Transmission of Severe Acute Respiratory Syndrome during Intubation and Mechanical Ventilation

Robert A. Fowler, Cameron B. Guest, Stephen E. Lapinsky, William J. Sibbald, Marie Louie, Patrick Tang, Andrew E. Simor, and Thomas E. Stewart

Interdepartmental Division of Critical Care Medicine, University of Toronto, Sunnybrook and Women's College Health Sciences Centre; Intensive Care Unit, Mount Sinai Hospital; and Department of Microbiology, Division of Infectious Diseases, University of Toronto, Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario, Canada

Nosocomial transmission of severe acute respiratory syndrome from critically ill patients to healthcare workers has been a prominent and worrisome feature of existing outbreaks. We have observed a greater risk of developing severe acute respiratory syndrome for physicians and nurses performing endotracheal intubation (relative risk [RR], 13.29; 95% confidence interval [CI], 2.99 to 59.04; p = 0.003). Nurses caring for patients receiving noninvasive positive-pressure ventilation may be at an increased risk (RR, 2.33; 95% CI, 0.25 to 21.76; p = 0.5), whereas nurses caring for patients receiving high-frequency oscillatory ventilation do not appear at an increased risk (RR, 0.74; 95% CI, 0.11 to 4.92; p = 0.6) compared with their respective reference cohorts. Specific infection control recommendations concerning the care of critically ill patients may help limit further nosocomial transmission.

Keywords: severe acute respiratory syndrome; endotracheal intubation; noninvasive; high-frequency oscillatory ventilation

Severe acute respiratory syndrome (SARS) is a newly recognized infectious disease that has led to international concern and response (1–4). Nosocomial transmission from ill patients to healthcare workers has been a prominent and worrisome feature of existing SARS outbreaks (4, 5). In Singapore and Toronto, healthcare workers have accounted for half of all SARS cases and approximately 20% of critically ill SARS cases (6, 7). There has been concern that specific ventilation strategies may place healthcare workers at greater risk of contracting SARS, and this has influenced early guidelines for the management of patients with SARS. There are yet few reports examining the nature and magnitude of this risk. This report describes the occurrence of high rates of transmission to healthcare workers caring for patients with SARS who required ventilatory assistance.

METHODS

To determine whether specific ventilatory strategies were associated with an increased risk of SARS development in healthcare workers, we undertook retrospective cohort analyses involving an intensive care unit (ICU) in which nine patients with SARS had been treated with various modes of ventilatory support. Seven patients with SARS were treated during the outbreak period; two patients were treated and discharged greater than 3 weeks before the outbreak and are not included. We considered and evaluated ventilatory exposures for the 2-week period before the outbreak, corresponding to the upper duration latency between exposure and SARS symptom onset in other series (2–4, 7, 8). Because of the concern of dispersal of respiratory droplets and secretions and limited available data, we chose to restrict our analysis to three particular respiratory practices to determine whether they conferred a high risk. We examined (*1*) the risk of developing probable or suspect SARS (1, 2) for physicians who performed endotracheal intubation for patients with SARS and respiratory failure versus physicians who cared for patients with SARS but did not perform endotracheal intubation, as well for nurses who assisted with endotracheal intubation versus nurses who cared for patients with SARS but were not present for endotracheal intubation; (*2*) the risk of developing SARS for nurses caring for patients with SARS with high-airflow, noninvasive positive-pressure ventilation (NIPPV); and (*3*) the risk of developing SARS for nurses caring for patients with SARS treated with high-frequency oscillatory (HFO) ventilation. In the later two groups, the comparison was to nurses caring for patients with SARS treated with conventional ventilation. Physicians formed the "at-risk" and control group for the first analysis, as all intubations were performed by physicians. For analyses of ventilatory techniques, nurses were considered rather than other healthcare workers (such as respiratory therapists or physicians) because of the greater likelihood for a longer duration of exposure and greater specificity of exposure (in the ICU studied, nurses generally care for one patient per shift, whereas respiratory therapists and physicians typically care for many different patients, with shorter durations of direct exposure to individual patients).

