention has been focused on the key role of personal protective equipment in the healthcare infection control armamentarium (6–8); however, much less emphasis has been placed on specific interventions that may minimize the increased infectious risk commonly associated with critical care delivery. Given the frequency of high-risk respiratory procedures such as intubation and delivery of aerosolized medications in the ICU, the delivery of critical care presents unique infection control challenges and unique opportunities to augment usual infection control practice with specific source-control efforts. Here, we summarize data regarding risks to critical care healthcare workers (10). Further, as SARS and other experiences have demonstrated, the risk of secondary transmission may be higher in the ICU than in other settings. Procedures common in the ICU setting such as endotracheal intubation (11, 12), open circuit suctioning (11), and bronchoscopy (6–9), which increase aerosolization of infectious material, have been associated with increased risk of secondary transmission. Therapeutic interventions such as noninvasive positive pressure ventilation (11, 13), administration of nebulized medication (11, 14), and manual ventilation (11, 15) may also play a role in the spread of infection, but data confirming or refuting this possibility are lacking. Because of the increased risk of respiratory virus transmission in the ICU, implementation of the best available infection control strategies to protect patients and healthcare workers from nosocomial infections in such high-risk units will be essential to limiting morbidity and mortality during a respiratory virus epidemic.

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SUBJECTS AND METHODS

Infectious Risk in Critical Care

During the SARS epidemic of 2003, >8000 infections were reported worldwide (9). Of the 351 cases reported in Canada, 72% were infected in a healthcare setting and 45% were in healthcare workers (10). Further, as SARS and other experiences have demonstrated, the risk of secondary transmission may be higher in the ICU than in other settings. Procedures common in the ICU setting such as endotracheal intubation (11, 12), open circuit suctioning (11), and bronchoscopy (6–9), which increase aerosolization of infectious material, have been associated with increased risk of secondary transmission. Therapeutic interventions such as noninvasive positive pressure ventilation (11, 13), administration of nebulized medication (11, 14), and manual ventilation (11, 15) may also play a role in the spread of infection, but data confirming or refuting this possibility are lacking. Because of the increased risk of respiratory virus transmission in the ICU, implementation of the best available infection control strategies to protect patients and healthcare workers from nosocomial infections in such high-risk units will be essential to limiting morbidity and mortality during a respiratory virus epidemic.
In the context of an epidemic, choices regarding appropriate therapeutic interventions may be complicated by the role a particular therapy may play in secondary disease transmission. For certain interventions, the benefit to the patient is well-documented and strategies to minimize transmission risk have been established. These interventions are usually easily recommended for use during the epidemic. For others therapies, however, the clinical benefit or the risk of secondary transmission, or both, remain uncertain (e.g., high-frequency oscillatory ventilation [HFOV] vs. low-tidal volume conventional mechanical ventilation). The increased risk of secondary transmission to a provider or other patients must be considered, in addition to the potential benefit of that therapy to the patient. These complex choices require detailed knowledge of the interventions, possible therapeutic alternatives, and modes of disease transmission.

**DISCUSSION**

**H1N1 Healthcare-Associated Infections and H1N1 Critical Illness**

Early data from the US 2009 H1N1 experience suggested that 50% of healthcare workers with documented H1N1 infections were infected in a healthcare setting (16). Although specific data on nosocomial H1N1 infection in critical care are not yet available, the significant risk to unprotected workers and patients from infectious agents in a healthcare setting must not be minimized. Further, the reports of numerous clusters of H1N1 causing severe critical illness (17–19) suggest that careful attention must be paid to infection control in the critical care setting. Should the autumn/winter northern hemisphere 2009 H1N1 experience match or exceed what has been predicted by US experts (20), it is likely that the numbers of patients needing critical care will dramatically exceed baseline US critical care demand (21). This increased risk in critical care is particularly important for two reasons: absenteeism attributable to occupational H1N1 infection may cripple an already stretched critical care workforce, and staff with high-risk profiles (e.g., comorbid respiratory disease) may experience serious complications from occupational infection, resulting in critical illness or death. Although the latter was a greater risk in the SARS epidemic of 2003, it remains a very real concern.

