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SARS in the critically ill patient

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Editors note: The severe acute respiratory syndrome (SARS) has become a challenge to those caring for critically ill patients. The infectivity virulence, with the need for ICU care in up to 20% of patients, poses a unique threat to our patients and ourselves. Indeed, many of the cases of SARS have been in healthcare providers caring for patients with SARS. The development of SARS in healthcare providers who are apparently using proper equipment suggests that additional steps must be undertaken to contain the disease. In addition to improved barrier methods, high-risk procedures and treatments must be avoided in these patients. The very nature of this disease demands that infection control techniques are executed immediately and perfectly when faced with a critically ill SARS patient. This requirement demands familiarity with infection control methods before starting the care of these patients. In this issue of *Critical Care Rounds*, Drs. Lapinsky, Hawryluck, and Wax, with the input of several experts in critical care, infection control, and infectious diseases have summarized their experience in reducing the risk associated with treating SARS patients. It is hoped that this will help the reader manage these patients and prevent the spread of this disease to other healthcare workers, patients, and the community.

John Granton, Editor

SARS, first recognized in late 2002, has now been documented in 26 countries worldwide, with significant outbreaks in China, Hong Kong, Singapore, and Toronto. At the present time, the disease has spread to over 8,000 individuals in 31 countries (WHO, 30/05/2003, updates available at www.who.int/csr/sarscountry/en/). Research into identifying the etiological agent and evaluating modes of disease transmission and treatment options is currently ongoing. Using electron microscopy and polymerase-chain-reaction of the virus isolated in cell culture, a novel *Coronavirus* has been isolated from patients meeting the case-definition for SARS.^{1,2} Preliminary serological studies suggest that this virus has not previously infected the U.S. population.¹ The viral genome has been sequenced and early PCR-based tests are at an evaluation phase. While the western world has only been aware of this condition for 2 months, considerable progress has been made in identifying the responsible viral organism; however, less is known about the mode of transmission and treatment of this disease. Likely mechanisms include droplet spread, surface contact, and possibly, airborne transmission. The recommendations herein are based on the sparse published data that is available, collaborations between physicians in many affected centres, recommendations from the World Health Organization (WHO) and the Center for Disease Control (CDC), and local experience.

Clinical features of SARS

Case definitions of SARS are currently based on the presence of epidemiological risk factors (close contact with SARS cases or travel to SARS "affected" areas), along with a combination of fever and respiratory symptoms, with or without hypoxia and/or chest x-ray



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Table 1: WHO definitions of live cases

SUSPECT

A person presenting after 1 November 2002 with history of:

- high fever (>38 °C)

AND

- cough or breathing difficulty

AND one or more of the following exposures during the 10 days prior to onset of symptoms:

- close contact with a person who is a suspect or probable case of SARS;
- history of travel, to an area with recent local transmission of SARS
- residing in an area with recent local transmission of SARS

PROBABLE CASE

- A suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR).
- A suspect case of SARS that is positive for SARS coronavirus by one or more assays.
See "Diagnostic testing" section below.

changes (Table 1).³ However, as SARS spreads into the general population, our ability to distinguish it from other community-acquired pneumonias based on such epidemiological linkages will become increasingly tenuous. Diagnostic tests will be crucial in the future, both to ensure that patients are rapidly isolated and treatment is initiated

The incubation period has been reported to be 2 to 10 days and early manifestations include influenza-like symptoms such as fever, myalgias, and headache. At present, it is not clear at what stage of the disease viral shedding occurs or whether someone who is infected, but asymptomatic, can infect others. The notion of "super spreaders" has been suggested to describe the occasional patient who is associated with spread to large numbers of contacts.