For each measure of association, factors previously identified to confer a greater risk of contracting SARS, such as age and presence of diabetes mellitus, were considered as potential confounders (7, 8). During the period of investigation, all patients were treated in negative-pressure isolation rooms, and healthcare workers wore gloves, gowns, N-95/PCM 2,000 masks, and hairnets. Eye or face shields were variably employed. Bronchoscopy and aerosol therapy were not performed. We explored the dose–response relationship between nursing exposure and the risk of developing SARS by examining not only absolute numbers of nurses affected in relationship to all exposed, but also the number of nursing shifts exposed in relationship to the total nursing shifts during the period of evaluation. We similarly compared dose–response relationships for physicians based on duration and degree of difficulty of intubation (greater than two attempts at passing the endotracheal tube, longer than 10 minutes of direct laryngoscopy/bag-mask ventilation, or copious patient secretions). Small sample sizes and limited information precluded determination of independent measures of association through multivariable logistic regression. We compared baseline normally distributed continuous characteristics (e.g., mean age ± SD) using Student's *t* test. As many comparisons contained small sample sizes, Fisher's exact tests were used to assess risk factors. Two-sided tests were used for all comparison, and 95% confidence intervals (CIs) were calculated for all relative risks (RRs).

RESULTS

The epidemic curve of healthcare workers who contracted SARS after caring for critically ill patients is presented in Figure 1. Between April 1 and April 22, 2003, there were 122 critical care staff at risk during the outbreak period, including 66 nurses, 18 nursing aids/patient assistants, 15 physicians, 18 respiratory therapists, 3 physiotherapists, and 2 other healthcare workers. All 122 members of the staff had exposure to patients with SARS during this period, but some had differential exposures, allowing for determination of the RR of certain exposures. Ten (8.2%)

(*Received in original form May 30, 2003; accepted in final form February 23, 2004*)

Correspondence and requests for reprints should be addressed to Robert A. Fowler, M.D., M.S., University of Toronto, Sunnybrook and Women's College Health Sciences Centre, 2075 Bayview Avenue, Room D4-78, Toronto, ON, M4N 3M5 Canada. E-mail: rob.fowler@sw.ca

Am J Respir Crit Care Med Vol 169. pp 1198–1202, 2004
Originally Published in Press as DOI: 10.1164/rccm.200305-715OC on February 27, 2004
Internet address: www.atsjournals.org

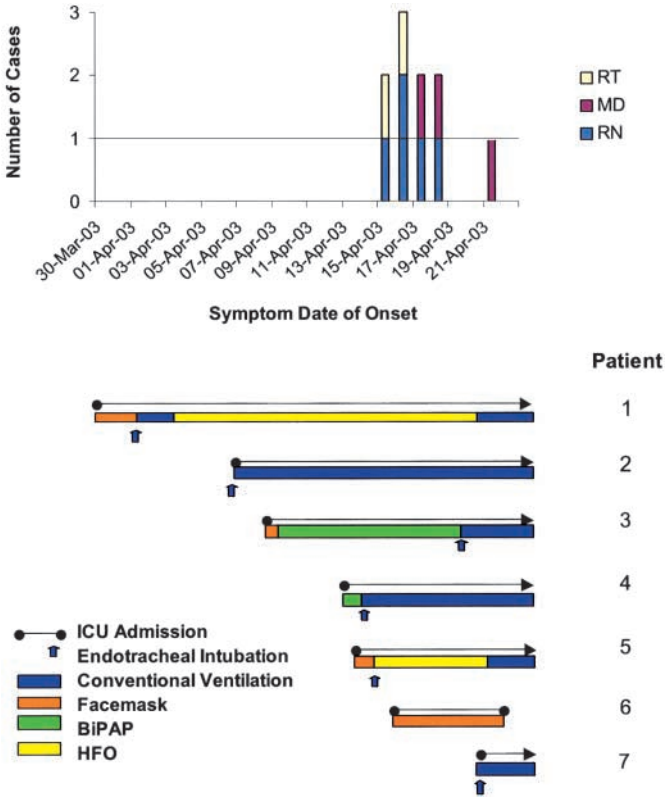

Figure 1. Epidemic curve of intensive care unit (ICU) healthcare workers who contracted severe acute respiratory syndrome (SARS) through patient care. BiPAP = biphasic positive airway pressure; HFO = high-frequency oscillatory; MD = physician; RN = registered nurse; RT = respiratory therapist.

