

March

12 March 2003 (Wed)

World Health Organization

◆ Causative agent

Unknown. No link has been made between the outbreaks in Hanoi and Hong Kong and the outbreak of Influenza A (H5N1) in Hong Kong reported on 19 February 2003. *[Press release]*

◆ Clinical Features

The signs and symptoms of the disease in Hanoi include initial flu-like illness (rapid onset of high fever followed by muscle aches, headache and sore throat). In some cases, this is followed by bilateral pneumonia, then progressing to acute respiratory distress requiring assisted ventilation. Early laboratory findings may include thrombocytopenia and leucopenia. *[Press release]*

◆ Isolation and precautions

Recommending patients with atypical pneumonia who may be related to the outbreak in Hanoi and Hong Kong be isolated with barrier nursing techniques. *[Press release]*

◆ Transmission

The disease appears to be confined to the hospital environment. Those at highest risk appear to be staff caring for the patients. *[Press release]*

15 March 2003 (Sat)

World Health Organization

◆ Case definition

Suspect case

A person presenting after 1 February 2003 with history of

- high fever ($>38^{\circ}\text{C}$), AND
- one or more respiratory symptoms including cough, shortness of breath, difficulty breathing, AND
- one or more of the following: close contact* with a person who had been diagnosed with SARS, or recent history of travel to areas reporting cases of SARS.

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Probable case

A suspected case with chest x-ray findings of pneumonia or respiratory distress syndrome, OR

A person with an unexplained respiratory illness resulting in death, with an autopsy examination demonstrating the pathology of respiratory distress syndrome without an identifiable cause.

* *Close contact means having cared for, having lived with, or having had direct contact with respiratory secretions and body fluids of person with SARS. [Press release]*

◆ Clinical features

In addition to fever and respiratory symptoms, SARS may be associated with other symptoms including: headache, muscular stiffness, loss of appetite, malaise, confusion, rash, and diarrhea. *[Press release]*

◆ Isolation and precautions

Patients with SARS be isolated with barrier nursing techniques. *[Press release]*

◆ Treatment

Patients with SARS be treated as clinically indicated. *[Press release]*

16 March 2003 (Sun)

World Health Organization

◆ Case definition

Suspect case

A person presenting after 1 February 2003 with history of

- high fever (>38°C), AND
- one or more respiratory symptoms including cough, shortness of breath, difficulty breathing, AND
- one or more of the following: close contact*, within 10 days of onset of symptoms, with a person who had been diagnosed with SARS, or
- history of travel, within 10 days of onset of symptoms, to an area in which there are reported foci of transmission of SARS.

Probable case

A suspect case with chest x-ray findings of pneumonia or respiratory distress syndrome, OR

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A suspect case with an unexplained respiratory illness resulting in death, with an autopsy examination demonstrating the pathology of respiratory distress syndrome without an identifiable cause.

* *Close contact means having cared for, having lived with, or having had direct contact with respiratory secretions and body fluids of person with SARS. [Weekly Epidemiological Record (78)12;81-88]*

◆ Isolation and precautions

Respiratory isolation, strict respiratory and mucosal barrier nursing are recommended for cases. *[Situation updates]*

◆ Transmission

Majority of cases have occurred in people who have had very close contact with other cases and over 90% of cases have occurred in health care workers. The mode of transmission has yet to be determined. Aerosol and/or droplet spread is possible as in transmission from body fluid. *[Situation updates]*

17 March 2003 (Mon)

World Health Organization

◆ Transmission

The disease is spread from person to person but only through close contact with a case. Almost all reported cases have been occurred in health workers involved in the direct care of reported cases or in close contacts, such as family members. There is no evidence that the disease spreads through casual contact. *[Situation updates]*

19 March 2003 (Wed)

Centers for Disease Control and Prevention, Atlanta, USA

◆ Case definition

Suspect case

Respiratory illness of unknown aetiology with onset since 1 February 2003, and the following criteria -

- documented temperature > 38°C
- one or more symptoms of respiratory illness (eg cough, shortness of breath, difficulty breathing, or radiography findings of pneumonia or acute respiratory distress syndrome)
- close contact* within 10 days of onset of symptoms with a person under investigation or suspected of having SARS or a person with