Our current understanding of the illness is that fever occurs in all patients and is often the presenting symptom; fever may occasionally be absent in the elderly. The clinical features can be found at the CDC website: <http://www.cdc.gov/ncidod/sars/>. The respiratory phase starts after 3-7 days with dry cough and shortness of breath. In some cases, these symptoms are followed by hypoxia and radiological evidence of patchy or focal infiltrates or consolidation, often with a peripheral distribution that may progress to diffuse infiltration. Pulmonary infiltrates may worsen during the first 10 days, and acute respiratory distress requiring mechanical ventilation has occurred in 10% to 20% of patients. The case fatality rate is approximately 3% to 12% depending on whether the denominator includes suspect and probable cases (3%) or probable cases alone (12%).^{4,6} While the mortality rate is higher in older patients, particularly those with pre-existing

co-morbidity (eg, diabetes and immunosuppression), we have also seen young, previously healthy people succumb to the disease. This may be due to higher viral loads or to their host response.

The disease runs for 7 to 14 days and a biphasic course has been described in some patients, with an initial illness, improvement, and subsequent deterioration. This worsening can present as recurrent fever 4 to 7 days after initial defervescence, new chest infiltrates on x-ray, or recurrent respiratory failure. In some patients, an initial mild to moderate respiratory illness may initially improve, later followed by a progressive deterioration requiring ventilatory support.

Laboratory findings in patients with SARS include thrombocytopenia and leukopenia (in particular, lymphopenia). Elevated creatine kinase (CK), lactate dehydrogenase (LDH), and transaminases have been noted. There is evidence that a peak LDH and an initial elevated white cell count may carry a poor prognosis.⁶ Epidemiological studies have recently been completed illustrating the clinical features of SARS and defining features related to outcome.⁷

Management

Diagnostic testing

Initial diagnostic testing, including blood cultures, sputum for Gram stain and culture, and serological tests, should include a search for other respiratory pathogens. Bronchoscopy is valuable to exclude other diagnoses, but is generally not recommended due to the high risk it poses to ICU staff. In patients who are immunosuppressed, and when concerns regarding other diagnoses are high, the risk of bronchoscopy must be balanced against the risk of exposure to staff. Specific tests for the virus, including antibody tests (ELISA and immunofluorescence), and polymerase-chain reaction tests are in development and evaluation stages.

Treatment

Empiric therapy for community-acquired pneumonia should be considered using antibiotics with activity against both typical and atypical respiratory pathogens. In all series of SARS described to date, therapy has included broad spectrum antibiotics including a fluoroquinolone or macrolide.^{4,6} The antiviral drug, ribavirin, has been used in the majority of patients treated in Hong Kong and in Toronto, without evidence of efficacy or a strong anecdotal suggestion that patients benefit (Table 2). The adverse effects of ribavirin are significant, particularly hemolytic anemia and electrolyte disturbances such as hypokalemia and hypomagnesemia. The drug is also teratogenic and this should be considered in the decision to treat patients. Although ribavirin was used in the initial outbreak in Toronto, it is no longer recommended.

Table 2: Treatment regimen for SARS. The regimen followed in Toronto as of April 11, 2003. See text for details on the use of ribavirin

Antibiotic therapy

- Respiratory fluoroquinolone or macrolide

Corticosteroids

- Methylprednisolone 40 mg IV q12h x 3 d followed by
- Prednisone 50 mg PO daily x 7 days
- Higher doses (methylprednisolone 2 mg/kg/d or short pulses of 500 mg/d IV) have been used in patients with deteriorating respiratory function

Anecdotal evidence suggests a benefit of corticosteroids, particularly in patients with progressive pulmonary infiltrates and hypoxemia. In some, but certainly not all, patients, a dramatic improvement has been noted following steroid therapy. Various regimens have been used in different centres, with methylprednisolone in doses ranging from 40 mg BID (similar to pneumocystis pneumonia therapy)⁸ to 2 mg/kg/day (similar to late-phase ARDS therapy)¹⁰ to pulse doses of 500 mg IV daily (Table 2).

Until recently, patients with a late deterioration were restarted on ribavirin and increased doses of steroids to avoid further deterioration. The evidence for such practices currently does not exist and benefit is uncertain. Physicians must remain vigilant and search for other causes for fever and secondary sources of infection.

