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SARS in Taiwan: an overview and lessons learned

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Summary

Objectives: This report aims to describe the epidemiology of severe acute respiratory syndrome (SARS) in Taiwan between March and July 2003, and to examine the public health response.
Methods: Surveillance for SARS was initiated on 14 March 2003. Response activities are described for the isolation of patients; contact tracing; quarantine of contact persons; fever screening for inbound and outbound passengers at the airport; and hospital infection control as assessed by mobile SARS containment teams.
Results: Between 14 March and 30 July 2003 a total of 668 probable cases of SARS were reported. Of the 668 cases, 181 (27%) were fatal. Compared to the survivors, fatal cases were more likely to be older ($p < 0.001$), male ($p < 0.05$), exposed through hospital contact ($p < 0.001$), and have a coexisting medical disorder ($p < 0.001$). Between 28 March and 30 July a total of 151,270 persons were quarantined. Among them, 46 (3.0/10,000) were subsequently classified as being probable SARS cases. At

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the time of the mobile team assessments, 46 (53%) hospitals had implemented WHO infection control recommendations.
Conclusions: In this outbreak, an emergency plan consisted of patient isolation and strict hospital infection control.

Introduction

The worldwide spread of a novel coronavirus that causes severe acute respiratory syndrome (SARS) proceeded with unprecedented rapidity, overwhelming many hospitals and public health systems in a matter of weeks.[1,2] As of 11 July 2003, a total of 8437 cases were reported from 32 countries.[3] In many locations, the introduction of the disease by ill travellers was soon followed by spread to health care workers and household contacts.[4,5]

This report describes the epidemiology of the SARS outbreak in Taiwan and proposes strategies for addressing response operations after any emerging outbreaks in the future. Further, the lessons learned from the response to this outbreak may help to improve current strategies for preventing outbreaks of infectious diseases and for distributing resources efficiently during response operations.

Background

Taiwan has a population of approximately 22,549,292. The main island is divided into 22 cities and counties. Taiwan, with its close proximity to the SARS epicenters of Guangdong and Hong Kong, and its extensive business and cultural ties, has many travellers from the most affected areas. Each year more than four million Taiwanese visit mainland China for business and tourism (Bureau of Immigration Ministry of the Interior) and the vast majority of flights return through Hong Kong. Although Taiwan was removed from the list of affected areas on 5 July 2003, it will remain at risk from the importation and spread of SARS should it re-emerge.[3,6]

Methods

Surveillance

On 14 March 2003, the day the first cases were reported, Taiwan's Department of Health initiated a system to respond to the potential spread of SARS resulting from the cases. A Task Force Committee established medical aid teams to address disruption in the quarantine system; to conduct rapid assessment by reviewing every reported SARS case within three days after the first case was reported; and to implement a legislative procedure for reporting SARS on 28 March. All suspected SARS cases were required by law to be reported to the Department of Health, and health authorities were required to deliver protective equipment including N-95 masks to the SARS hospitals immediately and to equip all healthcare workers with enhanced protective equipment.

Isolation of SARS cases

Beginning with the recognition of the first SARS case on 14 March, Taiwan moved aggressively to isolate all suspect or probable cases in negative pressure rooms and to equip all healthcare workers with enhanced protective equipment. Specially designed isolation rooms with HEPA filtered air, negative pressure under continuous electronic monitoring, and separate bathrooms and anterooms are commonly available in larger referral hospitals. Until 22 April most of the probable cases were cared for in such hospital settings. From 23 April to 8 May, the 277 new cases overwhelmed the capacity of the hospital system to care for all patients in negative pressure rooms.

Contact tracing

When a SARS case was reported, local public health workers pursued a case investigation and confirmed adequate home quarantine of all contacts. The case investigation reviewed the patient's history of exposure to patients with SARS or SARS-affected areas, reviewed the signs and symptoms as compared to the WHO case definition of SARS,[7] and collected information on the patient's recent close contacts.