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symptoms and a history of travel to an area with documented transmission of SARS as defined by WHO

- * *Defined as having cared for, having lived with, or having had direct contact with respiratory secretion and/or body fluid of a person suspected of having SARS. [Morbidity and Mortality Weekly Report (MMWR) 52(11);226-228]*

World Health Organization

- ◆ Causative agent

Research teams at two laboratories, in Germany and Hong Kong have detected particles of a virus from the Paramyxoviridae family in samples taken from SARS patients. Firm conclusions about the identity of the causative agent are premature. The failure of all previous efforts to detect the presence of bacteria and viruses known to cause respiratory disease strongly suggests that the causative agent may be a novel pathogen. *[Situation updates]*

21 March 2003 (Fri)

World Health Organization

- ◆ Causative agent

The infectious agent resembles the morphology of a Paramyxovirus. Scientists cannot, however, be certain about the identity of the virus, which may indeed be a new Paramyxovirus or another virus with a similar pathology. *[Situation updates]*

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Clinical features

Among patients reported worldwide as of 19 March 2003, incubation period has generally been 3-5 days (range: 2-7 days). The disease has been characterised by rapid onset of high fever, myalgia, chills, rigor, and sore throat, followed by shortness of breath, cough, and radiographic evidence of pneumonia. Laboratory findings have included thrombocytopenia and leukopenia. Many patients have had respiratory distress or severe pneumonia requiring hospitalisation, and several have required mechanical ventilation. *[MMWR 52(11); 226-228]*

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World Health Organization

- ◆ Clinical features

The incubation period of SARS is usually 2-7 days but may be as long as 10 days. The illness generally begins with a prodrome of fever ($>38^{\circ}\text{C}$), which is often high, sometimes associated with chills and rigors, headache, malaise and myalgia. At the onset of illness, some cases have mild respiratory symptoms. Typically, rash and neurologic and gastrointestinal findings are absent, although a few patients have reported diarrhea during the febrile prodrome. After 3-7 days, a lower respiratory phase begins with onset of a dry, non-productive cough or dyspnea that may be accompanied by or progress to hypoxemia. 10 – 20 % of cases are severe enough to require intubation and mechanical ventilation. The case-fatality among probable and suspected cases is around 3%. Early decrease in lymphocyte count with overall normal or decreased white cell count are observed. At the peak of the respiratory illness, up to half of patients have leukopenia and thrombocytopenia. Elevated creatine phosphokinase and hepatic transaminases levels have been noted. Renal function has remained normal in the majority of patients. *[Preliminary Clinical Description of SARS]*

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Isolation and precautions

Clinicians evaluating suspected cases should use standard precautions (eg hand hygiene) together with airborne (eg N95 respirator) and contact (eg, gowns and gloves) precautions. Until the mode of transmission has been defined more precisely, eye protection should also be worn for all patient contact. *[MMWR 52 (11);226-228]*

World Health Organization

- ◆ Isolation and precautions

Criteria for making decision regarding discharge

- Afebrile for 48 hours
- Resolving cough
- Improving chest x-ray changes

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- Returning to normal level, if previously abnormal
 - white cell count
 - platelet count
 - creatine phosphokinase
 - liver function tests
 - plasma sodium
 - c-reactive protein

Follow-up

Discharge patient should

- monitor and record their temperature twice daily
- remain at home for 7 days
- follow up at one week
- take convalescent serology at 3 weeks after onset

[WHO hospital discharge and follow-up policy for patient who have been diagnosed with SARS]

◆ Isolation and precautions

Respiratory precaution and barrier nursing are advised for all health care workers and visitors in close contact with reported cases. *[Weekly Epidemiological Record (78)12;81-88]*

◆ Treatment

The most efficacious treatment regime, if any, is unknown. *[Preliminary Clinical Description of SARS]*

◆ Treatment

No clinical improvement has been attributable to the use of antibiotics. The antiviral agent ribavirin, given intravenously in combination with high-dose corticosteroids, may have been responsible for some clinical improvement observed in critically ill patients in Hong Kong. Intensive and good supportive care, with or without antiviral agents, have also improved prognosis. *[Weekly Epidemiological Record (78) 12;81-88]*