Oxygenation and ventilation

Management is affected by the increased risk of droplet transmission of virus by certain procedures. Oxygen therapy using aerosol humidifiers may increase the risk of droplet spread. Other high-risk procedures include obtaining nasopharyngeal swabs, bag-mask ventilation, intubation, suctioning, chest physiotherapy in non-intubated patients, nebulized drug therapy, non-invasive ventilation and extubation (Table 3). If a ventilated patient desaturates and requires manual bag-valve-mask ventilation, it is important to turn the ventilator to “standby” prior to disconnecting to avoid droplet spray. In fact, in an intubated patient with SARS, we recommend avoiding this intervention unless there is an obvious mechanical ventilator failure, even in the event of a cardiac arrest.

The ventilatory management of patients with SARS is not different from other patients with ARDS.⁹ The use of high frequency oscillation may be associated with increased risk of droplet spread and exposure to respiratory secretions, and our practice is to avoid this intervention. Jet ventilation for those failing conventional ventilation may be used safely. Little experience exists with interventions such as nitric oxide (NO) and prone positioning. Anecdotally, the experience in Toronto and Singapore has been that NO offers little benefit.

Table 3: High risk procedures for transmission of SARS in the ICU

Procedure	Concern	Possible solution
Nasopharyngeal swabs	coughing	use nasal swabs
Bag-valve-mask ventilation	difficult to seal at face	limit as much as possible
Intubation	coughing, agitation	sedation & neuromuscular blockade
Suctioning	coughing, aerosolisation	in-line suctioning
Non-invasive ventilation	unfiltered aerosolized exhalation	avoid
High frequency oscillation	unfiltered exhalation uncontrolled secretions	avoid

Infection control precautions

This organism appears to be transmitted by droplet spread, although surface contamination and possibly airborne spread may play a role. Recent data suggest that the virus may remain viable for considerable periods on a dry surface (up to 24 hours). Staff education and continued vigilance are essential.

Infection control measures for healthcare workers exposed to patients are provided in Table 4.

To avoid repeatedly breaking the negative pressure barrier, individual rooms should be stocked with basic supplies. Modified cardiac arrest carts containing emergency drugs such as epinephrine, atropine, and bicarbonate, etc. should be available in the room in the event of urgent need. Staff should remain outside the negative pressure rooms as much as possible. This means timing bloodwork and administration of any therapies to minimize entries and using video camera equipment or windows to monitor SARS patients without exposing staff. An antechamber (preferably with a sink) helps maintain strict infection control precautions and avoids the potential contamination of a single door room.

Dress precautions

- An N-95 mask or equivalent is used for airborne precautions. It is important that manufacturer specifications be adhered to, eg, some N-95 masks maintain protection for 8 hours, some for only 4 hours. Touching the mask, or lifting it to wipe the face or nose should be avoided. It is crucial to maintain a close seal to the skin and to ensure proper fit.

- Contact precautions, including the use of double gowns (at least one of which is waterproof) and double gloves, hats and shoe covers. Gowns, gloves, hats, boots, masks, and goggles should be changed after seeing each SARS patient.

- Eye protection with non-reusable goggles or face-shield.

Table 4: Infection control precautions in the ICU

Staff education

- High-risk procedures, alternatives and precautions
- Ways of minimizing exposure and effective use of time when in the room
- Instructions to staff on how to “undress” and “re-dress” without contamination
- Importance of vigilance and adherence to all infection control precautions
- Importance of monitoring own health
- Information on SARS as it evolves

Dress precautions

- Airborne precautions using an N-95 mask or equivalent
- Contact precautions
- Eye protection with a non-reusable goggles or face-shield
- Pens, paper, other personal items should not be allowed into or removed from the room.
- Powered Air Purification Respirator (PAPR) hoods should be used during high-risk procedures