Mortality

Death certificates were obtained from the statistics division of the Ministry of Interior in Taiwan. Information from death certificates was used to determine the cause of death. Mortality was estimated by dividing the number of deaths by the total number of probable cases. It was based on cases with a known outcome and was irrespective of the immediate cause of death.[8]

Laboratory investigation

Nasopharyngeal swab or stool specimens were obtained from reported patients and tested for SARS-Co-V by the laboratory of the Center for Disease Control at the Department of Health in Taiwan. The viral RNA was extracted and reverse transcriptase polymerase chain reaction (RT-PCR) was completed for targets specific to various RNA viruses, including the influenza A and B viruses and SARS-Co-V. A specimen was considered RT-PCR-positive for SARS-Co-V if at least two different clinical specimens were positive (e.g., nasopharyngeal and stool), the same clinical specimens collected on two or more occasions during the course of the illness were positive (e.g., sequential nasopharyngeal aspirates), or if two different assays or repeat PCR using a new RNA extract from the original clinical sample on each occasion of testing were positive.[7]

Quarantine

Quarantine was implemented on 18 March for persons meeting one of two sets of criteria, designed as class A or class B. Class A included healthcare workers exposed outside isolation settings, family and other close contacts, and those on airplanes with ill SARS patients if seated within three rows in front or three rows behind the patient. Initially, the duration of quarantine was 14 days, but after 10 June this was revised to ten days in accordance with the incubation period for SARS.[1,5,6] Hospital staff and patients who had been in contact with a SARS patient were quarantined in a healthcare facility. All others were quarantined at home.

From 28 April to 4 July, those who returned from a WHO-designated SARS-affected area were considered class B, resulting in compulsory home quarantine for ten days.[6,9] Passengers arriving could choose to be quarantined in an airport transit hotel, at home, or at a quarantine site designated and paid for by their employer. If these options were not available, the traveller was quarantined at a government quarantine center located at a military base. On 9 June quarantine regulations were eased for the staff of Taiwanese companies based on mainland China who were returning to Taiwan for business. Travellers in this category were allowed to conduct business if they wore a surgical mask. Public health nurses from local health departments delivered food to the home three times a day. Body temperature was self-monitored three times a day and reported by telephone to the public health nurses. A surgical mask was worn whenever the quarantined individual entered a communal area within their own home. If he/she became sick during the home quarantine period, the driver of the ambulance took the patient to hospital dressed in a Tyvek suit, N-95 respirator and gloves. There were several hundred such ambulance trips for fever patients between mid-May and July in Taiwan.

Measurement of body temperature

After 10 April all airline passengers, outbound and inbound, were requested to have their body temperature taken at the airport. People whose body temperatures were higher than 37.5 °C were examined further by a physician.

Hospital infection control practice

Mobile SARS containment teams (mobile teams), a joint program by the Center for Disease Control in Taiwan and various teaching hospitals, were initiated three days after the first suspected SARS case was reported. Seventeen mobile teams, comprising infection control physicians, infection control nurses, rotating staff from the County Department of Health, staff from the Center for Disease Control, Taiwan, and staff from the Centers for Disease Control and Prevention in the USA, were deployed from 16 March to 10 May 2003. They observed and demonstrated the recommended SARS infection control practices and also provided personal protective equipment (PPE) to hospitals actively evaluating patients for SARS infection. Each team was equipped with an infection control checklist, personal protective equipment (PPE), blood specimen tubes, nasopharyngeal swabs, culture media, and a specimen cooler. Mobile teams evaluated infection control practices through observing hospital personnel, questioning current practices, and detecting the negative pressure of the isolation room using a strip of tissue paper at the entrance of a patient's isolation room.

Definitions

In this study, the WHO case definition as published in May 2003 was used. The results were later compared with those obtained by using the case definition published in August 2003. In May, a probable case of SARS was defined as a person presenting after 1 February 2003 with a history of fever higher than 38 °C and one or more of the following symptoms: lower respiratory tract illness (cough, breathing difficulty, shortness of breath) or radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) or autopsy findings consistent with pneumonia without identifiable cause. The person also needed evidence of one or more of the following exposures during the ten days prior to the onset of symptoms: to have had close contact with a person who is a suspect or probable case of SARS; to reside in an affected area.[7] A suspect case was a probable case without chest radiograph or pathological confirmation. Patients were excluded if an alternative diagnosis could fully explain their illness.[7]

On 14 August 2003 WHO proposed a new case definition, including laboratory confirmation. A clinical case of SARS was defined as a person presenting a history of fever higher than 38 °C and one or more symptoms of lower respiratory tract illness (cough, breathing difficulty, shortness of breath) and radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) or autopsy findings consistent with pneumonia without an identifiable cause. Patients were excluded if an alternative diagnosis could fully explain their illness.[10] A laboratory case was a clinical case with positive laboratory finding for SARS-Co-V.[10]

Statistical analysis

Statistical analysis was conducted using SPSS software (SPSS 10.0.5, Windows version).[11] Univariate analysis was used to identify factors associated with outcome. In the univariate analysis, the association between illness and categorical risk factors was assessed for statistical significance by the Chi-square test; the association for continuous variables was assessed using *t*-test. A two-sided *p*-value at a level of less than 0.05 was considered statistically significant. Odds ratios and 95% confidence intervals (95% CI) were also calculated.

