

Nosocomial Transmission of SARS

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Current Infectious Disease Reports 2003, 5:473–476

Current Science Inc. ISSN 1523-3847

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Severe acute respiratory syndrome is a newly emerged infectious disease with moderately high transmissibility. Nosocomial outbreaks were responsible for the propagation of the epidemic worldwide. Health care workers (HCW) are at particular high risk because of their close contact with patients, involvement in medical procedures, and handling of excreta/fomites. Good hospital organization and appropriate infection control strategies are essential to prevent/interrupt disease transmission from patients to HCWs (and vice versa) and among inpatients and HCWs themselves. Education and training should target broadly to all HCWs.

Introduction

During a 3-month period, a novel coronavirus caused more than 8000 probable cases of severe acute respiratory syndrome (SARS), resulting in 774 deaths [1]. When the epidemic began in early March of 2003, a global alert already had been issued by the World Health Organization (WHO) to warn against its propensity to spread among hospital health care workers (HCWs). This was because in Vietnam, where the syndrome was first recognized, more than 20 HCWs were infected by a single index case. Shortly afterwards, another nosocomial outbreak occurred in a regional hospital in Hong Kong in which 69 HCWs were infected [1]. It appeared that nosocomial transmission amongst HCWs and hospitalized patients is a particularly prominent feature of SARS. According to the WHO, it constituted the largest single group (19% to 57%) of probable SARS cases worldwide. This article reviews the possible mode of transmission of the SARS-associated coronavirus, its contributory factors, and the worldwide experiences in recognizing and managing such nosocomial outbreaks.

The Virus and Its Mode of Transmission

The SARS-associated coronavirus is a novel RNA virus that is genetically distinct from all known coronaviruses [2,3–5]. Relatively little is known about its physical and

virologic properties. Although the details of its mode of transmission must be elucidated, it is reasonable to speculate that inhalation of infectious droplets or aerosol and physical contact with a patient's body fluids/excreta (through hand or fomites) and the fecal-oral route of entry are likely to be important based on available epidemiologic data [1,6•,7–9,10•,11]. In the first week of illness, the amount of virus detected in respiratory secretion is relatively low. Findings from sequential quantitative reverse transcriptase-polymerase-chain reaction assays of nasopharyngeal aspirates suggested that the viral load might peak only at approximately day 10, after the onset of symptoms, and then decrease to lower levels [11]. It was thought that the patient is most infectious during this period. Although evidence to support airborne transmission of the virus is lacking, respiratory protection (eg, P100 or N95 mask) is recommended for HCWs, especially when involved in direct patient care [1,7]. Protective measures are further emphasized during high-risk procedures such as bronchoscopy or intubation [12,13]. It is now clear that the SARS coronavirus can survive in feces and urine for at least 1 to 2 days at room temperature and may persist up to 4 days in diarrhoeic stool because of its lower acidity [1]. Thus, body fluid or excreta-contaminated surfaces (eg, toilet bowls, bed sheets, and ward paper file covers) may serve as efficient means of viral transmission in the institution/hospital settings. However, the virus loses infectivity shortly after exposure to a range of commonly used disinfectants and fixatives (eg, < 5 minutes with 75% ethanol) [1]. Thus, proper hand washing practices and meticulous environmental cleansing are essential in preventing the transmission of disease.

Nosocomial Transmission of SARS

Nosocomial outbreaks of SARS were reported in Vietnam, Singapore, Hong Kong, Taiwan, Toronto, and mainland China [1,6•,14–19]. Based on a stochastic metapopulation compartmental model, it was estimated that SARS is only a moderately transmissible infection; in average, 2.7 to 3 secondary cases were generated from a primary case [9]. However, contact tracing in the Hong Kong epidemic showed that more than 22% of cases were related to hospital-related exposure [9]. Nosocomial amplification and super-spreader events are most likely responsible for the propagation of the epidemic [3,9,20].

Table 1 summarizes data from several reports of SARS nosocomial outbreaks. In Hanoi, Vietnam, where the first

Table 1. Summary of reports of SARS nosocomial outbreaks

	Vietnam [1]	Hong Kong [6•]	Canada [14]	Singapore [15]	Taiwan [17]	China [19]
Number of HCWs infected	20	85*	73	25	45	90
Number of inpatients and visitors infected [†]	—	53	38	20	92	6
HCW/non-HCW ratio	—	1.6	1.9	1.3	0.5	15
Index case	1	1	1	1	1	1
Contributing factor(s)	—	Use of nebulizer?	—	—	—	—

*Including 16 medical students.
[†]Including secondary and tertiary cases.
 HCW—health care worker.

