

Lack of SARS Transmission and U.S. SARS Case-Patient

Angela J. Peck,* E. Claire Newbern,*† Daniel R. Feikin,* Elmira T. Isakbaeva,* Benjamin J. Park,* Jason T. Fehr,‡ Ashley C. LaMonte,* Thong P. Le,§ Terry L. Burger,¶ Luther V. Rhodes III,¶# Andre Weltman,** Dean Erdman,* Thomas G. Ksiazek,* Jairam R. Lingappa,* and the SARS Pennsylvania Case Investigation Team¹

In early April 2003, severe acute respiratory syndrome (SARS) was diagnosed in a Pennsylvania resident after his exposure to persons with SARS in Toronto, Canada. To identify contacts of the case-patient and evaluate the risk for SARS transmission, a detailed epidemiologic investigation was performed. On the basis of this investigation, 26 persons (17 healthcare workers, 4 household contacts, and 5 others) were identified as having had close contact with this case-patient before infection-control practices were implemented. Laboratory evaluation of clinical specimens showed no evidence of transmission of SARS-associated coronavirus (SARS-CoV) infection to any close contact of this patient. This investigation documents that, under certain circumstances, SARS-CoV is not readily transmitted to close contacts, despite ample unprotected exposures. Improving the understanding of risk factors for transmission will help focus public health control measures.

On March 12, 2003, the World Health Organization (WHO) issued a global alert for severe acute respiratory syndrome (SARS) after outbreaks had been recognized in Vietnam, Hong Kong, and the People's Republic of China (1). The outbreak subsequently spread to Singapore, Taiwan, Canada, and elsewhere (2–8). In the United States, laboratory-confirmed SARS-associated coronavirus (SARS-CoV) infection was diagnosed in eight persons (9). Of these eight patients, only one may have been infected in the United States.

“Superspreading events,” in which a single person spread the infection to many other people, were an important component of SARS transmission globally. In

Singapore and Taiwan, for instance, single case-patients may have transmitted the virus to >60 persons (7,8). However, for most SARS case-patients, transmission was limited; for example, after the institution of intensive infection-control measures in Singapore, 81% of probable SARS patients had no evidence of transmission to other persons (7). By using mathematical models that included epidemiologic data (excluding superspreading events) from Singapore and Hong Kong, two to three secondary infections were estimated to result from single infectious case-patients before infection control measures were instituted (10,11). It is important to systematically assess risk associated with SARS transmission in order to implement effective control measures.

On April 14, 2003, a 52-year-old Pennsylvania resident was recognized as a probable SARS case-patient after his exposure to persons with SARS during a religious event in Toronto in late March (12). Some attendees of this event were infected with SARS-CoV through a chain of transmission linked to the first imported case of SARS in Canada, a woman who had become infected in Hong Kong (13–15). Overall, 20 probable and 11 suspected cases of SARS were identified in this religious community (14); the Pennsylvania patient was the only U.S. case. Before the Pennsylvania patient was recognized as a probable SARS case-patient and infection control practices were instituted, the patient interacted with numerous healthcare workers

*Centers for Disease Control and Prevention, Atlanta, Georgia, USA; †Philadelphia Department of Public Health, Philadelphia, Pennsylvania, USA; ‡Penn State College of Medicine, Hershey, Pennsylvania, USA; §Infectious Diseases Service, Bethlehem, Pennsylvania, USA; ¶Lehigh Valley Hospital and Health Network, Allentown and Bethlehem, Pennsylvania, USA; #Allentown Infectious Diseases Services, Allentown, Pennsylvania, USA; and **Pennsylvania Department of Health, Harrisburg, Pennsylvania, USA

¹Members of the Pennsylvania SARS Investigation Team: Marc-Alain Widdowson, Nino Khetsuriani, L. Clifford McDonald, Stephan S. Monroe, Suxiang Tong, James A. Comer, Daniel Jernigan, Matthew J. Kuehnert, Joseph S. Bresee, Sara A. Lowther, and Larry J. Anderson (CDC); Mary Theresa Temarantz, John P. Bart, William S. Miller, Mary Jo Lampart, and Carol Yozviak (Pennsylvania Department of Health); Shana Stites, (Bethlehem Bureau of Health); Susan Oliver, Debra Wilson, Carol Guanowsky, and Beverly Wasko (Lehigh Valley Hospital); Corwin A. Roberston (CDC) and New Jersey Department of Health and Senior Services); and Diane Krolkowski, Jeff Bomboy, and Reynaldo C. Guerra.

and other persons. We summarize the epidemiologic and laboratory investigations performed to identify persons exposed to the patient and to determine whether any were infected.

