

*Report*

# SARS: the new challenge to international health and travel medicine

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**SUMMARY** Severe acute respiratory syndrome (SARS), the first severe new infectious disease of this millennium, caused widespread public disruption. By July 2003, 8427 probable SARS cases had been reported from 29 countries with a case fatality rate of 9.6%. The new febrile respiratory illness spread around the world along the routes of international air travel, with outbreaks concentrated in transportation hubs or densely populated areas. The etiologic agent was identified as a novel coronavirus, SARS-CoV. The disease is transmissible person-to-person through direct contact, large droplet contact and indirect contact from fomites and unwashed hands. Saudi Arabia successfully prevented the entry of the disease by imposing travel restrictions, special entry requirements, screening procedures at airports, including temperature checks, and quarantine. Ongoing efforts are aimed at developing case investigation, case management and surveillance protocols for SARS.

## Introduction

In the first half of 2003, the global community saw the emergence and impact of severe acute respiratory syndrome (SARS), the first severe and easily transmissible new infectious disease of the new millennium. From Guangdong province of China, the SARS virus spread along international travel routes to 30 countries and became deeply embedded in 6 of them. By 11 July 2003, 8427 probable SARS cases had been reported from 29 countries with 813 deaths [1]. There was widespread public panic, and social stability was jeopardized in some of the hardest hit areas. Economists estimated the costs in the Far East alone at US\$ 30 billion. The containment of SARS, however, was achieved through the diligent application of centuries' old control

measures. The most pressing questions now are whether SARS is seasonal and could return in winter, and whether the SARS virus could hide in some animal or environmental reservoir and resurface when conditions again become favourable for spread to humans.

## Development of the SARS pandemic

The first cases of a life-threatening respiratory disease of unknown cause are now known to have appeared in Guangdong province in China in mid-November 2002 [2]. But it was only on 11 February 2003, that the World Health Organization (WHO) received the first official report of an outbreak of atypical pneumonia in the prov-

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ince, said to have affected 305 persons and caused 5 deaths. An infected medical doctor, who had treated patients in his hometown in Guangdong province, carried the SARS infection out of China on 21 February 2003 to Hong Kong. Guests and visitors to the hotel's ninth floor where he stayed seeded outbreaks in the hospital systems of Hong Kong, Viet Nam and Singapore days later [2].

Dr Carlo Urbani, a WHO epidemiologist who investigated the Hanoi outbreak, was the first to recognize the condition as a distinct entity. The WHO designated the illness as severe acute respiratory syndrome (SARS) in late February 2003. Considerable progress was achieved in the following months in understanding its epidemiology and clinical features. A collaborative network of scientists from 11 laboratories around the world worked hard and successfully identified the etiologic agent as a new species of coronavirus, now called SARS-CoV [3–5]. WHO confirmed the Guangdong cases to be consistent with the definition of SARS after its team was permitted on 2 April 2003 to visit the province.

SARS began spreading along air travel routes, as persons who came in contact with the earliest cases travelled internationally. Hanoi, Hong Kong, Singapore and Toronto were the initial "hot zones" for SARS, with rapid increases in the number of cases, especially in health care workers (who exposed themselves without barrier protection) and their close contacts. Subsequent chains of secondary transmission occurred outside the health care environment.

The new disease showed a clear capacity to spread around the world along the routes of international air travel. The maximum incubation period, estimated at 10 days, allows spread via air travel between any 2 cities in the world. Mounting evidence now points to certain source cases

making a special contribution to the rapid spread of SARS infection. An imported hospitalized SARS case infected health care workers and other patients; they infected their close contacts and then the disease moved into the larger community. Epidemiological analyses revealed that the outbreaks of greatest concern were concentrated in transportation hubs or densely populated areas.

### Clinical features and management

The Centers for Disease Control and Prevention (CDC) defines a "suspected case" of SARS as a person with onset of fever and lower respiratory tract symptoms (temperature > 38 °C or 100.4 °F) within 10 days of either travel to an area with documented transmission of SARS or close contact with a person believed to have SARS [6,7]. If a suspected case develops chest radiographic findings of pneumonia, acute respiratory distress syndrome (ARDS) or an unexplained respiratory illness resulting in death, with autopsy findings of ARDS without identifiable cause then he/she is reclassified as a "probable case" of SARS. Laboratory findings further reclassify suspected and probable cases into "laboratory positive", "laboratory negative" or "indeterminate". Household members or persons caring for or sharing personal items with a SARS patient are considered a "close contact" [6].