22 March 2003 (Sat)

Centers for Disease Control and Prevention, Atlanta, USA

◆ Case definition

Suspect case

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Respiratory illness of unknown aetiology with onset since 1 February 2003, and the following criteria -

- measured temperature > 38°C
- one or more clinical findings of respiratory illness (eg cough, shortness of breath, difficulty breathing, hypoxia, or radiography findings of either pneumonia or acute respiratory distress syndrome)
- travel within 10 days of onset of symptoms to an area with suspected or documented community transmission of SARS (excluding areas with secondary cases limited to health-care workers or direct household contacts)

OR

- close contact* within 10 days of onset of symptoms with either a person with respiratory illness with a history of travel to a SARS area or a person under investigation or suspected of having SARS.

* *Defined as having cared for, having lived with, or having had direct contact with respiratory secretion and/or body fluid of a patient suspected of having SARS. [MMWR 52(12);241-248]*

◆ Causative agent

Laboratory analysis had identified a previously unrecognised coronavirus in patients with suspected or probable SARS. The new coronavirus was isolated in Vero E6 cells from clinical specimens of two patients in Thailand and Hong Kong with suspected SARS. Sequence analysis suggests that this new agent is distinct from other known coronaviruses. Other laboratories collaborating in the WHO-led investigation have found similar results and also have isolated a different virus, human metapneumovirus, from some patients with suspected SARS. Information is insufficient to determine what roles these two viruses might play in the aetiology of SARS. [MMWR 52 (12);241-248]

World Health Organization

◆ Causative agent

A team of scientists from the University of Hong Kong has announced success in culturing the viral agent. While the Canadian researcher released findings suggesting that the metapneumovirus, which belongs to the paramyxoviridae family, may be the cause. It cannot be ruled out that an entire different virus from another family is responsible for the outbreak. [Situation updates]

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25 March 2003 (Tue)

World Health Organization

- ◆ Transmission

Report of a possible transmission of SARS on board a flight is under investigation. As “close” contact is possible during a flight for passengers sitting close to an infected person, such transmission cannot be ruled out. The evidence indicates that in-flight transmission is very unusual. *[Situation updates]*

26 March 2003 (Wed)

World Health Organization

- ◆ Causative agent

Research attention is increasingly focusing on the Coronavirus family, though viruses from the Paramyxovirus and other families are also being considered as scientists are casting the widest possible net in their search for the cause of SARS. Many are of the opinion that a diagnostic test could rapidly follow a conclusive identification of the pathogen. Experts in the network are also considering the theory that SARS is caused by co-infection with two new viruses that somehow need each other in order to cause severe disease in humans. Evidence is strongly pointing to a new virus, or possibly two new viruses, that have not previously been known to infect humans or cause severe disease.

Hypotheses include: a virus known to cause disease in an animal host has jumped the species barrier to infect humans, or a known human virus has mutated to acquire properties that are causing much more severe disease in humans. It is increasingly certain, however, that SARS is a serious new disease caused by a newly recognised pathogen. *[Situation updates]*

28 March 2003 (Fri)

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Causative agent

Although the etiologic agent has not been confirmed, laboratory data indicate that a metapneumovirus or a coronavirus are possible agents. Infection with a metapneumovirus, (ie, enveloped, single-stranded

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RNA virus) has been associated previously with respiratory disease with much less frequent occurrence of severe disease than SARS. Coronaviruses are enveloped, single-stranded RNA viruses that infect both humans and animals. [MMWR 52(12);241-248]

- ◆ Isolation and precautions

Infection-control recommendations should include precautions to prevent airborne, droplet, and contact transmission. [MMWR 52(12);241-248]

- ◆ Transmission

The mechanism of SARS transmission remains unclear. On the basis of the reported exposures for the majority of cases (ie, household contacts and healthcare workers), droplet and contact transmission appear to be the predominant modes. The cases in the outbreak in *Hotel M* and certain hospitals involving seriously ill patients suggest airborne or fomite transmission.

