Transmission and Control of SARS

Susan M. Poutanen, MD, MPH, FRCPC, and Allison J. McGeer, MD, MSc, FRCPC

Address
Toronto Medical Laboratories and Mount Sinai Hospital, Department of Microbiology, 600 University Avenue, Room 1470, Toronto, Ontario M5G 1X5, Canada.
E-mail: spoutanen@mtsinai.on.ca
E-mail: amcgeer@mtsinai.on.ca

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Severe acute respiratory syndrome (SARS) was first recognized in China in November 2002 and was subsequently associated with a worldwide outbreak involving 8098 people, 774 of whom died. The outbreak was declared contained on July 5, 2003, after the last human chain of transmission of SARS had been broken. Whether outbreaks of SARS will return is debatable, but no one disagrees that it is important to be prepared for this possibility. This article presents an overview of the transmission and control of SARS based on the current state of knowledge derived from published studies of the outbreak and on our own personal experience.

Introduction
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Transmission
During the outbreak, it was evident that SARS was readily transmissible from person to person, especially in health
care facilities. However, how transmissible, for what period, and by which modes was unclear. Since the outbreak, much effort has been placed on better understanding these issues.

Incubation and period of communicability

The incubation period of SARS is 2 to 10 days, with a mean of 4 to 6 days [15•]. Outliers include a small proportion (< 5%) of cases with incubation period as short as 1 day and as long as 14 days [15•]. There is no evidence of communicability before symptom onset, and transmission is infrequent during the first few days of illness. Risk for transmission appears to be greatest in patients who are most severely ill and peaks during the second week of illness, corresponding with the timing of peak viral load [15•,16].

Most countries considered SARS patients to be potentially infectious until 10 days after resolution of fever and signs of clinical improvement, and isolation precautions were not discontinued until this occurred. There is no evidence of transmission from anyone treated in this manner, and it is possible that isolation for a shorter time period would be sufficient. Despite the absence of transmission, SARS-CoV viral RNA remained detectable in respiratory secretions and stool and urine specimens for more than 30 days in some patients [17]. This may be explained by the fact that viral RNA does not necessarily correlate with the presence of viable virus; indeed, positive viral cultures were noted predominantly in the first 2 weeks of illness, with no positive cultures after the third week of illness [17]. There is no evidence of relapse of SARS-CoV infections.

Typical modes of transmission

SARS-CoV has been detected in respiratory specimens, stool, and to a lesser extent, in blood, urine, and conjunctival secretions [18]. Respiratory droplet and direct contact are the primary modes of SARS transmission. Evidence for this includes studies in Hong Kong and Toronto, Canada that show an increased risk for SARS in health care workers who entered the room of a patient with SARS, with increasing risk in those with closer proximity to the patient and those remaining in the room for a longer duration, suggesting that transmission is enhanced by close, prolonged contact [19•,20]. In addition, an increased risk in household members of patients with SARS has been shown in those who had close, prolonged contact with the index person, and in particular, in those who shared a bed, reported being within 1 meter of the index person, and dined together [21•]. Increasing risk was noted as the duration of time the symptomatic index patient spent at home increased. Exposure to respiratory secretions appears to pose a particular risk, with higher risks for SARS noted in health care workers who assisted with intubation, suctioned before intubation, manipulated oxygen masks, or were present during noninvasive ventilation of a SARS patient for more than 30 minutes [20•,22•], in addition to higher risks being noted in household members of SARS patients who were coughed at by the index person within 1 meter [21•]. A summary of the results of these studies is outlined in Table 1.

Whether exposure to fecal material poses a particular risk has not been as well-documented. However, given the high proportion of stool samples positive for SARS-CoV by molecular tests (up to 100% in some studies), one can propose that transmission through stool is likely [15•]. Although no study has documented the role of fecal-oral transmission, fecal droplet transmission was thought to have played a significant role in the Amoy Gardens community outbreak in Hong Kong. Fecal droplets were thought to have resulted from unsealed floor drain traps that permitted an open connection to the soil stack. Wide-spread transmission of these droplets was thought to have resulted from the temporary shutdown of the flush water system, powerful room exhaust fans, and a building layout permitting exhausted droplets to re-enter the building at other locations [23].