The incubation period for the disease varied from 2 to 10 days with a mean and median of 5 and 6 days respectively [8–12]. The classical presentation was of a febrile illness followed in 48–72 hours by dry cough, which progressed rapidly to cause respiratory compromise and hypoxaemia. This necessitated ventilator support in one-

quarter of the patients and led to mortality in 20%–45% of cases. The mortality was highest among elderly patients who had other co-morbid conditions [9]. Exposure to a high viral load was another factor suggested to explain the mortality from SARS among previously healthy young health care workers. Interestingly, SARS affected relatively few children and appeared milder in this age group [13]. Serological studies have shown that a symptomatic or sub-clinical infection is uncommon.

None of the therapeutic modalities tried in different parts of the world (broad-spectrum antibiotics, steroids, ribavirin, interferon, and retinovir/lopinavir) have shown conclusive evidence of curative effect on the disease and no standard regimen has been developed [14]. Current management of the disease therefore is purely supportive and efforts should be focused on appropriate infection control measures to prevent its spread.

### Infection control

The epidemiological features of the disease suggest that it is transmissible from person-to-person through direct contact, large droplet contact, and through indirect contact from fomites and unwashed hands [8]. The virus is present in the respiratory secretions of infected patients and has also been found in the urine and faeces, raising the possibility of faecal–oral spread in some situations.

It is critical that patients with suspected SARS be identified promptly to institute the isolation precautions needed to prevent the spread of the disease. Triage screening has been recommended, with a questionnaire to identify SARS symptoms and history of possible exposure. Patients suspected of having SARS need to be immediately sepa-

rated from other patients, given a mask and evaluated carefully by a health care worker wearing a gown, gloves, and N-95 respirator, ideally in a negative pressure room. One way of avoiding the spread of disease in hospitals is to set up a fever triage clinic outside the hospital emergency room, equipped with all necessary contact precaution supplies. These clinics were developed in Taiwan and Toronto during the peak of the SARS epidemic.

Patients who need to be admitted should be isolated in a negative pressure room in a special isolation ward, with restrictions on visitors and the number of health care workers involved in the patient care. Medical procedures such as bronchoscopy or respiratory nebulization of medications should be avoided. If the number of patients exceeds the hospital's capacity for negative pressure rooms, then the priority should be to keep patients with SARS pneumonia in isolation negative pressure rooms while maintaining other SARS patients in private rooms.

Restricting employees' access to hospitals with SARS patients and identifying the employees who are taking care of SARS patients are critical steps to ensuring that health care workers do not suffer unprotected exposure to SARS patients. Staff should be actively monitored for any signs and symptoms of SARS, i.e. new onset upper respiratory tract illness and high temperature, for early detection of cases. Health care workers with symptoms should be immediately confined to their homes with daily reporting of symptoms to the employee health department or infection control personnel at the hospital. All personnel involved in aerosol-generating procedures on patients with confirmed SARS should be quarantined for 10 days if

adequate precautionary measures were not taken during the procedure.

Intensive education of health care workers and family is mandatory. This includes proper infection control precautions, which should stress the 2 most likely modes of transmission of SARS: contact and respiratory droplets. Health care workers need personal protective equipment appropriate for standard, contact and airborne precautions (i.e. hand hygiene, gown, gloves and N-95 respirator) in addition to eye protection, and use of these should be enforced. Household members should be educated about the mode of spread of the disease and proper precautions when in contact with the infected person by wearing gloves and mask and washing and disinfecting the hands frequently. If they develop symptoms, they should call the public health department and arrange to be examined by a qualified person. This coordination is crucial to preventing the spread of the disease from infected family members to health care workers who may be unaware of the risk of SARS contact.

Suspect or possible cases that do not require admission to hospital should be managed as outpatients. These patients should be given clear instructions about hand hygiene practices with frequent hand washing and wearing a surgical mask to cover the mouth for coughing and sneezing. In addition, they should not share eating utensils, towels and bedding with family members until washed. These patients should remain at home until 10 days after the resolution of fever, if cough and other respiratory symptoms have resolved or improved. When no respiratory symptoms or fever are present, family members need not be restricted from going out and carrying out their usual activities including work or school.