Methods

Epidemiologic Investigation

Potential close contacts were identified through interviews with the case-patient, his family members, healthcare workers, and other persons. Additional clinical and contact information was obtained through review of medical records. "Close contact" exposures included any amount of time spent within 3 feet of the patient or 30 minutes or longer within 3 to 10 feet. Since evidence suggests that SARS-CoV is primarily transmitted by means of large respiratory droplets, usually spread within a 3-foot radius, we focused on contact within this range (16). Thirty minutes within the patient's immediate care area (3–10 feet) was chosen arbitrarily to divide shorter and longer exposures.

Contacts included persons exposed to the patient before and after his diagnosis as a probable SARS patient. Contacts were grouped according to sites of principal exposure: the term "healthcare workers" refers to employees or contractors of a healthcare facility, "healthcare-related contacts" includes non-healthcare worker contacts exposed in a healthcare setting, "household contacts" includes immediate family members, whether they resided in the same household or not, and "community contacts" includes persons exposed in other settings. Public health personnel, using standard data collection instruments, interviewed contacts regarding their type and duration of contact with the patient, use of personal protective equipment, and clinical symptoms after contact. Direct, unprotected contact with the patient's skin (i.e., without gloves) was defined as skin-to-skin contact, and unprotected contact with inanimate objects likely to have been touched by the patient, such as bedrails and clothing, was defined as skin-to-object contact.

Contacts were defined as prediagnosis or postdiagnosis contacts. Prediagnosis contacts were those exposed to the case-patient after his onset of symptoms (April 3) but before the patient's diagnosis of probable SARS (April 14). Postdiagnosis contacts were those exposed only after the diagnosis was made and infection control precautions were in effect. A convenience sample of postdiagnosis contacts was selected because strict infection control procedures had already been instituted, with all contacts wearing personal protective equipment; thus, unprotected exposures were not anticipated. Of the 32 persons with postdiagnosis exposure exclusively, 15 healthcare workers were selected for epidemiologic and laboratory evaluation.

Biologic Specimen Collection

Serum, whole blood (collected into a tube containing EDTA), oropharyngeal swab (swab of posterior pharynx), stool, and urine samples were requested from the case-patient twice weekly until day 21 after symptom onset and weekly for 2 additional weeks. In addition, a single nasopharyngeal swab specimen, nasal aspirate, and sputum sample were collected from the case-patient while he was hospitalized. The first set of specimens requested from his prediagnosis contacts included serum, whole blood, nasopharyngeal and oropharyngeal swab specimens, stool, and urine. Thereafter, specimens (serum, whole blood, oropharyngeal swab, and stool) were requested from prediagnosis contacts weekly until at least 22 days after the most recent exposure to the case-patient. Healthcare workers with postdiagnosis exposure submitted a single set of convalescent-phase specimens (>21 days after the last exposure), including serum, whole blood, and an oropharyngeal swab. Nasopharyngeal and oropharyngeal swab specimens were collected by using Dacron swabs with nonwooden handles. Swabs were immediately placed into viral transport medium and placed on ice. All specimens were stored at 4°C and shipped within 72 hours of collection to the Centers for Disease Control and Prevention (CDC).

Two postdiagnosis healthcare workers, in whom fever developed after they were exposed to the case-patient, provided weekly specimens rather than a single set. One prediagnosis healthcare-related contact participated until 22 days after exposure but did not provide serum or whole blood specimens, and four prediagnosis contacts (2 healthcare workers and 2 healthcare-related contacts) declined further participation after specimen collection at 8, 11, 11, and 21 days after exposure, respectively.

