

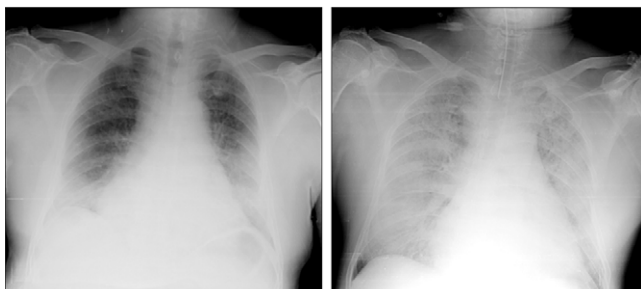
Preventing local transmission of SARS: lessons from Singapore

Clinical record

At 11:30 on 8 April 2003, a 64-year-old man presented to the National University Hospital emergency department (ED) complaining of light headedness for 3 days, and dry cough and body aches for 2 days. His general practitioner had recorded a temperature of 37.7°C. On further enquiry in the ED, he described mild dyspnoea and palpitations. For over 40 years, he had smoked 25 cigarettes a day, and had consumed at least 100 g of alcohol per day. He gave a history of hypertension, ischaemic heart disease and chronic atrial fibrillation. Regular medications included isosorbide dinitrate, aspirin, digoxin and candesartan. He had not travelled out of Singapore recently, nor did he report contact with anyone suspected of having SARS.

The patient's temperature was 36.0°C and he was noted to be "comfortable". Bilateral basal crackles were audible on auscultation. His chest x-ray showed cardiomegaly and non-specific bibasal infiltrates (Figure 1). Arterial blood gas measurement revealed a pH of 7.39, PO₂ of 61 mmHg, PCO₂ of 31 mmHg and an arterial oxygen saturation (SaO₂) of 91%, on an oxygen mask delivering a fraction of inspired oxygen (FiO₂) of 35%. He was assessed as having cardiac failure and admitted to an open, shared ward at 15:00. Admission blood results included a normal total white-cell count (9.3 x 10⁹/L), but lymphopenia (0.63 x 10⁹/L), and a lactate dehydrogenase level of 1770 U/L (normal range, < 700 U/L). Other measured parameters gave unremarkable results, but in hindsight these abnormalities may have been early pointers to the ultimate diagnosis.^{1,2}

Within hours of admission to the ward the patient's condition deteriorated rapidly. Although consistently afebrile during this period, respiratory distress and worsening hypoxia ensued, with SaO₂ at 91% on a "non-rebreather" mask with FiO₂ close to 100%. Echocardiography showed good ventricular function, inconsistent with heart failure. At 23:30, he was transferred to the intensive care unit (ICU), and 12 hours after presentation a temperature of 37.7°C was noted. Three hours later, because of further respiratory deterioration, he was intubated (Figure 2). He was transferred to the designated SARS hospital, and died on 12 April. The diagnosis was confirmed later when SARS coronavirus was identified in a throat swab on PCR testing, using primers developed by the Bernhard Nocht Institute.³ Postmortem examination showed "solid lungs" (> 1 kg each). Haemorrhagic infarcts were seen macroscopically. Microscopy showed diffuse alveolar damage, with inflammation and fibrous changes of the alveolar walls. The alveolar damage was not uniform in all parts of the lungs, but showed some temporal phasing; ie, severe damage was interspersed with an intermediate degree of damage and some relatively normal alveolar air sacs. Postmortem lung tissue specimens were also positive for SARS coronavirus.



1: Chest x-ray performed on 8 April at 12:06 showing non-specific bibasal infiltrates

2: Chest x-ray performed on 9 April at 02:34 showing extensive progression

THE NATIONAL UNIVERSITY HOSPITAL (NUH) has been designated as a "non-SARS" hospital in Singapore's health system. In theory, the hospital is to remain SARS free — by instituting measures to detect cases, providing isolation for suspected cases and referring probable SARS cases to Tan Tock Seng Hospital (the designated SARS hospital). The intention is that NUH continues to be part of a SARS-free segment of the health system. Evidence to date suggests that this is not easily achievable.