nosocomial SARS outbreak was reported, 20 HCWs were infected by an index case [1]. Shortly after, in a regional hospital in Hong Kong, one patient transmitted the infection to 112 individuals as secondary cases and 26 individuals as tertiary cases, including 69 HCWs (20 doctors, 34 nurses, and 15 allied health workers) and 16 medical students who worked in the index ward, plus 53 patients who were in the same medical ward or had visited relatives there [6•]. The index patient was administered salbutamol nebulizer because of its mucociliary clearance effect; whether this contributed to the spread of disease is being evaluated. In Toronto, of the 144 described cases, 111 (77%) were nosocomially transmitted. Among these patients, 73 (51%) were HCWs, including nurses, doctors, housekeepers, paramedics, and respiratory therapists [14]. These patients were linked to a hospitalized patient whose mother died from the disease at her home. In Taiwan, the index case of a nosocomial outbreak was a hospital laundry worker with diabetes mellitus and peripheral vascular disease [17]. The patient continued working and interacted frequently with patients, staff, and visitors for 6 days despite her early symptoms. The initial cluster of SARS cases included two nurses, one doctor, one administrator, a radiology technician, a nursing student, and another laundry worker. Subsequent epidemiologic investigations showed that 137 probable cases were associated with this nosocomial outbreak involving 45 HCWs (33%). In Singapore, unsuspected SARS cases were responsible for several nosocomial outbreaks [15]. An index case initially admitted for chronic renal disease and diabetes was readmitted for gastrointestinal bleeding, fever, and bacteremia. Chest radiograph was normal. When pneumonia developed and SARS was diagnosed, the patient had already caused 62 probable or suspected cases (25 HCWs, 20 inpatients, and 17 family and social contacts). Of these patients, 37 probable SARS cases (HCWs and visitors) were classified as secondary cases because of direct contact with the index case in hospital. As noted, nosocomial transmission is highly efficient, and HCWs were sometimes the predominant victims. The median infected HCW/non-HCW ratio estimated from these studies was approximately 1.6; the reasons for this are not entirely clear. SARS is being recognized as a new occupational disease [21].

Risk Factors for Disease Transmission

Nosocomial transmission of SARS can be subdivided into patient-to-HCW, HCW-to-patient, patient-to-patient (or “cross”), and HCW-to-HCW. Although factors that determine the spread of infection are being investigated, measures to interrupt/prevent disease transmission should be implemented immediately in these four categories. For patient-to-HCW transmission, close contact (eg, physical examination and feeding), direct physical contact with a SARS patient’s body fluid and excreta (eg, health care assistants and housekeepers), and engagement in high-risk activities such as airway suctioning (eg, physiotherapists) and endotracheal intubation (eg, intensivists) that generate enormous infectious aerosols are recognized risk factors [14–16,21]. In a recent report, the crude attack rates of SARS were in fact highest among health care assistants (79/1000), followed by nurses (51/1000), and physicians (38/1000) [22•]. Most of these cases had direct contact with SARS patients or were involved in their personal care. Fomite transmission (eg, excreta handling) may be the other explanation for a few cases. These observations were confounded by the problem of strict adherence to personal protective equipment. However, they illustrated the fact that preventive/protective measures and education must target much broader groups of HCWs than simply doctors and nurses [17,21].

It was speculated that the use of nebulizers, high-flow Venturi masks, and noninvasive positive pressure ventilation might facilitate the transmission of viral particles by generation of infectious aerosols [6•,7,13]. Before these issues are clarified, it is prudent to limit the use of this equipment or use in a strictly controlled manner (eg, in a negative-pressure room) for patients suffering from an unknown respiratory illness or SARS.

Because the SARS coronavirus transmits mainly through droplets and aerosols [10•], it would be unsurprising if distance is a key factor in determining the risk for infection among inpatients. According to several reports [15–17], patients in the vicinity (eg, neighboring beds) of patients with SARS were at high risk for acquiring the infection. In one institute, it was determined that risk for infection was several times higher in the same/adjacent cubicle

of an index case, compared to more distant cubicles in the same ward (Lee and Sung, Unpublished data). Thus, the space between patients is a major issue to address in medical wards that admit suspicious SARS cases. In general, distance between patient beds should not be less than 3 feet in case of a droplet infection. The avoidance of overcrowding in institutes is essential for all infection control, not exclusively for SARS.

Cross-infections between inpatients could be the result of fomite transmission and transmission through hands of HCWs. Thus, cohort nursing, dedicated medical equipment, and strict hand washing practices or glove changes after patient contact are important ways to interrupt disease transmission and should be strictly adhered to. The use of personal protective equipment (which also may protect patients), surveillance for illness among HCWs (if ill, promptly suspend from work and medically evaluate), limiting nonessential interactions among HCWs, and proper degowning procedures/areas are some important strategies to consider during a major outbreak situation to prevent HCW-to-patient and HCW-to-HCW SARS transmission [12].