The extent to which fomites play a role in the transmission of SARS through indirect contact also is unclear. Although there is no evidence to suggest that fomites played a significant role in the recent outbreak, the fact that SARS-CoV is able to survive up to 4 days at room temperature on several inanimate surfaces suggests that this mode of transmission is possible [24]. Evidence to support this includes a study in Hong Kong in which self-reported inconsistent hand hygiene practices were associated with an increased risk for SARS among health care workers who reported no contact with patients (odds ratio = 6.4 [1.6–36.2]; \( P = 0.004 \)) [25•]. In addition, in the Amoy Gardens outbreak, lack of household disinfection was associated with an increased risk in household members of patients with SARS [21•].

In addition to droplet and contact transmission, limited evidence suggests that airborne transmission may occur on occasion. The studies that suggested this possibility describe specific SARS clusters in which the pattern of transmission for a subset of individuals cannot be explained by droplet or contact transmission. For example, in a study assessing medical students exposed to a single patient, four students who were not within the 3-feet droplet risk zone [26] from the patient acquired SARS [19•]. In an investigation of a nosocomial outbreak in Toronto, one health care worker who had not worked in the index patient’s room acquired SARS [20•]. On a flight carrying a symptomatic person with SARS, 90% of the persons who became ill were seated more than 3 feet away from the index patient [27]. Although all of these examples are consistent with possible airborne transmission, alternate explanations implicating indirect contact transmission or unrecognized exposures also are possible. In addition, one can postulate that an enhanced droplet transmission mechanism exists in which droplets are capable of being transmitted beyond the traditional 3-feet radius from the index patient but are incapable of traditional airborne transmission.
Particularly worrisome during the outbreak were reported scenarios in which transmission occurred despite the use of droplet, contact, and airborne precautions. For example, a nurse who was wearing an N95 respirator, two sets of gowns and gloves, safety glasses, a face shield, hair cover, and shoe covers acquired SARS after providing bag-valve-mask ventilation to a patient with SARS [28]. In addition, at least two health care workers using N95 equivalent respirators, gown, gloves, and safety glasses, with or without a face shield, acquired SARS after assisting in the provision of noninvasive ventilation and a difficult intubation of a patient with SARS complicated by copious frothy secretions [29]. Common factors in these scenarios include being involved in a procedure that has the potential to generate aerosols (e.g., noninvasive ventilation, intubation) that is being performed on severely ill patients and requires close contact with the patient in the context of using N95 or N95 equivalent respirators that were not fit-tested. Potential explanations for the through-precautions transmission seen in these scenarios include the possibility of unrecognized breaches in precautions, contamination upon removal of precautions, or an airborne viral load high enough to overwhelm the non–fit-tested N95 or N95 equivalent respirators used. Whether N95 respirators require fit-testing in order to be effective in reducing airborne transmission has not been studied in the clinical setting. Although the United States has supported fit-testing for all N95 respirators since 1972, other countries such as Canada have only done so in response to SARS and specifically in response to the through-precautions transmission scenarios described earlier [29]. Further study is needed to definitely determine the role of fit-testing in preventing airborne transmission and to better understand the mechanisms responsible for through-precautions transmission.

### Basic reproduction number

Based on analyses of the outbreaks in Hong Kong and Singapore, the basic reproduction number for SARS, $R_0$, defined as the expected number of secondary infectious cases generated by an average infectious case in an entirely susceptible population, is estimated between 2.2 and 3.7 [30,31]. This is consistent with an infectious disease spread by contact or droplet transmission [15]. The relatively fast decrease in the effective reproduction number, $R_t$, to less than 1 noted after implementation of control measures, is suggestive of an infectious disease with relatively low efficiency in transmission that is readily controlled [31]. Data from recent seroprevalence studies support this showing that in typical situations relatively few people with exposure to patients with confirmed SARS-CoV infection actually became infected. For example, typical attack rates among health care workers in hospital settings who used no protection or inconsistent protection ranged from 0% to 8.5% [32–35]. Typical attack rates in household settings ranged from 4.6% to 8% [21,36]. Typical attack rates on flights were 0% to 0.5% [27,37], and no significant transmission was seen with casual contact in the community setting [38].

### Superspreading events

However, notable exceptions to this typical transmissibility are so-called superspreading events, in which transmission of SARS-CoV was shown to be highly efficient, with attack rates as high as 18% on one flight [27] and 60% [39] and...
73% [40•] in some hospital settings. For example, in Guangzhou, the index patient was shown to transmit SARS to 74 other individuals, with an associated large cluster of secondary infections giving rise to the outbreak in Guangzhou [41]. In Singapore, multiple superspreading events were described at the beginning of the outbreak, with one individual responsible for at least 40 other cases of SARS through direct contact [42]. In Canada, superspreading events also were described in the index hospital in Toronto, with one patient directly responsible for 19 other cases of SARS and with attack rates among exposed staff as high as 60% [39]. It has been proposed that the presence of a superspreading event was likely the dominant factor influencing which countries were significantly involved in the recent worldwide outbreak [40•].