**H1N1 Infection Control Guidance**

Based on lessons learned from the summer 2009 experience with transmission, morbidity, and mortality of the 2009 H1N1 virus, the Centers for Disease Control and Prevention has issued recommendations regarding infection control. Those have been reviewed and revised as data have accumulated in recent months. It is clear that no single action will provide complete protection for healthcare workers, but a multifaceted approach can help decrease the likelihood of healthcare-associated transmission. Comprehensive infection control programs should be built on a foundation of effective isolation procedures, as outlined by the Centers for Disease Control and Prevention, as well as aggressive hand hygiene and healthcare workers vaccination programs, both of which have been demonstrated to have significant impact on limiting nosocomial infections (6, 22–26). Centers for Disease Control and Prevention isolation guidance reflects concerns for increased risk with aerosol-generating procedures by recommending airborne isolation precautions in settings where such procedures are performed (6). Respiratory care infection control can then build on these recommendations, integrating best practices and available data specific to key interventions. It cannot be overemphasized that the implementation of the strategies discussed here should be considered adjuncts to the basic infection control guidance outlined by the Centers for Disease Control and Prevention.

**Masks for Contagious Patients**

Data on the mode of transmission of influenza is lacking. However, it is generally agreed to be multimodal, with respiratory droplet transmission serving as a major component of person-to-person transmission. Given that hypoxemia is one of the major H1N1 complications requiring hospitalization, the risk for viral dissemination from respiratory droplet aerosolization associated with oxygen mask use is a major concern (27). A few investigators have examined the implications of placing masks on infected patients to reduce spread of infection. The risks of increased work of breathing and re-inspiration of viral secretions with masks on patients having respiratory difficulty have not been investigated in detail but may be problematic (28).

In a recent study, Johnson et al (29) assessed the in vivo efficacy of surgical and N95 (respirator) masks to filter reverse-transcription polymerase chain reaction-detectable virus when worn correctly by patients with laboratory-confirmed acute influenza. Of 26 patients with a clinical diagnosis of influenza, 19 had the diagnosis confirmed by reverse-transcription polymerase chain reaction, and nine went on to complete the study. According to the authors, surgical and N95 masks were equally effective in preventing the spread of polymerase chain reaction-detectable influenza, but it is important to note that very few patients completed the study (29).

Several authors have examined the dispersal of respiratory droplets with the use of standard open oxygen delivery masks, including both a Venturi-type mask and a standard non-rebreather mask (27, 30, 31). One study (27) compared the use of the standard masks with side vents to a non-rebreather mask that could be used with a filter on the expiratory port, the Hi-Ox80 (Viasys Healthcare, Conshohocken, PA; Fig. 1). This study demonstrated that the visible plume of exhaled droplets was reduced with use of this filter, but change in measurable particle dispersal was not tested. It should be noted that although use of a Hi-Ox mask may reduce environmental contamination by an infected patient, it should not be expected to reduce a patient’s exposure to a potentially contaminated environment.

In certain situations, patients with possible infection may need to share rooms with patients who are known to be infected.
Noninvasive and Manual Ventilation

Noninvasive ventilation (NIV) has emerged as an important front-line treatment in acute exacerbations of COPD. In this instance, the prevention of intubation and attendant consequences reduce morbidity and mortality (33, 34). The use of NIV in hypoxemic respiratory failure, particularly in ARDS, is less clear and often results in failure (35–38), suggesting that the usefulness of NIV in mass respiratory failure associated with hypoxemia may be limited. In fact, early data from the 2009 H1N1 experience in Spain showed that the majority of patients treated with NIV for H1N1-associated respiratory failure went on to require invasive mechanical ventilation (19).