Coronaviruses are able to survive on environmental surfaces for up to 3 hours. Coronaviruses might be transmitted person-to-person by droplets, hand contamination, fomites, and small particle aerosols. [MMWR 52(12);241-248]

31 March 2003 (Mon)

Peer-reviewed journals

- ◆ Causative agent

The microbiological origins of SARS remained unclear. There was no evidence of infection by mycoplasma pneumoniae, Chlamydia pneumoniae, or Legionella pneumophila.

[Information based on 10 epidemiologically linked cases, published at www.nejm.org on 31 March 2003] [New England Journal of Medicine (NEJM) 348(20);1977-1985]

- ◆ Causative agent

The results of laboratory investigation were negative or not clinically significant except for the amplification of human metapneumovirus from respiratory specimens from 5 of 9 patients and the isolation and amplification of a novel coronavirus from 5 of 9 patients. In 4 cases,

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both pathogens were isolated. The role of the two viruses was not clear and requires further investigation.

[Information based on 10 cases from Canada published at www.nejm.org on 31 March 2003] [NEJM 348(20);1995-2005]

- ◆ Clinical features

The incubation period ranged from 2 to 11 days. Most patients had onset of symptoms 2 to 5 days after exposure.

All patients presented with fever (>38°C for over 24 hours), and most presented with rigor, dry cough, dyspnea, malaise, headache, and hypoxemia. Physical examination of the chest revealed crackles and percussion dullness. Lymphopenia was observed in nine patients, and most patients had mildly elevated aminotransferase levels but normal serum creatinine levels. Serial chest radiographs showed progressive air-space disease. Predominant abnormalities found on initial CT scans were subpleural focal consolidation with air bronchograms and ground-glass opacities. Two patients died of progressive respiratory failure; histological analysis of their lungs showed diffused alveolar damage.

[Information based on 10 epidemiologically linked cases, published at www.nejm.org on 31 March 2003] [NEJM 348(20);1977-1985]

- ◆ Clinical features

The most common presenting symptoms were fever (100%) and malaise (70%), followed by nonproductive cough (100%) and dyspnea (80%) associated with infiltrates on chest radiography (100%). Lymphopenia (89% of cases whose data were available), elevated lactate dehydrogenase levels (80%), elevated aspartate aminotransferase levels (78%), and elevated creatinine kinase levels (56%) were common.

Mechanical ventilation was required in 5 patients. 3 patients died, and five have had clinical improvement. Advanced age and tobacco smoking may be a risk factor for more severe SARS.

[Information based on 10 cases from Canada published at www.nejm.org on 31 March 2003] [NEJM 348(20);1995-2005]

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- ◆ Transmission

Transmission occurred only after close contact (eg household members, health care workers, or other patients who were not protected with contact or respiratory precautions). The observed patterns suggested droplet or contact transmission.

[Information based on 10 cases from Canada published at www.nejm.org on 31 March 2003] [NEJM 348(20);1995-2005]

- ◆ Treatment

There was no clinical response to combined therapy with a beta-lactam and a macrolide. Empirical treatment with a combination of a high dose corticosteroid and ribavirin coincided with clinical improvement.

[Information based on 10 epidemiologically linked cases, published at www.nejm.org on 31 March 2003] [NEJM 348(20);1977-1985]

- ◆ Treatment

Although the condition of 5 of 7 patients who had been treated with ribavirin had improved with therapy, the patient were treated with an array of therapeutic agents, and it was unclear whether ribavirin affected the clinical outcome. There is no definite therapy for adult respiratory distress syndrome (ARDS); therapy is supportive with the use of mechanical ventilation. The best approach for ventilating patient with SARS is not known, but it seems reasonable to adopt a lung-protective strategy that has been shown to decrease mortality in patients with ARDS.