critical care healthcare workers (five critical care nurses, two respiratory therapists, and three physicians) met the clinical case definition of probable SARS—all but one of these healthcare workers tested positive for SARS-coronavirus by polymerase chain reaction or serology. One healthcare worker did not have either test performed. All healthcare workers with SARS were subsequently hospitalized. Most received supplemental oxygen and antimicrobial therapy, but none became critically ill (7, 8). The mean age of healthcare workers with SARS was 35.1 ± 6.5 years and 36.2 ± 4.7 years among those without SARS ($p = 0.7$).

Healthcare workers and the nature of their exposures are described in Table 1. Nurses and physicians who directly participated in endotracheal intubation had a dramatically increased risk of subsequently developing SARS (RR, 13.29; 95% CI, 2.99 to 59.04; $p = 0.003$) (Table 2). This association was subsequently stratified based on the nurse or physician role. Physicians performing endotracheal intubation had a 3.8-fold greater likelihood of subsequently developing SARS than did physicians caring for patients with SARS who did not perform endotracheal intubation (RR, 3.82; 95% CI, 0.23 to 62.24; $p = 0.5$); however, this association was not statistically significant. Three intubations were deemed "difficult," whereas three were deemed not difficult. One of the three difficult intubations and one of the three nondifficult intubations were associated with physician acquisition of SARS. Only one physician was the primary intubator for more than one patient with SARS; however, this increased exposure was not associated with physician acquisition of SARS. Both among physicians who contracted SARS and those who did not, there was an equal (1:1:1) distribution of junior trainees, senior critical care trainees, and critical care attending physicians.

As the numbers of nurses who assisted and did not assist endotracheal intubation were much greater than physicians, we were able to define their risk more fully. Nurses who assisted in endotracheal intubation were much more likely to develop SARS than were nurses who cared for patients with SARS in the ICU at other times (RR, 21.38; 95% CI, 4.89 to 93.37; $p = 0.001$) (Table 2). Three of the five nurses who developed SARS assisted during intubation of patients with SARS. The risk was similarly high when examined as a function of nursing shifts of exposure compared with shifts worked when endotracheal intubation was not performed (RR, 33.0; 95% CI, 7.50 to 145.30; $p < 0.0001$).

Nurses caring for patients receiving NIPPV may have been more likely to develop SARS than nurses caring for patients with SARS treated with conventional ventilation (RR, 2.33; 95% CI, 0.25 to 21.76; $p = 0.5$), but this was not statistically significant (Table 3). This association was unchanged when examined by nursing shifts at risk because NIPPV was not used for prolonged periods and nurses generally cared for only one patient (one shift) in total. No nurses in this group assisted with endotracheal intubation per se, although nurses who developed SARS often had their first exposure to patients with SARS within the first 48 hours of their patient's admission.

Nurses caring for patients with SARS receiving HFO did not appear to have an increased risk of developing SARS than did nurses who cared for patients with SARS who received conventional mechanical ventilation (RR, 0.74; 95% CI, 0.11 to 4.92; $p = 0.6$) (Table 3). The association was similar when examined by nursing shift at risk (RR, 0.55; 95% CI, 0.1 to 3.12; $p = 0.8$), and neither reached statistical significance. In this group, similar to that observed with other interventions, SARS occurred in nurses caring for patients within 48 hours of their patient's admission to the ICU.

DISCUSSION

We have shown that physicians and nurses involved in the early critical care period and endotracheal intubation of patients with SARS are at a substantially increased risk of themselves contracting the illness. This association is particularly strong among nurses present during the period of endotracheal intubation. Physicians who actually place the endotracheal tube also appear to be at increased risk, although this association did not reach statistical significance, possibly because of the smaller numbers of physicians caring for patients with SARS during the outbreak. It is also interesting that the RR may be higher for nurses than physicians. This might be because of a longer duration of exposure that nurses likely had in the peri-intubation period, whereas physician exposure is often limited to the procedure itself. The relationship among other ventilation practices that may also lead to increased exposure to viral-laden droplets and subsequent transmission of SARS is less clear—no statistically significant association between NIPPV or HFO could be found by examining an outbreak within one ICU.