Environmental Specimen Collection

Sterile Dacron swabs with nonwooden handles were moistened with sterile saline or viral transport medium and rolled over environmental surfaces, including toilet and sink surfaces and other commonly touched items (e.g., door handles, telephones, remote controls, and toiletries) and placed in viral transport medium. Twenty environmental swab samples were collected from the patient's hospital room during his hospitalization (day 17 after illness onset), and 12 were collected from his home bedroom and private bathroom 3 days after hospital discharge (day 21 after illness onset). These were stored and shipped to CDC at 4°C.

Laboratory Testing

To test for evidence of infection with SARS-CoV, total anti-SARS-CoV serum antibody was measured by enzyme-linked immunosorbent assay (ELISA) and indirect fluorescent antibody test (17). Reverse transcription-polymerase chain reaction (RT-PCR) was

performed on nasopharyngeal and oropharyngeal swabs and stool and urine specimens; results were confirmed in separate CDC laboratories, with both negative and positive controls (17,18). Quantitative RT-PCR on stool specimens was conducted by using the TaqMan assay and standard curves generated from synthetic RNA transcripts (17). Viral culture in Vero E6 cells was performed on all RT-PCR-positive specimens (17).

Human Participants

This investigation was conducted as part of CDC's public health response to the SARS outbreak. Informed consent was obtained from the case-patient and contacts before epidemiologic information was obtained and biologic specimens were collected.

Statistical Analysis

Due to the non-Gaussian distribution of the data, the Wilcoxon rank-sum test was used to compare median durations of contact between different groups of persons. Prevalences of different types of exposures between the groups were compared by using Fisher exact test.

Results

Clinical History and Laboratory Findings for the Case-Patient

After traveling by automobile to an event held in Toronto on March 29 and 30, the previously healthy patient had onset of myalgias, subjective fever, chills, and diaphoresis on April 3 (Figure 1). Diarrhea developed on April 5, and the patient sought medical care at the emergency department of hospital A on April 6. The patient had a temperature of 38.2°C (100.7°F) and was discharged with a diagnosis of acute viral syndrome; no diagnostic testing was performed. During this emergency department visit, the patient did not report recent travel to Toronto to health-care providers. By April 10, despite taking oral amoxicillin for 3 days (initiated after telephone consultation with his primary care physician), a dry cough developed, which prompted him to visit his primary care physician. His physician referred him to an outpatient laboratory for phlebotomy and to hospital B for chest radiography; findings on the radiograph were normal, and the patient was sent home.

On April 14, the patient went to the emergency department of hospital B with dehydration, worsening cough, and severe shortness of breath. Within 2.5 hours of arrival, a diagnosis of SARS was suspected on the basis of a full travel history and new radiographic evidence of pneumonia. The patient was admitted to an airborne-infection (negative-pressure) isolation room, and the hospital instituted contact and airborne precautions for all healthcare workers