Data from the SARS experience suggest that there may be an increased risk of secondary infection with the use of NIV and with manual ventilation; however, the true risk posed by these interventions is unclear (13, 39–42). In some instances in Asia, NIV was used successfully without reports of caregiver infection. Caregivers did use appropriate personal protective equipment. In Canada, healthcare workers who were present for aerosol-producing procedures (aerosol therapy, intubation, NIV) were infected. This difference may be related to the level of personal protective equipment used. There is some controversy as to whether NIV is an aerosol-producing procedure, but the patient with an intact airway is capable of coughing when the mask is removed, thus expelling contaminated aerosol into the room. In the presence of leaks around the mask, the high flows produced by NIV may also propel aerosol droplets into the environment.

The decision regarding when to use NIV in an epidemic associated with mass respiratory failure must be based on thoughtful analysis of the patient benefits, the potential risks of spreading secondary infection with NIV use, and environmental factors such as availability of private isolation rooms. In the 2009 H1N1 outbreak, it may be reasonable for centers comfortable with NIV to consider its use in congestive heart failure or COPD patients with exacerbations attributable to H1N1, given the documented mortality benefit to NIV use in non-H1N1 patients with similar respiratory conditions. If NIV is used in this context, then a higher level of isolation precautions may be warranted. There are no compelling data for improved clinical outcomes for those patients with non-H1N1-associated rapidly progressive hypoxemic respiratory failure who have no underlying lung disease. Therefore, a much greater degree of caution is warranted in using NIV for H1N1-associated hypoxemic respiratory failure and ARDS.

Systematic investigation is warranted to clarify the degree to which these procedures contribute to viral transmission and how they may be implemented safely. Common sense and experience seem to suggest that a patient with an intact upper airway and cough is more likely to infect the environment than the intubated patient breathing through a ventilator circuit. Future investigations of NIV use should focus on whether a particular condition is likely to respond to NIV and whether the risk of secondary infection from its use is such that NIV utilization is unwise. The probability of limited ventilator resources in scenarios such as a severe influenza pandemic underscores the importance of clearly enumerating the risks of NIV use. Many inpatient NIV machines can be repurposed for ventilation with an endotracheal tube, so this equipment may be rendered useful even if NIV is not widely implemented (43).

Delivery of Inhaled Medications: Use of Metered-Dose Inhalers vs. Nebulizers

In patients with acute respiratory illness, inhaled medications, such as bronchodilators, are often a mainstay of early treatment. Such medications commonly are delivered to inpatients through nebulization. However, several studies have demonstrated that the use of a metered-dose inhaler (MDI) is as safe and efficacious as a nebulizer (44, 45) but can be delivered more quickly and with a reduced concern for cross-contamination. A spontaneously breathing patient receiving aerosol therapy via a mask or mouthpiece can contaminate the environment and place caregivers at risk. In this situation, use of MDI with a mask may be less likely to produce aerosols to contaminate the environment, and efficacy is unaffected. Therefore, the use of MDI with spacers and masks in a mass respiratory failure event seems prudent for medications that are available in this form. One major barrier to overcome in this context may be that of staff knowledge about MDI efficacy and patients’ willingness to use MDI in acute exacerbations of respiratory illness (46).

Mechanically ventilated patients present unique challenges for aerosol delivery of medications. MDI and nebulizers can be adapted for use in ventilator circuits. The nebulizer commonly connects to a T-shaped connector in the ventilator circuit and is driven by compressed gas from the wall source or the ventilator. When the ventilator is used, nebulization is typically in phase with inspiration, reducing medication waste. An MDI requires a spacer or connector with an integral actuator. The choice of devices is commonly dictated by the availability of medications in either MDI or unit dose form. Studies comparing the efficacy of the two delivery systems are limited (47–52). Although the available studies are small, enrolling <20, at least three of the studies showed no difference in efficacy between beta-agonist delivered by MDI or nebulizer.
nebulizer (50–52). A guideline from the American College of Chest Physicians and the American College of Asthma, Allergy, and Immunology states that the MDI and nebulizer can be used to deliver beta-agonists to mechanically ventilated patients, but the administration technique for both requires attention, given that multiple technical factors may impact the efficiency of aerosol delivery (53).