Results

Surveillance

The first two suspected cases were diagnosed in a couple on 14 March 2003. The man was a 54-year-old businessman who had travelled to Guangdong Province, China, on 5 February and returned to Taipei via Hong Kong on 21 February. On 25 February he developed fever and myalgia, and later a dry cough, but was not hospitalized until 8 March. Several hours after admission he was intubated and required mechanical ventilation for 13 days. His wife and son were exposed during the period before full protective measures were in place, and both developed SARS with a requirement for mechanical ventilation. The infections in the wife and son were confirmed by RT-PCR testing to be associated with the novel coronavirus associated with SARS worldwide.[12–14] On 26 March a resident of Hong Kong's Amoy Gardens flew to Taiwan and took a train to Taichung. The man's brother became Taiwan's first SARS fatality. Between 14 March and 19 April, 51 people met the criteria for a probable case (Figure 1).

Suddenly, in the last ten days of April, the number of cases began to increase steadily. The first increase was in patients and staff at Hospital H and was attributed to a laundry worker employed at the hospital, aged 42 years with diabetes mellitus

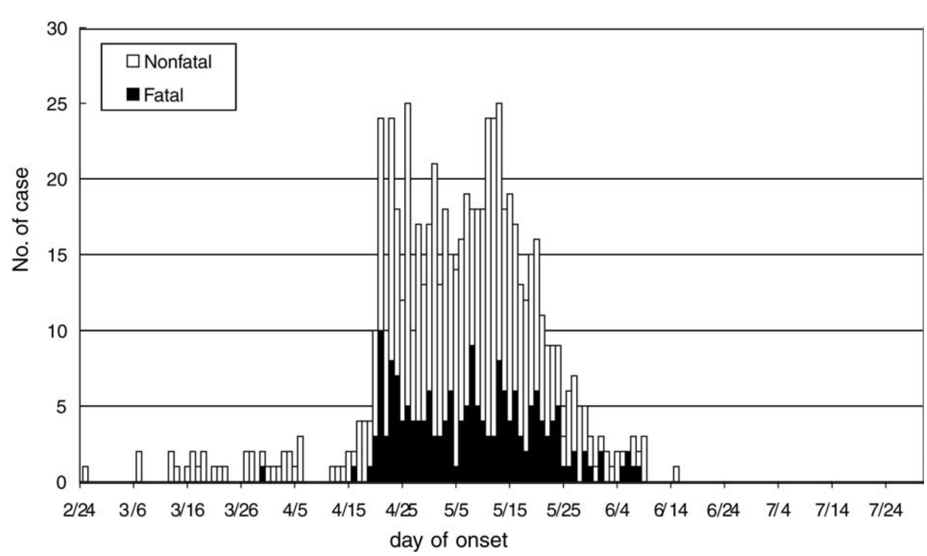

Figure 1 Number of cases and outcome of severe acute respiratory syndrome in Taiwan, February — July 2003.

and peripheral vascular disease. On 12 April he had a fever and diarrhea and was evaluated in the emergency department. The laundry worker remained on duty and interacted frequently with patients, staff, and visitors. He had sleeping quarters in the hospital's basement and spent off-duty time socializing in the emergency department. On 16 April, because of worsening symptoms, this worker was admitted to the hospital with a diagnosis of salmonellosis (infectious enteritis) and pulmonary edema. On 18 April he became short of breath. A chest radiograph showed bilateral infiltrates, and the patient was transferred to an isolation room in the intensive care unit with suspected SARS. This was a potential index patient because he had been symptomatic for six days before SARS was diagnosed. The number of potentially exposed persons was estimated at up to 10,000 patients and visitors, and 930 staff. On 24 April Hospital H was contained, and all patients, visitors, and staff were quarantined within the building.[15] During the period from 29 April to 14 June, a total of 151 SARS patients were transferred to 11 hospitals (mainly eight hospitals in Taipei city).

