ABSENCE OF INFECTION IN ASYMPTOMATIC CONTACTS OF INDEX SARS CASE IN FRANCE

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The first case of severe acute respiratory syndrome (SARS) in France was diagnosed in March 2003. We conducted a serological survey to assess whether or not asymptomatic persons who had been in contact with this patient during his infectious stage had been infected. They were interviewed and asked to provide a blood sample for SARS coronavirus immunoglobulin G antibody testing. Despite the likely high infectivity of the SARS patient, no asymptomatic SARS infection was found in any of the 37 contacts included. These findings support a SARS case definition that is essentially based on clinical and epidemiological assessment, should SARS re-emerge.

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Introduction

Soon after the severe acute respiratory syndrome (SARS) international alert was issued by the World Health Organization (WHO) on 12 March 2003, surveillance of SARS was set up in France to detect and isolate possible and probable SARS cases as early as possible. Contacts of SARS cases were identified, quarantined and followed up on a daily basis for ten days. By the end of the outbreak in July 2003, seven probable SARS cases had been identified, of which four were confirmed by serology or polymerase chain reaction (PCR). All cases had been infected outside France and no secondary SARS transmission occurred in France. We report the results of a serological survey conducted among the asymptomatic contacts of the index SARS case introduced in France on 23 March 2003.

Methods

The index patient had been infected in Hanoi, Vietnam, where he worked as a physician in a hospital where an outbreak of SARS had been reported [1]. He developed clinical symptoms on 20 March 2003 and travelled by plane to France on 22 March. Upon arrival in Paris, he presented to an infectious diseases hospital close to his home, and reported that he had been exposed to SARS patients in Hanoi hospital. He was admitted to a specific isolation unit and SARS coronavirus (SARS-CoV) infection was confirmed by PCR on nasopharyngeal aspirates. Viral RNA was detected in endotracheal aspirates and stool samples for 66 days after onset of symptoms (Dr Yazdanpanah, personal communication).

Active case finding among close contacts allowed the identification of four secondary SARS probable cases (of which three were confirmed), infected before their arrival in France: one case had had previous contact with the index patient in Hanoi and three had been infected during the flight [1].

The study population included all persons who had contact with the index patient during his infectious stage and who remained asymptomatic. The patient's infectious stage started from the date of travel on 23 March (while symptomatic) until the date when his biological samples tested negative for SARS-CoV on 26 May 2003. Contacts, as defined by WHO criteria [2], included the AF171 flight passengers seated in the same row, one row in front and one behind the patient, the crew members, the medical personnel responsible for passengers screening upon arrival at the airport, the taxi drivers who transported the patient from the airport to his home and from his home to the hospital, and the healthcare workers (HCWs) who cared for the patient in the hospital where he was admitted. The four symptomatic secondary probable cases of SARS, infected in Hanoi or during the flight, were excluded from the study.

After informed consent, contacts who agreed to participate responded to a standardised questionnaire administered by a physician. Data collected included demographic information, the nature, duration and type of contacts with the index patient, the use of personal protective equipment and the occurrence of any clinical symptom compatible with SARS. A blood specimen was then collected, frozen and sent to the National Reference Centre for Influenza, Institut Pasteur, Paris.

This retrospective serosurvey was conducted on a voluntary basis and received approval from our corresponding ethical committee.

Sera were tested for SARS-CoV immunoglobulin G antibodies using an indirect immunofluorescence assay.

Results

We identified 65 eligible contacts, of whom 37 (57%) agreed to participate : five of the six airline passengers, one taxi driver who drove the patient on a thirty minute journey from his home to the hospital, and 31 (61%) of 51 HCWs who cared for the patient (11 nurses, 7 auxiliary nurses, 6 radiographers, 5 kinesitherapists and 2 physicians). Aircraft crew members and airport attendants could not be included because their respective companies refused to provide staff lists. Interviews and blood sampling took place from 24 May to 24 June 2003.