## Global action

WHO issued a global alert on 12 March 2003 about cases of severe atypical pneumonia with unknown etiology that appeared to place health workers at high risk. On 15 March 2003, WHO increased the level of the global alert to a rare emergency travel advisory for international travellers, health care professionals, and health authorities to the perceived worldwide threat to health from SARS. The Global Outbreak Alert and Response Network (GOARN) teams from WHO provided support at all the main outbreak sites.

WHO regarded every country with an international airport, or bordering an area having recent local transmission, as being at potential risk of an outbreak. The lack of vaccine and effective treatment forced health authorities to resort to control tools dating back to the earliest days of empirical microbiology: isolation and quarantine. Countries around the world, guided by WHO, adopted aggressive and unprecedented measures including travel restrictions, special entry requirements, screening procedures at airports including temperature checks and quarantine. Other control measures included public information and education to encourage prompt reporting of symptoms, early identification and isolation of patients, vigorous contact tracing, and management of close contacts. These succeeded to a large extent in containing the disease.

Hospitals, schools, and borders were closed, and several governments advised their citizens not to travel to hard-hit areas. Some airlines decided not to carry passenger with a fever of 37.5 °C or above on any of their flights regardless of local government regulations. Hong Kong adapted an electronic tracking system used in criminal investigations for contact tracing and mon-

itoring of compliance with quarantine. Singapore deployed its military forces to assist in contact tracing and to enforce quarantines that halted the normal lives of thousands of people [7]. The country also banned visitors at public hospitals.

On being notified by Singapore, through WHO, Germany removed a physician from Singapore (returning from New York after attending a medical conference who had symptoms suggestive of SARS) along with his 2 accompanying family members from their flight at a stopover in Frankfurt, immediately isolated them and placed them under hospital care. This prompt action saved Germany from any further spread.

The WHO announced in late June that Hong Kong and Beijing, the 2 most severely affected areas, had interrupted transmission. Toronto and Taiwan followed shortly afterwards. On 5 July 2003, the WHO decided [15], on the basis of country surveillance reports, that all known person-to-person transmission of SARS-CoV had ceased and the global SARS outbreak was contained as it removed Taiwan from its list of areas with recent local transmission of the disease. The human chains of SARS virus transmission appeared to have been broken everywhere. While the containment was a milestone, nations were cautioned against becoming complacent, and to maintain vigilance against the re-emergence of the illness that resulted in over 800 deaths worldwide, mostly in China and Hong Kong, and for which there is no simple treatment. Some experts say it could be seasonal.

## Saudi Arabia

Saudi Arabia had a special reason for concern. It has a large expatriate working population of 5.3 million persons coming from

various regions of the world. Around 2 million international pilgrims from over 140 countries visit Mecca, the focal point of Islam, for the annual *hajj* pilgrimage; a smaller number visit the country throughout the year for the individual and shorter *umra* pilgrimage. The country also receives a large number of business travellers the year round. Were measures not taken immediately to prevent the entry of SARS, it would spread quickly and wreak havoc.

Acting promptly, the Saudi Ministry of Health, on 10 April 2003, banned the entry of people who had visited any of the 5 SARS-stricken South East Asian countries—China, Hong Kong, Taiwan, Singapore and Viet Nam. The ban was enforced to protect both citizens and expatriates in the country. Saudi Arabian citizens were advised against travelling to SARS affected countries. The Saudi missions in China, Singapore, Hong Kong and the Philippines were instructed to stop issuing *umra* visas indefinitely. Isolation wards were designated in major hospitals in all regions to quarantine all suspected cases of SARS and admit confirmed SARS cases. The Sahari hospital, a new tuberculosis hospital in Riyadh, was the designated hospital for the Central region. Mass media was used extensively to increase awareness of SARS among the population.

Customs, passport and health employees at international airports were ordered to put on masks while dealing with flights arriving from countries with cases of SARS. All arriving passengers were required to fill in a mandatory health declaration form for immigration clearance. At the same time, the health officers at the airport distributed a health alert card with information about SARS. The card advised persons to contact doctors or designated hospitals if they later developed symptoms suggestive of

SARS, such as high fever ( $> 38^{\circ}\text{C}$ ,  $> 100.4^{\circ}\text{F}$ ), dry cough, shortness of breath or breathing difficulties.