There is a limited understanding of what causes superspreading events, but it is generally believed that a combination of host, environment, and virus interactions is involved. Host factors, such as age, underlying illness, and increased severity of SARS symptoms may be associated with increased viral shedding, permitting more efficient transmission. Shen et al. [40•] have shown that cases associated with superspreading in Beijing were more likely to be older patients with high case fatality rates. Increased opportunity for exposure through increased interaction with patients (such as that which typically occurs in hospitals settings) may further aid transmission. This is confirmed in the study by Shen et al. [40•], which showed that superspreading patients in Beijing were more likely to have higher numbers of close contacts than were patients unassociated with superspreading. Although association with aerosol-generating procedures was not seen in Beijing, it has been proposed as an alternate explanation that may further facilitate transmission in superspreading events. Inadequate infection control precautions also may be partly responsible, and after the implementation of control measures in Beijing, superspreading events were greatly reduced [40•]. Whether strain variations in SARS-CoV or coinfections with other organisms might play a role in these situations has not been fully assessed. Superspreading events are not unique to SARS but also have been described with other diseases such as Ebola, rubella, and measles [40•,42]. Additional investigation is needed to further understand the role of various determinants of superspreading events in SARS.

Identification of cases
In order to identify cases early in the course of a patient’s illness, implementation of surveillance programs is needed at the hospital and community level. Given the uncertainty as to whether SARS will return and the costs associated with implementing surveillance programs, surveillance efforts ideally would not be restricted to SARS but would be incorporated into general surveillance efforts for other potentially communicable infectious diseases, which are already in place in most institutions and community settings.

Surveillance for SARS is complicated because clinical features alone cannot distinguish SARS from other respiratory infections or from the many possible explanations for fever and pulmonary infiltrates in patients with multiple comorbidities. Surveillance is further complicated because adequately sensitive rapid diagnostic tests are unavailable early in the disease [16]. Thus, surveillance for SARS should rely on screening for patients who have compatible clinical features in the context of potential SARS-CoV exposure. Epidemiologic risks to consider include: exposure to settings where SARS activity is suspected or documented; a person with an epidemiologic link to a cluster of persons with unexplained respiratory illness, especially when such a cluster occurs within a single health care facility setting; a health care worker with direct patient-care responsibilities; or a laboratory worker in a laboratory that contains live SARS-CoV [43•].

Upon identification of possible cases of SARS on the basis of these clinical and epidemiologic factors, appropriate infection control precautions should be initiated and laboratory testing for SARS and alternative diagnoses that might explain the illness should be completed. Infection control precautions should be continued until SARS has been ruled out or alternative diagnoses have been identified that fully explain the patient’s symptoms.

Appropriate infection control precautions
Updated infection control practice recommendations for use with patients with possible or confirmed SARS are available [44••]. As evidence accumulates regarding the effectiveness of infection control measures used in the recent outbreak, revisions of these recommendations are being made. A summary of some of the most informative studies regarding effectiveness of specific infection control precautions is presented here and outlined in Table 2.

Seto et al. [45•] completed a case-control study involving 254 health care workers, 13 of whom acquired SARS, from five Hong Kong hospitals. They noted that the risk for acquiring SARS after direct care of a patient with SARS was significantly reduced with the use of N95 respirators or surgical masks and gowns, and hand-washing. Multivariate
analysis revealed masks (N95 respirators or surgical masks) to be the only significant protective measure. The authors contend the fact that surgical masks and N95 respirators were effective, with the finding that 30% of noninfected staff did not use masks of any type, supports that transmission is not typically airborne. Loeb et al. [22•] completed a retrospective cohort study among 43 nurses, eight of whom acquired SARS after working in one of two Toronto critical care units with SARS patients. They noted that the consistent use of N95 respirators was significantly more protective than was not wearing a mask. The consistent use of surgical masks also reduced the risk, but not significantly. N95 respirators appeared to reduce the risk more than did surgical masks, but not significantly. The use of gowns and gloves was not shown to significantly reduce the risk for SARS. Lau et al. [25•] completed a case-control study involving 72 health care workers with SARS and 144 matched controls from Hong Kong. They noted that transmission of SARS occurred despite almost all of the study respondents using N95 respirators or masks when providing direct care for patients with SARS, suggesting that masks were not sufficient to prevent transmission of SARS. The use of gloves, gowns, goggles, and caps was significantly associated with a reduced risk for acquiring SARS, but the high degree of collinearity in the use of these precautions made it difficult to ascertain which measure was most important. Other findings included an increased risk for SARS among health care workers who perceived there to be an inadequate supply of personal protection equipment and among those who received less than 2 hours of SARS infection control training.