Our study also offers insights into the importance of timing of SARS transmission from critically ill patients to healthcare workers. Although symptoms in workers arose over a 7-day period, we feel it was important to examine potential exposures in the 14 days before the date of onset, corresponding to upper limits of latency from exposure (7, 8). Transmission often appeared to occur within 48 hours of patients' admission to the ICU and often involved acute patient respiratory stabilization through endotracheal intubation and mechanical ventilation. There may be a number of potential explanations for this. First,

TABLE 1. DESCRIPTION OF HEALTHCARE WORKERS WHO DEVELOPED SEVERE ACUTE RESPIRATORY SYNDROME

Healthcare Worker	Occupation	Nature of Exposure
1	Registered nurse	Cared for patient treated with conventional ventilation during one 12-hour shift; assisted with intubation
2	Respiratory therapist	Routine respiratory care for multiple 12-hour shifts; assisted with intubation
3	Respiratory therapist	Routine respiratory care for multiple 12-hour shifts; assisted with intubation
4	Registered nurse	Cared for patient treated with NIPPV for one 12-hour shift; present before, during, and after intubation
5	Registered nurse	Cared for patient treated with HFO for one 12-hour shift
6	Registered nurse	Cared for patient treated with HFO, conventional ventilation for one 12-hour shift; assisted with intubation
7	Physician	Cared for all patients during multiple shifts; performed intubation
8	Physician	Cared for all patients during multiple shifts; performed intubation
9	Registered nurse	Cared for patient treated with conventional ventilation for two 12-hour shifts; present for intubation
10	Physician	Cared for all patients during multiple shifts, helped to perform intubation

the clinical deterioration that often precipitates transfer to an ICU may be associated with increased tachypnea, dyspnea, or coughing and thus increased dispersal of infectious respiratory droplets. As well, deterioration may involve the changes in respiratory support that also increase the likelihood of secretion dispersal. Although patients were treated in negative-pressure isolation rooms and full droplet precautions were in place before the onset of the outbreak, a compromise in such protective barriers may have been more likely with both patient deterioration and transfer (5). With increased awareness, education, and vigilance to infection control procedures; the addition of face shields, personal respirators for high-risk activities such as endotracheal intubation, the addition of bacterial–viral filters (ClearGuard 3; Intersurgical Ltd., Berkshire, UK) on the exhalation valve of all mechanical ventilators; diminished exposure to acutely ill patients with SARS requiring stabilization and intubation; and possibly because of fewer other ventilation practices associated with a high risk of droplet dispersal (such as NIPPV), further nosocomial transmission was stopped within this ICU.

There are several limitations of our analysis. The small sample size and limited available data preclude extensive stratification or meaningful multiple logistic regression that might identify other and independent predictors. Certain associations may be altered by important confounding or effect-modifying variables we were unable to consider. Several other critical care interventions may be associated with a greater risk for transmission of SARS to healthcare workers. For example, patients receiving HFO typically have severe respiratory disease and may therefore produce a larger quantity or concentration of virus in sputum or expiratory gas than less ill patients, producing an increased risk for transmission of SARS to healthcare workers on this basis alone, irrespective of mode of ventilation. If this were the case, however, this would strengthen our observation that no conclusive positive association exists between HFO use and SARS transmission. We did consider the effects of known potential common confounders such as age and diabetes mellitus on the associations we report (7, 8). We were able to stratify risk of endotracheal intubation according to physician or nursing exposure. Among physicians, we did not find a clear trend toward a greater or lesser risk based on the level of training. Additionally, and again somewhat surprisingly, we did not detect a clear trend toward an increased risk for performing multiple intubations or among difficult intubations. This quite possibly relates to the small sample size of our associations and may be further clarified in an ongoing multicenter epidemiologic investigation.