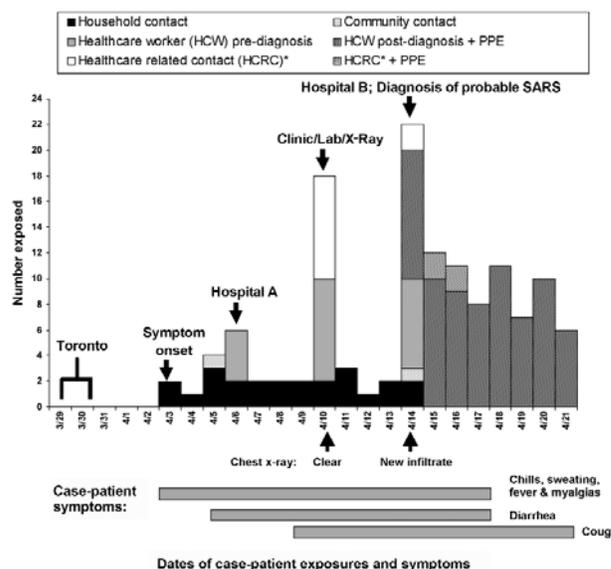


Figure 1. Timeline: severe acute respiratory syndrome (SARS) case-patient symptoms and total daily number of contacts from date of symptom onset to date of hospital discharge. Contacts indicated regardless of their subsequent participation in this investigation. Close contact was defined as any contact within 3 feet or contact within 3 to 10 feet for an extended duration (two persons). Repeated contacts by the same person over successive days are shown as independent events. *Healthcare-related contact refers to non-healthcare worker (HCW) contacts in a healthcare setting (persons in waiting rooms of physician office and referral laboratory, curtained area in the emergency department, and two persons who reportedly used personal protective equipment [PPE] and visited the case-patient in his hospital room on 4/15 and 4/16).

in contact with the patient, restricted visitation to this patient, and immediately notified public health authorities. Serum samples collected on April 14 (day 11 of illness) demonstrated antibodies to SARS-CoV. Admission vital signs included a temperature of 37.7°C (99.9°F) and oxygen saturations of 90%–91% on room air. The patient was given supportive care (including 2 days of supplemental oxygen), inhaled fluticasone propionate/salmeterol twice daily, and antimicrobial drugs (levofloxacin for pneumonia and metronidazole for diarrhea associated with laboratory-confirmed *Clostridium difficile* infection). His highest documented temperature while hospitalized was 38.1°C (100.6°F) on April 15. After the patient was hospitalized for 4 days, his fever and systemic symptoms resolved, and he was discharged on April 21 (hospital day 7) with a persistent but improving cough. He did not require aerosolized nebulizer treatments, intubation, or admission to an intensive care unit during his hospitalization.

The case-patient's serum specimens from days 11 to 32 after illness onset demonstrated anti-SARS-CoV antibodies (Figure 2). Additional analysis showed an increase in antibody titer over time (19). All respiratory specimens and the only urine sample tested negative by RT-PCR for

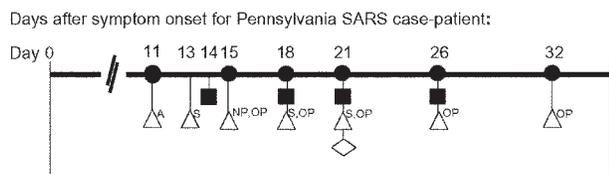


Figure 2. Clinical specimens collected and laboratory results for Pennsylvania severe acute respiratory syndrome (SARS) case-patient, April 2003. Symbols of specimens and method of testing: serum anti-SARS-CoV antibody, ○; stool RT-PCR; ■; urine RT-PCR, ◇; and respiratory RT-PCR, △; A, nasal aspirate; S, sputum; NP, nasopharyngeal swab; OP, oropharyngeal swab. Black shading indicates laboratory-positive specimen. Viral cultures of all stools and respiratory specimens were also performed and were negative.

SARS-CoV. However, serial stool specimens collected on days 14, 18, 21, and 26 after the onset of illness were positive by RT-PCR. Quantitative PCR showed the copy number in the first collected stool to be 16- to 40-fold higher than that in all subsequent stools (19). Viral cultures of all stools and respiratory specimens were negative for SARS-CoV, and all environmental specimens were negative by RT-PCR for SARS-CoV.

Epidemiologic and Laboratory Results for Contacts

The principal potential exposure sites that were investigated included sites for healthcare worker and healthcare-related contact exposures (emergency department of hospital A; primary care physician's office; referral phlebotomy laboratory; and emergency department, radiology suite, and inpatient facility of hospital B), the patient's home, and community settings in which the patient reported having had close contacts.

Prediagnosis Contacts

Thirty-four potential prediagnosis contacts were identified, and questionnaires were collected from 26 (76%) of them. The eight remaining potential prediagnosis contacts, who did not complete questionnaires, included seven healthcare-related contacts (six who were present in a laboratory waiting room at the same time as the case-patient and one radiology staff member) and one community contact (a retail salesperson). Of these eight persons, two could not be contacted, five did not complete more detailed interviews but did not recall specific interaction with the patient or report any subsequent illness, and one reported brief contact with the patient with no subsequent symptoms and declined to answer further questions.