Based on these studies and on the fact that the patterns of transmission of SARS suggest droplet and contact modes of transmission, one can suppose that isolating patients with SARS and implementing droplet precautions using surgical masks and contact precautions for all persons interacting with them are likely sufficient to prevent the transmission of SARS from these patients to others. However, despite the lack of definitive studies showing an involvement in transmission through fomites, routine environmental cleaning and disinfection also should be completed; 0% sodium hypochlorite, 75% ethanol, and 2% phenol have all been shown to inactivate SARS-CoV within 5 minutes [24]. In addition, because of potential for possible airborne transmission associated with aerosol-generating procedures and because airborne transmission cannot be ruled out altogether in some cases occurring in the recent outbreak, the use of N95 respirators and negative pressure rooms (when available) is likely prudent until further studies better define the role of possible airborne transmission. Whether N95 respirators require fit-testing needs further study, as described earlier. In addition to the protective measures described earlier, given the reported cases of through-precautions transmissions, additional measures to reduce the opportunity of transmission also should be enforced. These include minimizing the number of health care workers and visitors permitted in the patient’s room, minimizing the time spent by health care

| Protection used consistently | Seto et al. [45•] | Loeb et al. [22•] | Lau et al. [25•] |
|-----------------------------|-------------------|------------------|------------------|
| N95 respirator or surgical mask* | 0.02 (0.001–0.4) | 0.23 (0.07–0.78) | 0.50 (0.20–20)† |
| N95 respirator* | 0.03 (0.002–0.6) | 0.22 (0.05–0.93) | N/A |
| Surgical mask* | 0.06 (0.003–1.1) | 0.45 (0.07–2.7) | N/A |
| N95 respirator vs surgical mask‡ | N/A | 0.50 (0.06–4.2) | N/A |
| Gloves | 0.47 (0.1–1.6) | 0.45 (0.1–1.5) | 0.05 (0.001–0.34) |
| Gown | 0.07 (0.004–1.2) | 0.36 (0.1–1.2) | 0.11 (0.02–0.41) |
| Goggles | N/A | N/A | 0.16 (0.05–0.40) |
| Cap | N/A | N/A | < 0.0001 |
| Hand-washing | 0.19 (0.05–0.78) | 0.14 (0.03–0.43) | 0.001 |
| Any mask/ respirator, gloves, gown, and hand-washing | 0.09 (0.005–1.6) | N/A | N/A |

*Compared the risk associated with the consistent use of the mask/respirator indicated with the risk of not wearing any mask/respirator. The risk associated with the consistent use of paper masks also was studied by Seto et al. [45•] and was not found to be significantly reduced compared with the risk of not wearing any mask/respirator (estimated RR = 0.5 [0.1–2.4]; P = 0.51).
‡All but one of the cases and all of the controls used N95 respirators or surgical masks when providing direct care to patients with SARS.
†Compared the risk associated with consistent use of N95 respirators to the risk associated with the consistent use of surgical masks.
N/A—not assessed; RR—risk ratio; SARS—severe acute respiratory syndrome.
workers and visitors in the room and specifically minimizing the time spent in close contact with the patient, keeping to the side of the patient (out of direct droplet range), only having the most experienced personnel perform procedures on the patient, providing adequate medication to suppress cough and vomiting with the goal to minimize droplets produced from the patient, and avoiding transporting patients with SARS when possible. Furthermore, ensuring an adequate supply of protective equipment and providing intense training with regard to its appropriate use is important, as documented by Lau et al. [25•].