Proximity and duration of contact to a patient with SARS have previously been found to be associated with a higher risk of viral transmission (9). We attempted to explore the effects of duration of exposure by examining healthcare worker risk in terms of both patient exposures and number of shifts exposed. Among nurses caring for patients with SARS, we evaluated dose–response exposure among nurses who cared for more than one patient with SARS and also among those who worked more than one shift with individual patients, without demonstrating obvious important trends. Because respiratory therapists were found to have exposures to nearly all patients and ventilation

TABLE 2. ASSOCIATION OF ENDOTRACHEAL INTUBATION WITH THE DEVELOPMENT OF SEVERE ACUTE RESPIRATORY SYNDROME AMONG PHYSICIANS AND NURSES

Any Involvement with Intubation	n	Developed SARS	RR	95% Confidence Interval	p Value
All healthcare workers					
Yes	14	6	13.29	2.99–59.04	0.003
No	62	2			
For nurses					
Yes	4	3	21.38	4.89–93.37	0.001
No	57	2			
For physicians					
Yes	10	3	3.82	0.23–62.24	0.5
No	5	0			

Definition of abbreviations: RR = relative risk; SARS = severe acute respiratory syndrome.

TABLE 3. ASSOCIATION OF VENTILATION STRATEGIES WITH THE DEVELOPMENT OF SEVERE ACUTE RESPIRATORY SYNDROME AMONG HEALTHCARE WORKERS

Ventilation Mode	n	Developed SARS	RR	95% Confidence Interval	p Value
Patient treated with NIPPV					
Yes	6	1	2.33	0.25 to 21.76	0.5
No*	28	2			
Patient treated with HFO					
Yes	38	2	0.74	0.11 to 4.92	0.6
No*	28	2			

Definition of abbreviations: HFO = high-frequency oscillatory; NIPPV = noninvasive positive-pressure ventilation; RR = relative risk; SARS = severe acute respiratory syndrome.

* Conventional ventilation is the reference, with an odds ratio of developing SARS = 1.

strategies in the ICU over any given shift, we were unable to evaluate their risk in light of particular independent exposures. During the period of investigation, there was extensive bi-daily screening of all healthcare workers for symptoms and signs of SARS. If there was any suspicion of healthcare worker illness, they were assessed and placed under home quarantine observation, minimizing the chance that exposure and illness could have resulted from staff-to-staff contacts as opposed to direct patient care.

Certain high-risk components of SARS nursing care, such as tracheal suctioning, may also be an important confounder in this type of analysis. Tracheal suctioning was generally not performed among patients with SARS ventilated with either NIPPV or HFO. In-line, closed system endotracheal suctioning was used for patients with SARS receiving endotracheal intubation. If indeed endotracheal suction might increase the risk of respiratory droplet dispersion, this would likely act to dilute any estimate of positive association discovered between NIPPV, HFO, and nursing acquisition of SARS.

The ICU SARS Working Group of the Provincial Operations Committee of Emergency Management Ontario (an agency of the Solicitor General of Ontario) and others have developed guidelines for procedures such as endotracheal intubation, cardiopulmonary resuscitation, and mechanical ventilation in critical care areas during a SARS outbreak (10, 11). The guidelines include specific recommendations on the use of personal protection devices specify that the most qualified individual available should perform endotracheal intubation and that therapies such as prolonged NIPPV and aerosolized bronchodilator or humidification therapies generally should not be initiated where safe alternatives are available. It has been recommended by many clinicians involved in the Asian SARS outbreak that noninvasive ventilation may be preferred over early endotracheal intubation and mechanical ventilation because of the risk to healthcare workers involved with endotracheal intubation (12). Although noninvasive ventilation might be considered for patients with the expectation of very near-term improvement, much the same as for patients with hypoxemic cardiogenic pulmonary edema or hypercarbic respiratory failure because of a chronic obstructive pulmonary disease exacerbation (13, 14), observational studies of critically ill patients with SARS report that this form of acute lung injury is unfortunately generally not rapidly reversible.