Health personnel checked all incoming passengers for fever. Within weeks, thermal scanners were installed before immigration clearance at the 3 international airports at Riyadh, Jeddah and Damman in Saudi Arabia to identify persons with raised body temperature. This non-intrusive check did not affect passengers, as it did not delay them. Passengers with temperature below  $38^{\circ}\text{C}$  were allowed to proceed for immigration clearance as normal. Those with body temperature above  $38^{\circ}\text{C}$  were taken for a secondary temperature check. Where fever was confirmed, the staff asked the passenger a series of health-related questions recommended by the WHO: if they have other symptoms of SARS, such as cough, breathing difficulty or shortness of breath; if they or their family members have had close contact with any person/s who have been diagnosed with SARS; and if, in the last 10 days, they had travelled to any SARS-affected areas. When SARS was suspected, the passenger was to be referred to the airport health department for follow-up to be kept under observation for 10 days. Saudi Arabian citizens and expatriate workers returning from or transiting through SARS-affected countries within the incubation period of SARS, when cleared by checking for fever and symptoms in the airport, were quarantined in their homes; staff from the Ministry of Health visited them daily to check their temperature until the 10th day.

The measures were further stepped up on 28 April 2003. The Saudi Ministry of Health set up a special committee in Riyadh with branches throughout the country to coordinate efforts to fight the disease. The Ministry barred entry to nationals of SARS-affected countries as a precautionary mea-

sure. All international airlines were notified not to transport any passenger coming to the Kingdom from the SARS-hit countries via a third country unless that passenger had stayed at least 10 days in that third country after departing from the last SARS-stricken station.

The Saudi Arabia and 6 other Gulf countries met in Qatar in the first week of May to coordinate their efforts against SARS. The countries agreed to inform each other about SARS cases registered among their citizens or expatriates.

The ban on passengers coming to Saudi Arabia from countries affected by SARS was lifted on 8 July 2003 following positive reports from WHO that no new cases had been reported for the past 20 days, including Canada and China. The Saudi Arabian health authorities, however, continued to monitor the country's entry points in order to prevent the incursion of any potential SARS-carrier. For the subsequent *hajj* (at the end of January/beginning of February 2004), plans were made that all pilgrims coming from the earlier SARS endemic countries would not be allowed to enter the country unless there was evidence on his/her passport that he/she had been outside of the country for a minimum of 10 days immediately prior to arrival in Saudi Arabia.

## Perspective

SARS is a particularly serious threat for public health internationally. It also had far-reaching economic and social consequences. Alerted by WHO, all countries with imported cases, with the exception of provinces in China, were able through rapid case detection, immediate isolation, strict infection control, and vigorous contact tracing to successfully prevent further transmission.

The high level of mass media attention focused on SARS and the concerted work of medical professionals, together with WHO's pragmatic leadership role, helped create widespread awareness of the severity of the infectious disease threat, and united the global community. Scientists and clinicians in various countries collaborated and pooled expertise and resources to combat the shared threat. This helped health authorities to identify imported SARS cases quickly, prevent a SARS outbreak, and thus avoid the devastating consequences seen elsewhere. The SARS experience in countries like Viet Nam and Singapore showed that immediate political commitment at the highest level can prove decisive in combating the spread of the disease.

SARS has posed important challenges for medical professionals. There are concerns over the future evolution of outbreaks as the virus belongs to a family notorious for its frequent mutations. Genomic studies have shown a remarkable genetic conservation of the virus; there appears little likelihood of mutation to a benign infection with attenuated symptoms. With neither herd immunity nor attenuation of the virus, the next epidemic when it occurs will have large-scale outbreaks with severe symptoms. Efforts are on to devel-

op case investigation, case management and surveillance protocols for SARS in the post-outbreak environment.

The major challenges of the disease are its poorly understood epidemiology and pathogenesis, its non-specific and common initial symptoms, the limitations in the available diagnostic tests and the vulnerability of hospital staff, the human resource vital for SARS control [8]. The requirement for intensive care for SARS cases is a strain on hospital resources. A rapid diagnostic test needs to be developed urgently for diagnosing SARS within days of onset for differentiating it from other atypical pneumonias. Research should be intensified to identify the possible animal reservoir. A global database on SARS has to be developed and an evidence-based approach used for therapeutic approaches for SARS treatment [2].

The efforts at combating the threat of SARS have revealed the strengths and weaknesses of national, regional and global capacities to respond to infectious disease threats. Areas for urgent improvement have now been highlighted in the health surveillance systems of various countries. These need to be addressed so that countries are adequately prepared when the world is next confronted with SARS or another infectious disease pandemic.

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