Environment/Equipment

- Negative pressure isolation rooms with ante-chambers, and doors closed at all times
- Individual isolation rooms stocked with basic supplies and emergency drugs
- Alcohol-based hand and equipment disinfectants
- Gloves, gowns, masks, and disposal units should be readily available
- Use of video camera equipment or windows to monitor patients
- Careful and frequent cleaning of surfaces with disposable cloths & alcohol-based detergents
- No equipment should be shared

Transport

- Avoid patient transport where possible
- Reflect on need for investigations and whether the benefits justify the transportation risks.
- Intubated patients should have a filter (Conserve PALL 50) inserted between the bag-valve and the swivel connector.
- Infection control should be alerted

Ventilation

Avoid	Use
Nebulizers	Filters on bag-valve-mask
Non-invasive ventilation	
High frequency oscillation	Two filters per ventilator
Normal saline instillation prior to suctioning	Scavenger system for exhalation port

• Staff should change into hospital scrubs upon arrival and change into their own clothing at the end of the day to avoid fomite spread. Scrubs should not leave the hospital and should be sterilized after each use.

• Pens and paper should not be brought in and out of negative pressure isolation rooms. Pagers and watches should be left outside or be carefully covered to avoid contamination.

• Powered Air Purification Respirator (PAPR) hoods should be used by all members of the ICU team in the room during ALL high-risk procedures such as intubation and bronchoscopy.

• ALL precautions must be in place before staff enter the room no matter what is happening with the patient.

ICU environment

• Surfaces, including nursing stations, computer keyboards, etc. must be carefully and frequently cleaned with alcohol-based disinfectants

• No equipment should be shared

• When changing linens, air turbulence should be minimized

• No eating at nursing stations. Protective gear must be removed and not hung around neck when eating/drinking

• Staff must monitor their own health and most centres have set up screening mechanisms for staff on arrival at work.

In the ICU, the risk of droplet spread is increased with various procedures (Table 3). Efforts to avoid viral spread include avoiding nebulizers for drug administration and limiting or avoiding non-invasive ventilation. Nebulized humidification for oxygen therapy may carry similar risks and our practice is to provide nonhumidified oxygen using nasal prongs or a venturi mask. A non-rebreather mask with an expiratory port allowing gas filtration is available and may be of value. During bag-mask-valve ventilation, a filter should be used on the expiratory port. High-risk procedures include endotracheal intubation and bronchoscopy. Intubation should be performed by the most skilled person available, using the method with which they are most comfortable. Awake intubation may be associated with patient agitation and coughing that can severely compromise infection control precautions.

The Working Group on Adjunctive Protective Equipment for High-risk Procedures

The development of SARS in care providers who were performing high-risk procedures demanded that special precautions and vigilance be instituted in these circumstances. In addition, training on the proper use and handling of protective equipment and the performance of procedures to minimize exposure must be given, potentially on a large scale. To facilitate this process, a working group on adjunctive protective equipment for high-risk procedures in SARS patients was developed for hospitals in the Greater Toronto Area (GTA). The next step for this group is to devise clear procedures for using the protection devices

described below and to create effective training material. Furthermore, a plan for purchasing, distributing, and implementing these protection devices on a large scale needs to be created by the government. Having a large number of trained personnel who have undergone a detailed education process would help. The current availability of simulators and airway mannequins should be assessed in institutions that require these devices and plans for sharing or purchasing such training devices should be generated.

The mandate of this group was:

- to review options for adjunctive protection systems during high-risk situations when caring for SARS patients
- to evaluate candidate systems under simulated resuscitation situations
- to provide recommendations regarding use of adjunct systems and choice of adjunct systems

Methods included:

- a demonstration of 3 adjunctive protective systems by industry representatives and the Toronto Emergency Medical Services-Chemical Biological Radionuclear (EMS-CBRN) team members
- discussions and questions regarding advantages/disadvantages of each system
- simulated resuscitation scenarios with a SARS patient requiring intubation (operators only had 1 prior practice attempt at using gear, not a difficult airway situation)