It is also important to note that the use of a nebulizer in the ventilator circuit is associated with an increased risk of ventilator-associated pneumonia. The causative mechanism may include breaking of the circuit or handling of the nebulizer between uses. A nebulizer left in the circuit continuously can fill with condensate and aerosolize this contaminant (54–56). If the nebulizer is removed from the circuit, the physical breaking of the circuit, cleaning, and storage of the device may all contribute to an increased infection risk. Taken together, these factors suggest that MDI should be used to deliver inhaled medications whenever possible in the context of a respiratory virus epidemic. Further, great care should be taken in the care and handling of ventilator circuits when the use of nebulizers is necessary, to limit patient risk for secondary complications and healthcare worker risk for exposure to healthcare-acquired infection.

Ventilator Circuit Filtration

Another key issue to be addressed in critical care infection control is that of ventilator circuit filtration. The use of filters for inspired gases, expired gases, or within the heat–moisture exchanger is a subject of debate. It is recommended that ventilators that draw air from the room for patient delivery have a filter on the inspiratory inlet, particularly in the presence of contagion. Such a strategy has not been demonstrated to reduce ventilator-associated pneumonia, but its utility in the presence of other respiratory pathogens remains uncertain (57, 58). For the most part, filters before the ventilator’s drive mechanism are meant to protect the internal components, not patients. The inlet of most ventilators can be modified to include a high-efficiency particulate air filter or chemical, biological, radiologic, and nuclear filter, but there are no data on the role of these filters in preventing secondary infection.

Filters used in the expiratory limb of the ventilator circuit are intended to protect the delicate flow and pressure monitoring components. They have been recommended by some for infection control. Although there is a theoretical risk to caregivers, the actual risk for secondary infection from expired gas from intubated patients has not been documented (59). The answer may vary by device (e.g., configuration of ventilator circuit, location of exhalation valve, and use of active humidification or aerosol delivery). It is unclear which is a more dangerous, unfiltered exhaled gas or possible staff exposure when breaking the circuit to change the filter. Further, the use of heat–moisture exchangers with a filter has not been shown to reduce the ventilator-associated pneumonia rate or to alter contamination of the environment. Heat–moisture exchangers with a filter may reduce bacterial contamination of the environment, but do so at an increased risk of occlusion and increased resistance. High-efficiency particulate air heat–moisture exchangers improve filtration capabilities but tend to have more limited humidification performance (60).

Rescue Therapies

Available data on the number of critically ill H1N1 patients requiring very high levels of ventilatory support suggest that careful attention be paid to what is known about infectious risk associated with the delivery of therapeutic modalities that are often considered “rescue therapies” (i.e., therapies of unproven benefit that may be tried in the event that conventional critical care support has failed). In the past, the therapies in this group have been considered “cosmetic” in the treatment of ARDS in that oxygenation is improved, but impact on outcomes has not been demonstrated. This finding may be influenced by the fact that most ARDS patients die of multiorgan system failure rather than respiratory failure (61). Given the profound, life-threatening hypoxemia that has been noted in many early 2009 H1N1 critically ill patients, these therapies may prove to be extremely useful adjuncts in this patient population.

High-Frequency Oscillatory Ventilation

The use of HFOV poses additional infection control challenges in the event of epidemic or pandemic respiratory illness (59, 62). Standard HFOV use involves constant venting of unfiltered, aerosolized gas from the mean airway pressure control diaphragm into the patient room. The entire basic system includes one exhalation valve and two high-pressure dump valves with a design that prevents filtration. Some centers have developed scavenging and filtration techniques (62) that may decrease the risk of environmental contamination, but no published data exist regarding the impact of these systems on infection control. Additionally, filtered HFOV circuits have been developed since the SARS experience. Although these circuits may be an important contributor to the critical care infection control armamentarium, some concern exists regarding whether the addition of filters to these circuits may alter airways resistance, or if they have appropriate efficacy in reducing environmental contamination in clinical settings. No published studies answer either of these questions, but some data suggest that airways resistance is not significantly impacted by the addition of filters to HFOV circuits (Gentile M, unpublished data).