Case clusters at eight additional hospitals in Taiwan have been linked to the initial outbreak at Hospital H. Preliminary data suggested that many of these clusters occurred when pre-symptomatic patients, or patients with SARS whose symptoms were attributed to other causes, were discharged or transferred to other healthcare facilities. SARS later spread to multiple cities and regions of Taiwan, including several university and private hospitals. Four of these hospitals, including a 2300-bed facility in southern Taiwan, discontinued emergency and routine services.[15]

Morbidity

Between 14 March and 30 July 2003, a total of 3032 patients were reported to the Department of Health in Taiwan as having possible SARS. Among them, 668 (22%) patients met the May WHO criteria for a probable case. Among these probable cases, 53 (8%) were reported to have travelled to mainland China and Hong Kong in the ten days before the onset of illness, 41 (6%) were close contacts of a known case, 376 (56%) were hospital-related of whom 120 (19%) were health care workers (17 doctors, 63 nurses, and 40 allied health care workers) and 256 (38%) were in the same medical ward or had visited their relatives there (Table 1). Exposure for 198 (30%) could not be determined. There were 319 (48%) male patients and 349 (52%) female patients; their mean age was 51.2 ± 20.3 years. A total of 112 (17%) had coexisting medical conditions: diabetes in 39, cardiovascular disease in 29, chronic pulmonary disease in 13, chronic liver disease in three, chronic renal failure in ten, cancer in 13, immunologic disease in five. Most of the health care workers were previously healthy. All patients were ethnic Chinese.

The most common symptoms at presentation were fever (96.9%), cough (62%), breathing difficulty (28.6%), diarrhea (18.7%), sputum production (15.1%), sore throat (14.4%), myalgia (13.8%), headache (12.1%), and rigor (11.8%). Less common symp-

Table 1 Demographic characteristics of SARS patients and relationship to fatal outcome, 2003.

Variable	Probable cases			*p*-value
	Living N (%) (*N* = 487)	Deceased N (%) (*N* = 181)	Total N (%) (*N* = 668)	
Mean age in years	47.2 ± 21.1	61.8 ± 18.2	51.2 ± 20.3	<0.001
Sex				<0.05
Female	272 (78)	77 (22)	349 (52)	
Male	215 (67)	104 (33)	319 (48)	
Contact tracing				<0.001
Imported	51 (96)	2 (4)	53 (8)	
Household close contact	37 (90)	4 (10)	41 (6)	
Health care workers	103 (86)	17 (14)	120 (18)	
Doctor	*14*	*3*	*17*	
Nurse	*59*	*4*	*63*	
Allied	*30*	*10*	*40*	
Hospitalized patient	138 (54)	118 (46)	256 (38)	
Not identified	158 (80)	40 (20)	198 (30)	
Coexisting medical disorder				<0.001
No	439 (79)	117 (21)	556 (83)	
Yes	48 (43)	64 (57)	112 (17)	

toms included general malaise (7.3%), rhinorrhea (4.9%), and vomiting (4.6%).

Mortality

Of the 668 patient cases, 181 (27%) were fatal. This was a crude mortality rate to provide a comparison with other countries that used this method. Of the 64 (57%) who died with coexisting medical conditions, 22 had diabetes, 21 cardiovascular disease, nine had cancer, five had chronic pulmonary disease, three had chronic renal failure, three had immunologic disease and one had chronic liver disease (Table 1). The average age of patients who died was 61.8 ± 18.2 years (males 64.9 ± 16.9; females 57.6 ± 19.2). Compared to cases that survived, the fatal cases were older (61.8 ± 18.2 years vs 47.2 ± 21.1, $p < 0.001$), more often male (RR = 1.50, 95% CI 1.2—1.9, $p < 0.05$), and more often had a coexisting medical condition (RR = 2.7; 95% CI 2.2—3.4, $p < 0.001$).

The mortality by age and sex are shown in Table 2. Males had higher mortality than females (32.6% vs 22.1%, $p < 0.05$). For males, the age-specific mortality ranged from 9.4% for persons aged 0—29 years to 52.5% for those over 60 years. The risk of fatality was significant ($p < 0.001$) among patients who were older than 60 years (RR = 5.6; 95% CI = 2.4—13.0). For females, the age-specific mortality ranged from 8.1% for persons aged 0—29 years to 57.1% for person over 60 years. The risk of fatality was significant ($p < 0.001$) among patients who were older than 60 years (RR = 7.1; 95% CI = 3.7—13.6). It can be seen that mortality increased significantly ($p < 0.0001$) with age for males (Chi-square for linear tread = 37.8) and females (Chi-square for linear tread = 52.8)

Based on the WHO case definition of August,[10] there were 346 confirmed cases with 73 deaths (directly due to SARS, 37; SARS-related, 36). The mortality using this definition would be 21.1% (73/346), or 10.7% (37/346) when calculated according to the proposed method.