Stage 1: Donning standard and adjunct protective gear

Stage 2: Entry to patient room and appropriate care leading to intubation of the patient

Stage 3: Removal of adjunct protective gear, decontamination procedures

General recommendations

- N-95 masks underneath adjunctive gear can provide a back-up device as a respiratory barrier in the event of an adjunct device failure.
- Prior to donning adjunct protective gear, N-95 mask placement must be checked to ensure it will not slip after donning hoods.
- Eye protection should include an elastic band or other device to ensure that the glasses/goggles will not slip position while under the hood.
- An electronic stethoscope with external speaker should be available for high-risk intubations to confirm endotracheal tube placement (a standard stethoscope cannot be used while wearing adjunct protective hoods). Other methods for confirming tube

placement, such as CO₂ detectors and/or esophageal detection devices, should be used.

- At least 1 appropriately trained person in full protective gear (N-95 mask, face shield, gown, gloves) must assist personnel exiting a room following a high-risk procedure. The exiting personnel should move as little as possible to avoid aerosolization of virus. All procedures for removing protective equipment should be done slowly and carefully. Removal of the equipment may be the period of highest risk for cross-contamination and requires special attention.
- Easily visible step-by-step checklists for entry and exit may help achieve total compliance with procedures.
- Clear procedures must be created for any adjunct device to ensure consistent and safe use.
- Thorough training of personnel on the use of adjunct devices and protocols is mandatory. The use of simulators or intubating mannequins, combined with hands-on training with the equipment under observation by someone familiar with the device/protocols, is helpful. Videotaped demonstrations would also likely benefit new users.

Mechanical ventilators

Mechanical ventilators should have two filters (eg, Conserve 50 PALL filters) that are placed in such a way to eliminate the exhalation of viral particles into the environment and to protect as much as possible the inside of the ventilator from contamination. One filter should be interposed between the distal end of the expiratory tubing and the ventilator itself and the second should be placed on the exhalation outlet of the ventilator. Ideally, the exhalation port should then be connected to a central scavenging system that would eliminate release of viral particles into the ICU.

Transportation of patients with SARS.

Transporting a SARS patient for testing is an infection control challenge. SARS patients should never be transported while being supported by bag-valve-mask ventilation and they should preferably be intubated. The risks and benefits of any procedure should be considered prior to transporting a patient. If bag ventilation is used, a filter should be placed between the bag and the endotracheal tube. Infection control should also be consulted for their advice on proper precautions.

Limiting visitors and personnel

An important component of infection control is limiting contact between the patient and personnel and visitors. It is crucial that staff do not work if they

are ill, even if the diagnosis is not clear. Staff who come into unprotected contact with a SARS patient are subject to a compulsory 10-day quarantine period at home. Visitors are currently restricted in Toronto hospitals and all are screened for symptoms of SARS and adhere to the same precautions as hospital staff in gowning, gloving, wearing N-95 masks, and goggles. Visits with SARS patients are prohibited even on compassionate grounds.

Conclusion

The Severe Acute Respiratory Syndrome has resulted in significant challenges for critical care medicine and likely will change the ICU environment for some time to come. In affected areas, policies are changing on a daily basis as more information about the virus and the disease are obtained. The ability of this disease to incapacitate staff has resulted in staff safety becoming a priority to maintain adequate critical care services. The concept of "universal precautions" now includes strict respiratory and contact precautions. The guidelines and recommendations discussed in this article will change as our knowledge grows. Information and communication technology have played an important role in allowing collaboration and rapid transfer of information. It is only through such sharing that we can hope to improve the mortality and morbidity of our patients, and stay healthy and well ourselves.

Further information:

Updated information on SARS can be obtained from:
Center for Disease Control: www.cdc.gov
World Health Organisation: www.who.int/csr/sars/
New England Journal of Medicine:
nejm.org/earlyrelease/sars.asp
www.medtau.org; www.cdc.gov/ncidod/sars

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