Although the patient reported no contact history with a patient with SARS, and had not been to any recognised Singapore SARS "hot spots", it later transpired that his brother was ill in hospital and was subsequently shown to be the index case of a SARS cluster involving 62 cases at Singapore General Hospital.

SARS spread in hospital

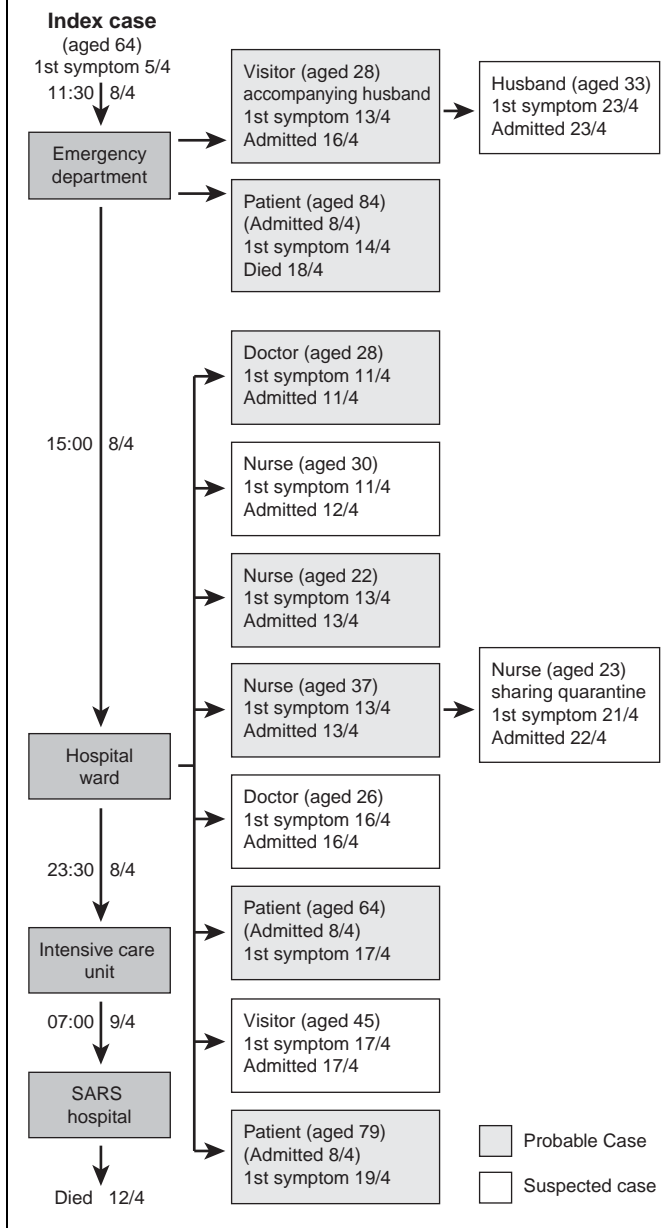
The patient was in the emergency department (ED) for 3 hours and the ward for 9 hours. During this time he was not isolated, as he gave no contact history for SARS and was afebrile. Furthermore, at that time in Singapore, gowns, gloves and masks were not consistently worn by staff, and were generally reserved for those caring for identified suspected cases. During the 12 hours, there was disease transmission to one doctor, two nurses, three patients and a visitor (Box 1). Other cases — a doctor, a nurse and a visitor — remain "suspect", and second generation cases are beginning to present. A total of 132 contacts were identified for the 12-hour period, each person requiring varying levels of intervention from counselling through to home or hospital quarantine.

Unfortunately, the first doctor infected (Box 1) was not initially identified as a contact, as she had worn gloves, a gown and an N-95 mask. Infection may have been a result of inadequate eye protection when transferring the patient to the intensive care unit (ICU). She was in the hospital on the day of her first symptoms, and, as a result, four wards (around 100 patients) were quarantined.