Superspreading Events

The term superspreading is used to describe situations in which a single index case results in a large number of secondary cases (eg, more than 10 contacts), including HCWs, family and social contacts, or the patient's visitors at the hospital [15,23]. Similar phenomenon had been described in other infectious diseases such as rubella, laryngeal tuberculosis, and Ebola virus [23]. It is uncertain whether viral factors (eg, viral load, extent of viral shedding), environmental factors (eg, use of nebulizers, leaking sewages), host factors (eg, immunocompromised patients, renal failure), or the combinations of these are important to determine the occurrence of such superspreading events. In a Singapore epidemic, of the first 201 probable cases reported, 103 patients were infected by just five source cases [15]. Because most superspreading events occurred in the hospital setting, it served as a source of disease amplification and propagation of the epidemic.

Unsuspected SARS Cases

Patients with unsuspected SARS are the most challenging issue in hospital infection control. Unrecognized cases were implicated in several outbreaks in Singapore, Taiwan, and Toronto [15–17]. Absence of fever, presence of comorbidities, and other atypical manifestations of SARS are a few of the reasons these cases were not promptly recognized and isolated. Although fever $> 38^{\circ}\text{C}$ was included in the case definition of SARS (which was a retrospective observation), the patient's temperature during diagnosis may be below this number or normal. According to a study by Booth *et al.* [14] from Toronto, only 85% of their patients had fever

$> 38^{\circ}\text{C}$ documented during admission. A similar observation was made by a group of Hong Kong investigators: during evaluation at a screening clinic, only 81% of patients had high fever, although all confirmed cases eventually fulfill the case definition of SARS [24]. Fever may initially improve, but recurred at a mean of $8.9 (\pm 3.1)$ standard deviation days [11]. In addition, some patients may never mount a fever response to coronavirus infection, as with other already known causes of pneumonia. Elderly patients occasionally may not have fever [23,25,26]. According to experience in our center, approximately 3% of elderly patients (aged > 65 years) had no documented fever even in the presence of progressive pneumonia. In addition to patients with senility, patients with comorbidities and/or patients who are immunocompromised may again present with an afebrile respiratory illness and pneumonia (eg, chronic renal failure, long-term steroid therapy) [25]. In addition, plain chest radiographs may be difficult to interpret in patients with pre-existing chronic pulmonary diseases (eg, pulmonary fibrosis) and in the presence of pulmonary edema (eg, congestive heart failure). Also, radiologic features of SARS may mimic some of these conditions [27]. There is no reason that patients with SARS could not present with active medical or even surgical conditions (eg, acute pulmonary edema, exacerbation of chronic obstructive airway disease, influenza, bacteremia, acute abdomen, and hip fracture) [15–17,23,26]. Excluding respiratory symptoms, diarrhoea could be the predominant manifestation of SARS. In a report from Hong Kong (which included more than 1400 cases) [20], up to 27% of patients had the symptom initially. Watery diarrhoea may begin to develop or recur in up to 73% of cases after the first week of illness (mean 7.5 ± 2.3 days) [11]. To further complicate the issue, diarrhea could occur in the absence of pneumonia on the radiograph [28]. A high index of suspicion is necessary in diagnosing such cases. When the more typical features of SARS emerge as the disease progresses (eg, in the second week of illness), the viral load is already at its peak, and infection might have spread to other individuals if not isolated properly. A clear history of close contact with known SARS patients should be very helpful under these circumstances. Nevertheless, it cannot replace a good infection triage system with initial isolation facilities [18,29]. Recent data from a nosocomial outbreak in Hong Kong showed that infections began among HCWs exposed to patients with unsuspected SARS located in low-risk general medical wards instead of designated high-risk areas, where alertness and infection control practices are of the highest stringency [22].

Hospital Infection Control

Expert recommendations for hospital infection control of SARS are available from Centers for Disease Control and Prevention and WHO web pages [1,7]. A case-control study published early in the epidemic demonstrated that use of surgical face masks and disposal gloves and gowns was

significantly associated with noninfection among HCWs [10•]. For HCWs involved in high-risk activities (eg, bronchoscopy, intubation), N95 or N100 respirator, goggles, and visors, in addition to gloves and gowns, are advisable. However, the organization and strict implementation of various infection control measures is probably just as important. Interrupting disease transmission should target the four categories previously mentioned and prevent secondary cases generated from patients with unsuspected SARS. Developing a fever case triage system, limiting the patient's visitors, designating "police nurses," educating to ensure adherence to personal protective equipment, and even relatively minor issues such as keeping inanimate objects inside wards, should be designed and adapted to each hospital setting [12,29•].

Conclusions

Nosocomial transmission of SARS is responsible for the amplification and propagation of the epidemic. The combinations of viral, host, and environmental factors are important to the occurrence and extent of these nosocomial outbreaks. Meticulous infection control measures and good organization are essential in limiting the spread of SARS in the hospital setting.

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