Laboratory examination

Nasopharyngeal swab and stool specimens obtained from reported patients were examined by the laboratory at the Center for Disease Control, Department of Health in Taiwan. From April through August 2003, RT-PCR tests of coronavirus were detected from 3032 patients, and 346 were positive. The frequency of RT-PCR positive for SARS coronavirus varied significantly between probable cases (37.5%), suspected case (3.5%), and excluded (0.9%).

Quarantine

Between 28 March and 11 July, a total of 151,270 (class A, 55,315; class B, 95,955) had been quarantined. Among the persons placed under class A quarantine, 112 were suspected patients of whom 34 or 6.1/10,000 were subsequently classified as having probable SARS. Among the persons placed under class B quarantine, 21 were suspected cases of whom 12 or 1.3/10,000 were subsequently classified as having probable SARS.

Measurement of body temperature

Between 10 April and 29 July 2003, the total number of passengers who had their temperature taken was 2,760,379 (inbound, 1,317,159; outbound, 1,443,220). Among them, 2134 (0.08%) had fever, of whom four or 1.4/1,000,000 were subsequently classified as having probable SARS.

Hospital infection control practices

Selected infection control practices in place at the time of the mobile team visits are summarized in

Table 2 Mortality of severe acute respiratory syndrome by age and sex in Taiwan, February — July 2003.

Age group (years)	Male[b]			Female[c]		
	Cases (N)	Deaths N (%)	Relative risk[a] (95% CI)	Cases (N)	Deaths N (%)	Relative risk[a] (95% CI)
0—29	53	5 (9.4)	1.0 (Referent)	111	9 (8.1)	1.0 (Referent)
30—59	144	35 (24.3)	2.6 (1.1—6.2)*	168	28 (16.7)	2.1 (1.0—4.2)*
≥60	122	64 (52.5)	5.6 (2.4—13.0)**	70	40 (57.1)	7.1 (3.7—13.6)**
Total	319	104 (32.6)		349	77 (22.1)	

[a] χ^2 test.
[b] Chi square for linear trend = 37.8, $p < 0.0001$.
[c] Chi square for linear trend = 52.8, $p < 0.0001$.
* $p < 0.05$.
** $p < 0.001$.

Table 3 Selected SARS infection control practices at the time of visit for hospitals investigated by mobile teams in Taiwan, March — May 2003.

Infection control practices	Frequency *N* = 86	%
Administrative measures		
Written ICP protocol for SARS	83	97
Triage and segregation of possible SARS case-patients	46	53
Non-SARS patients admitted to same ward	66	77
Restricted traffic outside patients' rooms	59	69
Hospital policy prohibited visitors from patients' rooms	65	76
Environmental engineering measures		
Private rooms for SARS case-patients	79	92
Handwashing facilities immediately outside patients' rooms	75	87
Separate dressing area for PPE and anteroom	64	74
Negative air pressure at patients' doors documented by mobile team	56	65
Personal protective equipment		
N-95 or better respirator used by hospital staff	62	72
Hospital staff used eye protection	62	72
Hospital staff used single gown with apron or double gowns	62	72
Hospital staff used double gloves	62	72
Hospital staff used head and foot covers	62	72

SARS: Severe acute respiratory syndrome; ICP: Infection control practices; PPE: Personal protective equipment.

Table 3. Between 16 March and 10 May mobile teams assessed a total of 86 hospitals. Fifty-three percent of the study hospitals had triage and segregation of possible SARS case-patients, but 24% (21/86) did not prohibit visitors from patients' rooms and 31% (27/86) did not restrict traffic outside the patients' rooms.

Of the study hospitals, 87% (75/86) had hand-washing facilities immediately outside patients' rooms or anterooms. At the other 11 hospitals, hand-washing facilities were at a location further from the anteroom. Seventy-nine (92%) had private rooms for SARS case-patients and 72% (62/86) had N-95 or better respirators in stock. Seventy-two percent used at least one layer of protective gown and had access to eye protection, head covers, and foot protection.