SARS spread in the community

Community spread involving at least five individuals is now also linked to our patient before his admission. His wife and two of his three children have SARS, as does a taxi driver who took him to work just before hospital presentation. The patient was a vendor at one of Singapore's largest markets. As the extent of our patient's cluster became clearer, there was major concern in Singapore with the identification of another market vendor and his family with SARS. The ramifications of spread within a crowded market place prompted the unprecedented move by health authorities to place 2500 individuals on home quarantine orders for 10 days. The value of quarantine is an ongoing debate, but it is one of the few measures that can be taken during an infectious disease outbreak.⁴ Instituting this

1: Hospital transmission from index case ("1st symptom" included fever, myalgia, cough or dyspnoea)



safeguard has caused significant financial hardship to individuals and disrupted the flow of food supplies in Singapore.

There are numerous lessons to be learned from this case.

Lesson 1: Contact histories

Although a contact history, by our understanding, was clearly present, our patient did not appreciate this. We would regard an unwell brother in hospital, whom he had visited a week earlier, as a significant contact. Had this information been forthcoming at the initial general practitioner visit or on ED presentation, the whole scenario may

2: World Health Organization case definitions of severe acute respiratory syndrome (SARS)

The WHO case definitions of SARS, revised as of 1 May 2003, for a suspected and a probable case of SARS⁶

Suspect case

1. A person presenting after 1 November 2002 with history of: high fever (> 38°C) AND cough or breathing difficulty AND one or more of the following exposures during the 10 days prior to onset of symptoms:

- close contact with a person who is a suspect or probable case of SARS

- history of travel, to an area with recent local transmission of SARS
- residing in an area with recent local transmission of SARS

2. A person with an unexplained acute respiratory illness resulting in death after 1 November 2002, but on whom no autopsy has been performed AND one or more of the following exposures during the 10 days prior to onset of symptoms:

- close contact with a person who is a suspect or probable case of SARS

- history of travel to an area with recent local transmission of SARS
- residing in an area with recent local transmission of SARS

Probable case

1. A suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome on chest x-ray.

2. A suspect case of SARS that is positive for SARS coronavirus by one or more assays.

3. A suspect case with autopsy findings consistent with the pathology of respiratory distress syndrome without an identifiable cause.

have been prevented. At that time, patients “with” versus “without” a contact history were managed differently. Now, in response, we have de-emphasised the importance of a lack of contact history.

Australia must ensure rapid identification of a potential index case at points of initial contact in hospitals, community clinics and general practices across the country.

Lesson 2: Clinical triggers for isolation

As well as giving no contact history, the patient presented afebrile and gave no history of a fever > 38.0°C, which many regard as essential to confirm a diagnosis.⁵ We have now learned that fever may appear later, particularly in individuals with comorbidities. Our patient’s other medical problems, including excess alcohol consumption and cardiac disease, may have contributed to the absence of fever. It is also possible that patients with such fulminant disease may be relatively immunocompromised, impairing their ability to mount a fever. Most certainly, and with the benefit of hindsight, our patient had fulminant disease, progressing from being “comfortable” to respiratory failure requiring intubation in 15 hours. It is probable that he had a high viral load, which would explain the rapid deterioration in his condition as well as his infectivity.

Fever is essential to the World Health Organization case definition of SARS (Box 2),⁶ but clinicians must not confuse

Lessons from practice

- The clinical features used to manage suspected SARS cases should not be confused with a surveillance case definition used for epidemiological purposes
- An outbreak of SARS in Australia will most likely occur in a hospital after spread from an unidentified case. The extent of spread will depend on the patient's infectivity and the time to isolation
- Lowering the threshold for respiratory and contact isolation of a possible SARS case allows a period of observation until the diagnosis is clarified
- Given the consequences of a major SARS outbreak, resources for appropriate infection control systems must be made available

an epidemiologically useful definition with clinical criteria. If fever is present at admission, the situation is much clearer, but cases such as this one have prompted us to change the threshold criteria for initial isolation.

At NUH, any patient with fever or respiratory symptoms or a chest x-ray abnormality not otherwise explained is initially admitted to one of our newly created "fever wards". In the first 4 weeks of our engagement with SARS, there have been 394 admissions (including 65 staff) to these wards, with 23 individuals (4.3%) referred as suspect or probable SARS cases. Such a practice consumes considerable resources with a low yield of cases. The patient described, however, demonstrates the heavy costs of not isolating.