The 26 prediagnosis contacts who completed questionnaires included 4 household contacts (15%), 17 healthcare workers (65%), and 5 others (19%), including 4 healthcare-related contacts (4 persons in a waiting room or curtained area in the emergency department) and 1 communi-

ty contact (a bank teller) (Table). The median age of prediagnosis contacts was 41.3 years (range 15.7–90.1); the only 2 contacts over age 65 were healthcare-related contacts.

Of these 26 persons, nearly all (92%) had contact with the patient during the 3 days when he sought medical care (Figures 1, 3). All household contacts and healthcare workers with prediagnosis contact had close unprotected exposures (within 3 feet), compared with 40% of the other contacts; this finding was significantly different only for healthcare workers ($p = 0.006$; $p = 0.17$ for household contacts) (Table). However, household contacts had the longest median duration of exposure per person, 60 times longer than the median duration per person among prediagnosis healthcare workers (459 vs. 7.5 minutes, $p = 0.04$) and 15 times longer than among other contacts (459 vs. 30 minutes, $p = 0.008$). Household contacts and healthcare workers had similar degrees of skin-to-skin contact (50% vs. 53%, $p = 1.00$) and skin-to-object contact (100% vs. 71%, $p = 0.53$). The patient and household contacts attempted to limit interactions throughout his illness and began wearing surgical masks when they interacted after April 9.

All contacts were monitored for fever and respiratory symptoms during the 10 days after exposure to the case-patient. Eleven (42%) of the 26 prediagnosis contacts reported fever and/or lower respiratory tract symptoms (defined as cough, wheezing, or shortness of breath/difficulty breathing) during the surveillance period. Of the 26, 1 (4%) reported fever alone, 9 (35%) reported respiratory symptoms alone, and 1 reported both. The person with both fever and respiratory tract symptoms was a household contact who reported sore throat and cough before contact; fever developed after contact, thus meeting the CDC clinical case definition for a suspected SARS case (9,20). Seven (41%) of 17 healthcare workers with prediagnosis contact were furloughed from work for 3 to 10 days due to unprotected close contact or the presence of respiratory symptoms. Four (57%) of these persons had lower respiratory tract symptoms, and three (43%) were asymptomatic or had only mild symptoms (sore throat, headache, or rhinorrhea).

Prediagnosis contacts provided a total of 86 serum and whole blood samples, 90 oropharyngeal swabs, 25 nasopharyngeal swabs, 18 stool samples, and 4 urine specimens (Table). The household contact who met the suspected SARS case definition provided a single nasopharyngeal swab, stool, and urine samples, and acute- and convalescent-phase (37 days after contact) serum specimens, whole blood samples, and oropharyngeal swabs. The other contact with fever provided a single nasopharyngeal swab and stool sample and three oropharyngeal swabs, serum specimens, and whole blood samples (up to 22 days after contact). The median time after contact to