Inhaled Nitric Oxide/Prostanoids

The ability of inhaled nitric oxide to reliably improve oxygenation in early ARDS (63) makes it a potentially useful therapeutic option in the H1N1 patient with refractory hypoxemia when conventional therapy fails. Inhaled nitric oxide is delivered in a nitrogen/nitric oxide mixture proportional to ventilator flow. The sampling system of the INOvent or INOmax DS (IKARIA, Clinton, NJ) draws 230 mL/min from the inspiratory limb of the ventilator circuit through a filter, across the gas analyzers, and out to the ambient environment (64, 65). Additional filters can be placed on this line, but there is no evidence of ambient contamination.

Aerosolized prostanoids are a cheaper alternative to inhaled nitric oxide with similar effects (66). Drug delivery requires continuous nebulization and poses the attendant risks associated with that procedure, as previously described. An inspiratory filter is routinely used during prostaglandin delivery, because the aerosol can foul expiratory pressure and flow sensors. Filters must be routinely changed to avoid occlusion, which would require frequent breaking of the circuit and potential environmental contamination.
**Prone Positioning**

As with HFOV and inhaled nitric oxide/prostacyclin, the impact of prone positioning on clinical outcomes remains a subject of debate, but its impact on improving oxygenation (67) makes it a potentially useful resource in the management of H1N1-associated severe ARDS. Some have reported increased incidence of endotracheal tube dislodgement (68), but that finding has not been demonstrated uniformly (67). The available evidence suggests that this complication is unlikely to impact patient outcomes (69); however, the theoretical infectious risk to the healthcare workers by disruption of the ventilator circuit or dislodgement of the endotracheal tube should be taken into account in the implementation of this therapy and appropriate precautions taken.

**CONCLUSION**

**Situational Assessment and Priority Action Items for Planners**

Respiratory care equipment may directly impact disease transmission, but patient and equipment selection have yet to be sufficiently addressed by traditional sources for infection control guidance. This limited consideration likely results from under-representation of respiratory care practitioners within infection control professional societies and government advisory committees. Also, infection control guidance for respiratory viruses frequently provides a one-size-fits-all summary set of recommendations, which rarely acknowledge the complex equipment variables and differences in risk to patients across a range of clinical practice sites. Uninfected, at-risk, critically ill patients generally have limited cardiopulmonary reserve to tolerate the complications of a healthcare-associated infection such as influenza. Therefore, secondary transmission may have fatal consequences in the ICU, even if the pathogen is of limited virulence overall, as with the current outbreak of 2009 H1N1. Hence, infection control strategies appropriately differ in critical care settings compared to other inpatient settings, even if such differences add complexity to infection control messaging.

To best guide use of respiratory care interventions during outbreaks of respiratory-transmitted pathogens, it is vital that we build an appropriate knowledge base. At present, strategies for delivery of inhaled medications, use of NIV for patients with respiratory conditions likely to benefit from it, selection of respiratory ancillary equipment for invasively ventilated patients, and determination of the safest rescue modalities for refractory hypoxemia remain a matter of expert opinion. We must advance the evidence base regarding transmission risk, with specific attention to collecting data on meaningful outcomes in the clinical environment. Data on transmission risk alone, however, are insufficient to generate meaningful guidance on therapeutic interventions. Recommendations for use of therapeutic interventions must be based on expert analyses of the therapies' effectiveness and the risk of transmitting disease.

Given the need to understand the risk of transmission of therapeutic respiratory interventions, the potential impact of transmission on patients with limited cardiopulmonary reserve, and the effectiveness of the therapies, relevant infection control advisory committees must increase participation by clinicians with respiratory care expertise. Professional societies such as the American Association of Respiratory Care, American College of Chest Physicians, American Thoracic Society, American Association of Critical-Care Nurses, and Society of Critical Care Medicine should consider assembling expert committees to provide recommendations and define a research, policy, and training path toward appropriate respiratory care intervention guidelines for respiratory-transmitted pathogens. These societies should also urge increased participation with government advisory committees on infection control for respiratory-transmitted pathogens in healthcare settings.

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