Contact tracing and quarantine
An additional component to controlling the spread of SARS is tracing all close contacts of symptomatic SARS patients, isolating those who are symptomatic, and quarantining those who are asymptomatic for the 10-day incubation period after their exposure. Such measures were instituted in many of the countries involved in the recent outbreak, including China, Taiwan, Hong Kong, Singapore, and Canada. However, given the limited understanding of transmission that existed at the beginning of the outbreak, in some areas of the world close and remote contacts of symptomatic and asymptomatic patients with SARS were quarantined, as opposed to limiting quarantine to only close contacts of symptomatic patients with SARS, who are now appreciated as being the only contacts that have significant risk for acquiring the disease. In Taiwan, by the end of the epidemic, 131,132 people had been placed in quarantine, with failure to comply punishable by fines of $1765 to $8824 and incarceration of up to 2 years [46]. In Beijing, approximately 30,000 residents were quarantined in their homes or quarantine sites [47•]. These numbers would be lower had quarantine been limited to only close contacts of symptomatic cases. In Beijing, by limiting quarantine in this way, the number of persons quarantined would have been reduced by approximately 66% [47•]. Typically, quarantined persons were asked to stay where they were quarantined, wear surgical masks when near others, take their temperature two to three times a day, and seek medical attention promptly if they developed fever (≥ 38° C) or other symptoms compatible with SARS. Phone calls or visits from public health officials occurred regularly to check on the status of quarantined persons.

The use of quarantine as a strategy in the control of infectious diseases is controversial given the ethical and legal issues regarding its negative associated impact on civil liberties. In addition, the effectiveness of quarantine has been questioned because of the difficulty of tracing all at-risk contacts and ensuring observance of the rules of quarantine in all quarantined persons. As a strategy in the control of SARS specifically, one could argue that the effectiveness of quarantine should be further questioned given the lack of evidence of transmission during the incubation period before the onset of symptoms. However, the role of quarantine is not only to prevent transmission during the incubation period, should that be associated with a particular infection, but it also can facilitate early detection and management of symptomatic cases by enforcing compliance with reporting the onset of symptoms. In Beijing, the effectiveness of quarantine is supported by the fact that no secondary transmission to relatives or other contacts was detected from any person who had SARS while quarantined [47•]. Analysis has shown that restricting quarantine in Beijing to only those who had close contact with an actively ill patient with SARS would not have compromised its effectiveness [47•]. The decision to implement quarantine needs to be made in conjunction with local public health authorities.

Outbreak response
In the event that the recognition of SARS is delayed and an outbreak ensues that is not readily controllable using the aforementioned strategies alone, other additional control strategies should be considered in order to expedite control of the disease. Central to this is the designation and coordination of an interdisciplinary outbreak team with excellent communication capabilities. Decisions need to be made regarding implementation of more drastic control measures, such as hospital-wide screening and visitor restrictions, closing hospitals, removing exposed or symptomatic groups to designated hospitals, or managing exposed or symptomatic cohorts in place. All of these strategies were used in different circumstances in Singapore with positive effect [48]. Additional control measures to consider include airport screening and travel restrictions, although the usefulness of these strategies in terms of their contribution to the control of infectious diseases has not been systematically studied.

Paradigm shift
SARS has opened the world’s eyes to the existence of emerging infectious diseases that have the capability of causing worldwide outbreaks within a relatively short span of time. Given the threat of the return of SARS and the ongoing threat of other emerging infectious diseases, it is prudent to consider a general paradigm shift regarding the approach to potentially infectious persons. Implicit in this is the need to educate health care workers in addition to the general public. Health care “new normal” directives implemented in Ontario, Canada that suggest addressing all patients presenting with respiratory illness as potentially infectious until proven otherwise and that reinforce that ill health care workers should stay at home until they are well are an example of the implementation of this paradigm shift [49]. In addition, “healthy habits” posters directed at the general public and created by the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia are an excellent example of the kind of basic health hygiene education that should be reinforced [50]. In so doing, the goal is to change the way that infectious diseases are managed in health care and by the public, in
order to increase the emphasis on the prevention of transmission of such diseases, with the ultimate goal of possibly averting a worldwide outbreak of the next newly emerged infectious disease.

Conclusions
SARS is a newly recognized infectious disease that caused a worldwide outbreak affecting 8098 people in 26 countries from November 2002 through July 2003. Studies have shown that transmission occurs primarily through droplet and contact, but airborne transmission cannot be ruled out. Superspreading events, although the exception to the rule, play a significant role in propagating transmission, especially in hospital settings. Control depends on the identification of cases and early implementation of isolation and appropriate personal protective measures, contact tracing, and possibly the implementation of quarantine for asymptomatic contacts. These were the measures that permitted the control of the worldwide 2002 to 2003 outbreak and will hopefully prevent another outbreak from becoming as widespread, should SARS re-emerge.

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