Table. Characteristics of contacts of SARS case-patient—Pennsylvania, 2003

Variable	All contacts (N = 41) (%)	Prediagnosis ^a			Postdiagnosis ^a healthcare workers (n = 15) (%)
		Healthcare workers (n = 17) (%)	Household contacts (n = 4) (%)	Other ^b (n = 5) (%)	
Age (y)					
≥50	9 (22)	4 (24)	0	3 (60)	2 (13)
18–49	31 (76)	13 (77)	3 (75)	2 (40)	13 (87)
<18	1 (2)	0	1 (25)	0	0
Male	10 (24)	4 (24)	1 (25)	2 (40)	3 (20)
No. minutes of total contact per person, median (range)	28 (1–741)	7.5 (1–30)	459 (241–741)	30 (10–150)	110 (10–280)
Types of contact,					
Within 3 feet	38 (93)	17 (100)	4 (100)	2 (40)	15 (100)
Skin to object	17 (41)	12 (71)	4 (100)	1 (20)	0
Skin to skin	13 (32)	9 (53)	2 (50)	1 (20)	1 (7)
Use of PPE ^c	13 (32)	0	0	0	13 (87)
Postexposure symptoms ^d					
Fever	4 (10)	0	1 (25)	1 (20)	2 (13)
Respiratory symptoms	11 (27)	7 (41)	1 (25)	2 (40)	1 (7)
Met case definition (suspect case)	2 (5)	0	1 (25)	0	1 (7)
Furloughed from work, no. (%)	11 (27)	7 (41)	2 (50)	1 (20)	1 (7)
Total no. of specimens collected (average/person)					
Serum	125 (3)	63 (3.7)	14 (3.5)	9 (1.8)	39 (2.6)
Nasopharyngeal swab	35 (0.9)	17 (1)	4 (1)	4 (0.8)	10 (0.7)
Oropharyngeal swab	124 (3)	64 (3.8)	14 (3.5)	12 (2.4)	34 (2.3)
Stool	21 (0.5)	10 (0.6)	3 (0.8)	5 (1)	3 (0.2)
Urine	4 (0.1)	0	4 (1)	0	0
No. of days from last contact to last serum collection, median (range) ^e	28 (8–37)	28 (8–29)	29 (28–37)	16.5 (11–28) ^e	25 (22–30)

^aPrediagnosis contacts were those exposed to the case-patient after his onset of symptoms (April 3, 2003) but before his diagnosis with probable severe acute respiratory syndrome (SARS) (April 14). Postdiagnosis contacts were those exposed only after the diagnosis was made and infection control precautions were in effect.

^bOther, 4 contacts with healthcare-related exposure and 1 community exposure.

^cN95 respirator, gown, gloves. To be counted as having worn personal protective equipment (PPE), contact had to have worn it for every interaction with the case-patient.

^dSymptoms occurring during the 10-day period after contact with the case-patient.

^eMedian and range for "other" category is for 4 contacts, since 1 contact did not provide any serum specimens.

collection of the last serum specimen was 28 days (range 8–37). All specimens tested negative for SARS-CoV.

Postdiagnosis Contacts

Some contacts had unprotected exposures within 3 feet on the day SARS was diagnosed in the case-patient; the most prolonged of these were 210 minutes for a household contact and 30 minutes, including skin-to-skin contact, for a community contact (Figure 3). However, nearly all contacts were protected after diagnosis (Figures 1, 3; Table). The sample of 15 postdiagnosis healthcare workers was protected with fit-tested N95 respirators, gowns, and gloves (goggles were added on day 2 of hospitalization). Postdiagnosis healthcare workers had a median age of 39.1 years (range 24.6–51.7). Despite much longer median durations of exposure compared with those of the prediagnosis healthcare workers (110 vs. 7.5 minutes/person, $p < 0.005$; Table), postdiagnosis healthcare workers had only two unprotected close contacts, one failure to wear a gown, and one failure to wear an N95 respirator and gloves during skin-to-skin contact.

After contact with the patient, two (14%) postdiagnosis healthcare workers reported fever. One of these persons

also reported a cough 2 days after exposure to the case-patient and, therefore, met the clinical case definition for suspected SARS (9,20). This person was admitted to the hospital for 1 night with a diagnosis of respiratory syncytial virus infection (antigen-positive nasal aspirate) and asthma exacerbation. Neither of these symptomatic postdiagnosis healthcare workers had breaches in personal protection equipment. All specimens from postdiagnosis healthcare workers tested negative for SARS-CoV, including specimens from both contacts with fever, each of whom provided a single nasopharyngeal swab and weekly oropharyngeal swabs, serum specimens, and whole blood samples (up to 27 and 28 days after contact).