Among the 37 contacts, the male to female ratio was 0.65 and median age was 33 years (range 24-64 years). The median time interval between first exposure to the index case and blood collection was 70 days (range 30-91 days), and the median time interval between last exposure and blood collection was 33 days (range 10 - 87 days).

None of the participants reported fever or other symptoms related to SARS within 10 days after first exposure. However, three contacts reported a non-febrile rhinitis, myalgia that lasted for two days and a cough that lasted for three days. For these three persons, clinical examination, blood counts and chest radiographs were normal.

Of the 31 HCWs, thirty (97%) reported having always worn at least one protective respirator (N95 type), gloves and goggles when caring for the patient. One HCW reported contacts with the patient during two days: he did not wear any protective equipment during the first day but did do so on the second day. The taxi driver did not wear any protective device, but the patient himself wore a surgical mask during the taxi journey. The flight passengers seated close to the patient did not wear any protective equipment.

All 37 serologic samples (100%) tested negative for SARS-CoV immunoglobulin G antibodies.

Discussion

Our study did not show any SARS-CoV infection among asymptomatic contacts of a confirmed case of SARS. Healthcare

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workers in the hospital where the patient was admitted had made preparations to admit the index patient and were warned of his potential SARS diagnosis. As a consequence, they were able to adopt adequate protective behaviours as reported during their interviews. The transmission risk for HCWs was high, since the patient was severely ill and the exposure period included his peak contagious period, that is, in the course of the second and third weeks after the onset of the disease. Furthermore, the risk of secondary transmission from this patient was ascertained a couple of days after the illness onset, when three secondary cases were found to have occurred during the flight [1]. In addition, potentially aerosol-generating invasive procedures had been carried out during the patient's care. They consisted of endotracheal intubation and aspiration and could have fostered transmission, despite the use of personal protective equipment, as reported by Ofner et al [3].

The absence of asymptomatic or subclinical SARS-CoV transmission among HCWs in our study is consistent with reports from other countries that did not show any evidence for asymptomatic SARS infections [4,5,6,7,8] or reported it as uncommon (1.4 to 2.3%)[9,10,11], despite larger series and greater exposure (from 87 persons in Singapore to 1147 in Guangzhou, China).

Available studies on SARS transmission indicate that inflight transmission is rare but can occur, especially in 'superspreading events' [12,13,14]. In a previous article, we showed that SARS transmission occurred from the French index patient during his flight from Hanoi to Paris [1]. In the study reported here, we explored further the serological status of asymptomatic passengers, crew members and airport personnel who had been in contact with the patient during his flight and upon arrival. Unfortunately, this study in the aircraft was limited to five passengers, because airline company internal management considerations prevailed. Like Breugelmans et al [12], we deplore the lack of collaboration with the travel industry, regarding it as a major public health risk that is directly amplified by international travels.

Our study had some limitations. First, refusal to participate for some HCWs may have biased our results. In particular, the HCWs who refused to participate may have adopted protective measures less strictly and felt more at risk of having been infected. For those who participated, recall bias was probably not present, since interviews took place soon after events. However, some HCWs may have reported appropriate protective practices that they felt they should have adopted, rather than their own behaviours during patient care. Secondly, for some participants, blood collection took place at week 2 after contact with the patient; this delay may have been too short to allow detectable seronconversion rates. A second sample collected at least 30 days after last day of exposure would have allowed to confirm the absence of seroconversion among asymptomatic contacts.

In conclusion, like other studies, we showed no asymptomatic or subclinical SARS infection among close contacts of an index patient, despite his severe clinical condition. These findings support the WHO SARS case definition that is essentially based on clinical and epidemiologial assessment, should SARS re-emerge.

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Contributors

The authors contributed as follows: Stéphane Le Vu contributed to the design, planning, implementation and analysis of the study and drafted the manuscript. Yazdan Yazdanpanah contributed to the data collection and made comments on the manuscript. Julien Emmanuelli and Isabelle Bonmarin contributed to the study design and planning. Dounia Bitar contributed to the manuscript drafting. Jean-Claude Desenclos contributed to the study conception, implementation and reviewed the manuscript.

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