Overall, at the time of the mobile team visits, 46 (53%) hospitals implemented recommendations of triage and segregation of possible SARS case-patients, private negative pressure isolation rooms, minimal PPE for all staff entering patients' rooms, and effective visitor policies (visitors restricted from patients' rooms).[16,17]

Discussion

This reported outbreak of SARS in Taiwan caused 668 probable cases with severe deterioration of pulmonary function and 181 deaths. Consistent with other findings,[18,19] healthcare workers in Taiwan were at higher risk of infection from SARS. Within three months, SARS developed in 120 healthcare workers after exposure at work in the medical ward where the index patient was hospitalized. All had unremarkable medical histories. Recent reports suggest that infection control practices can be effective in some settings.[20,21] Just over half (53%) of Taiwanese hospitals had implemented recommended infection control practice at the time of the mobile team visits; however, as with another report,[22] an outbreak occurred among hospital healthcare workers.

As more becomes known about the transmission of SARS-associated coronavirus infections, infection control practices at hospitals evaluating patients for SARS will need to evolve. Even as the SARS epidemic appears to wane,[23] being prepared for SARS infection control remains important among hospitals. Future studies should evaluate the effectiveness of specific infection control practices, as well as assess the implementation of effective measures in countries affected by SARS.

In this study, a substantial difference was documented in both the number of cases and the mortality rate after applying the WHO definition proposed in August 2003. It is important to note that the later definition, published after the outbreak was over, was developed to serve a different purpose. In May 2003, the case definition focused on the clinical picture, and was deliberately sensitive in order to identify most suspected cases and implement control measures for SARS. The case definition in August was modified to increase specificity by focusing on laboratory confirmed cases. In addition, the new definition allows for the calculation of a low mortality mainly by permitting deaths in SARS patients to be attributed to other underlying diseases and therefore not contribute to the numerator. Including SARS patients regardless of etiology would prevent subjectivity and provide more uniform data for comparison across countries.

Quarantining the contacts is a new challenge to the public. Within this period between 28 March and 30 July, a total of 151,270 persons (0.7% of the population of Taiwan) were quarantined. Only 46 (class A, 34; class B, 12) were subsequently classified as probable cases. In humans infected with the virus there is a wide range of reported incubation periods, from five to 15 days, before patients become symptomatic.[18,19] This lag time allows apparently healthy people to travel by air almost anywhere in the world after they have been exposed. Once they become symptomatic, the disease is most likely spread through person-to-person transmission.[24] As expected, based on the known transmission patterns for SARS,[19,20] the fact that transmission appeared to occur from patients in the symptomatic phase of illness, but not from those who were in the pre-symptomatic phase, suggests that the risk of transmission varies by the phase of illness. It is likely that persons who were in contact with patients with the pre-symptomatic phase were at low risk. The fact that transmission has been limited to only close contacts of patients, such as healthcare workers and family members who were not using contact or respiratory precautions, suggests that either droplet secretions or direct contact probably played a role.[4] SARS patients should limit interactions outside the home and should not go to work, school, out-of-home childcare or other public areas until ten days after the resolution of fever. In Taiwan, family and other close contacts, those on airplanes with ill SARS patients (if seated within three rows in front or three rows behind the patient), and those returning from SARS affected areas were given strictly compulsory home quarantine for ten days. It must be considered whether in the future household members or other close contacts of SARS patients need to limit their activities outside the home as recommended by the USA CDC.[25]

Epidemiologic investigation and laboratory studies suggest that most patients with illnesses meeting the case definition of SARS in Taiwan were linked to a common source. To date, 37.5% of cases identified in this report were confirmed positive.

In this study, some clinical and laboratory features were identified on presentation that were associated with death. Advanced age, being male, and coexisting underlying medical conditions were independent predictors of mortality from SARS. Information on hepatitis B status was not systematically collected, a risk factor reported elsewhere.[26]

SARS has already become a global health hazard, and its high infectivity is alarming. The decrease in worldwide incidence is gratifying; but it may simply reflect the seasonal variation in the transmission of the virus.[24] Some experts have predicted the return of SARS in the cool season. Containing an outbreak at an early stage affords a greater chance of success than does a later response and clearly puts less strain on the healthcare system. Future strategies to control the spread of SARS need to emphasize the greater risk to certain populations: health care workers, older people, and people who have chronic diseases. Isolation of cases, stringent infection control measures in hospitals, and vigilant surveillance at both community and population levels are imperative.[26–28]

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