Discussion

This investigation provides the first detailed epidemiologic analysis of persons exposed to a U.S. patient with serologically confirmed SARS. Despite substantial contact with many persons, this case-patient did not transmit SARS-CoV, which is in contrast to experiences in Singapore (7), Taiwan (8), and Canada (15), where in some circumstances, limited contact to some case-patients led to many secondary infections. Similar lack of transmission

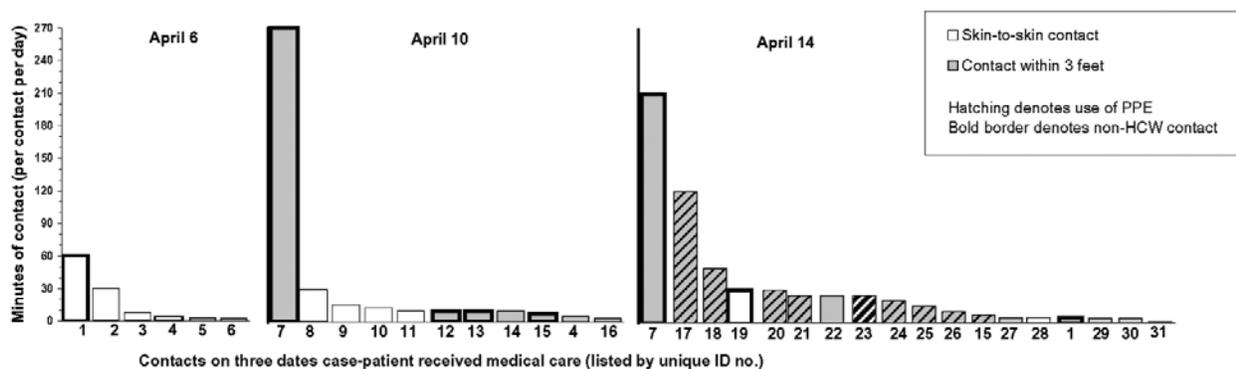


Figure 3. Duration of exposure for close contacts within 3 feet on the three dates when the case-patient with severe acute respiratory syndrome sought medical care. Four contacts (three household contacts and one healthcare worker) had contact with the patient on 2 of these days. Two healthcare workers had both protected and unprotected contact (shown with hatching).

from probable SARS case-patients has been documented in other settings (7); however, detailed exposure data have not been provided. Our findings demonstrate that in certain situations, even in the context of prolonged close contact without use of personal protective equipment, SARS-CoV may not be transmitted.

Certain aspects of this case-patient's illness may account for the lack of transmission. The case-patient did not have a cough until almost 1 week after symptom onset, and his respiratory secretions were negative for SARS-CoV by RT-PCR 11 days after symptom onset, although his stool specimen remained positive by RT-PCR for 26 days. In a report of the Hong Kong outbreak, viral RNA was identified in 68% of nasopharyngeal aspirates by the second week of illness (21); one interpretation of the negative results in this case-patient is that virus load in respiratory secretions may have been low. In addition, although the patient's stool specimens were positive for SARS-CoV by RT-PCR, the fact that viral cultures were negative suggests that any virus present in stool might not have been infectious.

Even before diagnosis, but after his first healthcare encounter, the patient was concerned about having SARS after learning that other attendees of the Toronto religious retreat were infected. This concern led the patient and his household contacts to take precautions after the patient's onset of cough; these precautions included the intermittent use of surgical masks, which have been shown to be effective in reducing the risk for SARS-CoV infection (16). Routine cleaning and surface decontamination of the case-patient's household and hospital settings may have further reduced transmission. Finally, no medical procedures associated with increased risk for transmission, such as intubation or aerosolized nebulizer treatments, were performed on this patient (3). Taken in combination, low virus load in respiratory secretions, virus in stool that was potentially noninfectious, use of surgical masks by the case-patient and family, active infection control measures, and lack of

aerosol-generating medical procedures may have all contributed to the lack of SARS-CoV transmission found in this investigation. Quantifying the impact that these and other factors have on the risk for transmission will require further epidemiologic evaluation around transmission events.