Isolation beds can protect hospital staff and others from patients with atypical presentations. A patient's likelihood of having SARS becomes clearer after 48 hours of monitoring respiratory symptoms, temperature, white cell count (for lymphopenia) and chest x-rays.

Lesson 3: Preventing a SARS outbreak in Australia

The lead time Australia has to establish healthcare systems to cope with SARS, as well as our geographical barriers — allowing assessment of newly arrived travellers for fever and typical symptoms of SARS — should provide us with a primary level of protection.^{1,2} In countries with the resources to implement full and effective contact and respiratory isolation for all suspect patients, local transmission of the virus has been almost non-existent.⁷ The incubation period of around 10 days is long enough, however, to permit a first presentation of an individual with SARS anywhere in Australia. Early identification of potential cases requires sustained clinical vigilance at all points at which patients enter the health system. Health administrations must ensure accountability of these processes nationwide.

Provided there is consistent early identification of imported suspect cases, then Australia's healthcare system can manage these patients with appropriate isolation to prevent secondary transmission. All the nurses and patients involved with our patient were identified as contacts and isolated (Box 1). Their quarantining possibly prevented escalation of this nosocomial outbreak.

The fact that this disease presents and spreads foremost as a nosocomial infection permits us to provide community protection by focusing efforts in the health sector.⁸ Our experience with this patient, and similar atypical cases, informs us that patients with SARS cannot invariably be identified on admission. Thus, in addition to the low clinical thresholds to isolation, NUH has instituted the wearing of masks for all staff and visitors to provide a level of protection from unidentified cases. Staff with any patient contact wear a mask, gown and gloves, and sometimes eye cover as well. The documented spread to hospital visitors has seen Singapore limit non-essential attendance at all hospitals and exclude children visitors.

Patients presenting with overt symptoms suggestive of SARS, including fever, are unlikely to be the source of an outbreak. Unidentified SARS cases not in isolation have to date been responsible for most outbreaks. Individuals requiring hospital admission who have been in affected countries in the preceding 10 days may be infected or incubating the disease. Monitoring and possible isolation of these patients should be considered.

Lesson 4: Ensuring rapid control of an Australian outbreak

A second tier of public health protection should be invoked once secondary transmission has occurred. This will be instrumental in Australia's (or a region's) chance of remaining SARS free. The response will need to be in hours, not days, and must use all available epidemiological resources for contact tracing, quarantine and isolation. Government, health jurisdictions, and clinicians must act collaboratively and proactively.⁹ Unfortunately, experiences in Singapore suggest that the spread of SARS, while being somewhat controllable, is very difficult to fully extinguish once established. Observations from Frankfurt³ and Vietnam,¹⁰ where single, imported cases led to limited secondary and no tertiary spread, suggest that preparedness, drastic measures and some luck can help "get the cat back in the bag".

Each health jurisdiction in Australia must have a plan for managing a local SARS outbreak, which should include prompt hospital and community responses, and an ability to meet potential needs at short notice. Central monitoring will ensure that all jurisdictions are adequately prepared.

Lesson 5: Resources for a potential outbreak

Australia's defences begin at entry points to the country and are followed up at entry points to health facilities. With local transmission, the battle turns to the wards and the community setting. Our patient's unrecognised illness resulted in infection of numerous others in the community and in hospital. Furthermore, it led to the closure of four hospital wards and a major produce market. Contact tracing and quarantine has involved thousands of people. The economic impact on individuals and the whole country is profound, affecting tourism, education and employment. The current Australian guidelines for SARS prevention¹¹ are a useful interim effort, but arguably could go further in some areas, as outlined above.

There is no financial justification for limiting resources to avoid the establishment of SARS in Australia. There are substantial costs involved in preventing local disease transmission, but these will be insignificant compared with the costs of managing a SARS outbreak, which will extend well beyond the health sector. Every reasonable avenue must be pursued to keep Australia SARS free for as long as possible.

Addendum: At the time of publication, one of the sons of the Index patient has died from SARS and another patient from the same ward has become a probable SARS case, with an onset of symptoms 14 days after exposure (April 22), raising concerns over a prolonged incubation or an unidentified intermediate infection.

The son of the husband and wife infected via the ED is also now a probable SARS case.

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