These preliminary observations and others within the greater Toronto healthcare system have precipitated an ongoing epidemiologic investigation into the specific nature of risk of transmission between patients with SARS and healthcare workers. This investigation, with the assistance of infection control officers of hospitals of the greater Toronto area, local departments of public health, and the Centers for Diseases Control and Prevention, is likely to offer a detailed understanding of the mode of transmission and best means of prevention. In the interim, we advise caution in initiating procedures that may be associated with increased dispersal of respiratory droplets in patients with SARS. Our brief report highlights that there may be risks with many forms of support and that decisions should likely be made on an individual patient basis with due attention to the hazards for both patients and healthcare workers.

Conflict of Interest Statement: R.A.F. has no declared conflict of interest; C.B.G. has no declared conflict of interest and University of Toronto has a suppliers contract to receive full body protection suits to minimize risk of SARS transmission; S.E.L. has no declared conflict of interest; W.J.S. has no declared conflict of interest; M.L. has no declared conflict of interest; P.T. has no declared conflict of interest; A.E.S. has no declared conflict of interest; T.E.S. has no declared conflict of interest.

Acknowledgment: The authors acknowledge the dedication, bravery, and professionalism of nurses, respiratory therapists, physicians, and supporting staff of the greater Toronto area healthcare system during this crisis.

References

1. World Health Organization. Severe acute respiratory syndrome (SARS). *Wkly Epidemiol Rec* 2003; 78:81–83.
2. Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K, Tellier R, Draker R, Adachi D, Ayers M, *et al.* Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003;348:1995–2005.
3. Tsang KW, Pak LH, Gaik C, Yee WK, Wang T, Chan-Yeung M, Lam WK, Seto WH, Yam LY, Cheung TM, *et al.* A cluster of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1977–1985.
4. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, *et al.* A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1986–1994.
5. Centers for Disease Control and Prevention. Cluster of severe acute respiratory syndrome cases among protected health-care workers: Toronto, Canada, April 2003. *MMWR Morb Mortal Wkly Rep* 2003;52: 433–436.
6. Lew TWK, Kwek T-K, Tai D, Earnest A, Loo S, Singh K, Kwan KM, Chan Y, Yim CF, Bek SL, *et al.* Acute respiratory distress syndrome in critically ill patients with severe respiratory distress syndrome. *JAMA* 2003;290:374–380.
7. Fowler RA, Lapinsky SE, Hallett D, Detsky AS, Sibbald WJ, Slutsky AS, Stewart TE, Toronto SARS Critical Care Group. Critically ill patients with severe acute respiratory syndrome. *JAMA* 2003;209:367–373.
8. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, Walmsley SL, Mazzulli T, Avendano M, Derkach P, *et al.* Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003;289:2801–2809.
9. Scales DC, Green K, Chan A, Poutanen SM, Foster D, Nowak K, Raboud JM, Saskin R, Lapinsky SE, Stewart TE. Illness in intensive care staff after brief exposure to severe acute respiratory syndrome. *Emerg Infect Dis* 2003;9:1205–1210.
10. Interim directives to all Ontario acute care hospitals for high-risk procedures in critical care areas during a SARS outbreak. Accessed April 29,

2003. Available from http://www.health.gov.on.ca/login/sarsrep/docs/dir_inter_infec_control_050103%20.pdf.
11. Centers for Disease Control and Prevention. Interim domestic guidance on the use of respirators to prevent transmission of SARS. Accessed May 6, 2003. Available from http://www.cdc.gov/ncidod/sars/respirators.htm.
12. Zhong NS, Zeng GQ. Our strategies for fighting severe acute respiratory syndrome (SARS). *Am J Respir Crit Care Med* 2003;168:7–9.
13. Keenan SP, Kernerman PD, Cook DJ, Martin CM, McCormack D, Sibbald WJ. Effect of noninvasive positive pressure ventilation on mortality in patients admitted with acute respiratory failure: a meta-analysis. *Crit Care Med* 1997;25:1685–1692.
14. Pang D, Keenan SP, Cook DJ, Sibbald WJ. The effect of positive pressure airway support on mortality and the need for intubation in cardiogenic pulmonary edema: a systematic review. *Chest* 1998;114:1185–1192.