This investigation had some limitations. We chose a nonrandom sample of postdiagnosis contacts; however, since no SARS-CoV transmission to unprotected prediagnosis contacts was documented, the sampling scheme likely did not bias our findings toward lack of transmission. Furthermore, surveillance for fever and respiratory symptoms was ongoing in all contacts whether they participated in the investigation or not. We also cannot eliminate the possibility of some false-negative laboratory results, given that sensitivity of serologic assays and RT-PCR is lower early in illness (17,18,21). Nevertheless, Peiris et al. (21) showed that immunoglobulin (Ig) G isotype-specific antibody to SARS-CoV was detected in 93% of patients meeting a probable SARS case definition by day 28 after onset of symptoms, and the mean time to seroconversion was 20 days. Since serum samples were obtained for 22 of the prediagnosis contacts (85%) by day 20 and for 14 (54%) by at least day 28 after last exposure to the case-patient, that we missed seroconversions seems unlikely.

This patient was recognized as a probable SARS case-patient 2.5 hours after arrival in the emergency department, which was relatively rapid, given that neither WHO nor CDC had included Toronto as part of the interim SARS case definitions at the time of this patient's diagnosis. Toronto was subsequently added to the list of areas with suspected or documented community transmission in response to reports of SARS transmission among attendees at the gathering that led to this patient's infection (12,15). However, since very short exposure times have been associated with extensive SARS transmission elsewhere (16), vigilance is needed when caring for patients with recent exposure to a setting with an ongoing SARS outbreak,

even if local transmission has not been recognized. Draft guidelines are available to help identify future SARS case-patients (22), but since we do not know which patients with SARS will transmit readily, droplet and airborne infection control precautions should be implemented if a diagnosis of SARS is suspected.

Although this case-patient did not transmit SARS-CoV, many persons were symptomatic after contact with him, including two persons who met the suspected SARS case definition. To date, no asymptomatic SARS-CoV infection or transmission before onset of symptoms has been definitively documented. Until a diagnostic test is developed that is sensitive early in SARS-CoV infection, illness in a healthcare worker, household contact, or other close contact of a SARS case-patient remains the best existing criterion for requiring furlough or isolation of that person (23–25). However, due to the nonspecific clinical signs and symptoms of SARS (i.e., cough and fever), the clinical case definition has a low positive predictive value. This situation presents a challenge both for the management of close contacts of SARS patients and for surveillance for new SARS cases, particularly during the viral respiratory season, and emphasizes the need to identify an epidemiologic link as quickly as possible. Most (82%) symptomatic persons in this investigation had some degree of rhinorrhea, a symptom present in <25% of patients in descriptions of early clinical manifestations of SARS-CoV infection (5,6,26).

This type of epidemiologic investigation can be used in future investigations of transmission surrounding individual SARS case-patients; however, since such investigations are quite resource-intensive, this method would be most useful if applied to SARS case-patients linked to multiple transmission events, to assess risk factors associated with patients who readily transmit SARS-CoV. While factors contributing to SARS transmission are likely to be complex, additional data on the relationship between the natural history of infection and viral shedding, the types and duration of contacts with SARS patients, the effectiveness of infection control measures, and the contribution of each of these factors to transmission should help focus public health control measures to efficiently reduce SARS transmission.

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Dr. Peck is an Epidemic Intelligence Service Officer in the Respiratory and Enteric Virus Branch at the Centers for Disease Control and Prevention, Atlanta, Georgia. Her recent field epi-

demiology experiences include outbreak investigations of viral respiratory illnesses in healthcare facilities and the implementation of a hospital-based encephalitis surveillance project in Thailand.

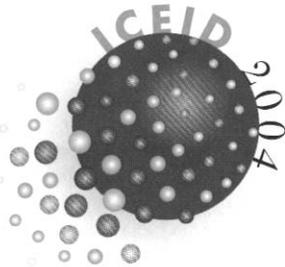
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Address for correspondence: Angela J. Peck, Centers for Disease Control and Prevention, National Center for Infectious Diseases, Division of Viral and Rickettsial Diseases, Respiratory and Enteric Virus Branch, 1600 Clifton Road N.E., Mailstop A34, Atlanta, GA 30333, USA; fax: 404-639-4960; email: apecck@cdc.gov

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