[Information based on 10 cases from Canada published at www.nejm.org on 31 March 2003] [NEJM 348(20);1995-2005]

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1 April 2003 (Tue)

World Health Organization

◆ Case definition

Suspect case

A person presenting after 1 November 2002 with history of

- high fever ($>38^{\circ}\text{C}$), AND
- cough or difficulty breathing, AND
- one or more of the following exposure during the 10 days prior to onset of symptoms
 - close contact with a person who is a suspected or probable case of SARS, or
 - history of travel to an affected area
 - residing in an affected area

Probable case

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

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

Exclusion criteria

A case should be excluded if an alternative diagnosis can fully explain their illness.

Reclassification of cases

As SARS is currently a diagnosis of exclusion, the status of a reported case may change over time:

- A case initially classified as suspect or probable, for whom an alternative diagnosis can fully explain the illness, should be discarded.
- A suspect case who, after investigation, fulfil the probable case definition should be reclassified as "probable".
- A suspect case with a normal CXR should be treated, as deemed appropriate, and monitored for 7 days. Those cases in whom recovery is inadequate should be re-evaluated by CXR.
- Those suspect cases in whom recovery is adequate but whose illness cannot be fully explained by an alternative diagnosis should remain as "suspect".
- A suspect case who dies, on whom no autopsy is conducted, should remain classified as "suspect". However, if this case is identified as being part of a chain transmission of SARS, the case should be reclassified as "probable".
- If an autopsy is conducted and no pathological evidence of RDS is found, the case should be "discarded". [*SARS information*]

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2 April 2003 (Wed)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Causative agent The agent causing SARS has not been fully characterised [Situation updates] ◆ Transmission The outbreak in Hong Kong has developed an unusual pattern of transmission. This pattern is different from what is being seen in the vast majority of other SARS outbreak, and is not yet fully understood. There may involve transport of the virus from one person to another via some type of environmental means. [Situation updates]
4 April 2003 (Fri)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Transmission The health authority of Hong Kong is investigating sewage samples and sewage pipe as the source of outbreak occurring in Amoy Gardens Block E. [Situation updates]
7 April 2003 (Mon)	<p>Peer-reviewed journals</p> <ul style="list-style-type: none"> ◆ Clinical Features The clinical, laboratory and radiological features of 138 cases of suspected SARS during a hospital outbreak in Hong Kong was reported. The most common symptoms included fever (100%); chills, rigor, or both (73.2%); and myalgia (60.9%). Cough and headache were also reported in more than 50% of patients. Other common findings were lymphopenis (69.9%), thrombocytopenia (44.8%) and elevated lactate dehydrogenase and creatine kinase levels (71% and 32.1 % respectively). Peripheral air-space consolidation was commonly observed on thoracic CT scanning. A total of 32 patients (23.2%) were admitted to ICU; 5 patients died, all of whom had co-existing conditions. In a multivariate analysis, the independent predictors of an adverse outcome were advance age (per decade OR 1.80 95% CI 1.16 to 2.81), a high peak lactate dehydrogenase level (per 100U per litre

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2.09; 1.28 to 3.42), and an absolute neutrophil count that exceeded the upper limit of the normal range on presentation (1.60, 1.03 to 2.50).

[published at www.nejm.org on 7 April 2003] [NEJM 348(20);1986-94]

World Health Organization♦ **Diagnosis**

Three diagnostic tests are available and all have limitations. The ELISA detects antibodies reliably but only from about day 20 after the onset of clinical symptoms. It therefore cannot be used to detect cases at an early stage before they have a chance to spread the infection to others. The second test, an immunofluorescence assay (IFA), detects antibodies reliably as of day 10 of infection, but is a demanding and comparatively slow test that requires the growth of virus in cell culture. The presently available PCR molecular test for detection of genetic material of SARS virus is useful in the early stages of infection but produces many false-negatives, meaning that many people who actually carry the virus may not be detected, thus creating a dangerous sense of false security for a virus that is known to spread easily in close person-to-person contact.

[Situation updates]

♦ **Transmission**

Evidence that the causative agent is excreted in faeces has focused attention on the possibility of an oral-faecal route of transmission, though no conclusions have been reached. *[Situation updates]*

8 April 2003 (Tue)

Peer-reviewed journals♦ **Causative agent**

50 patients with SARS were studied. A virus belonging to the family of Coronaviridae was isolated in two patients. By using serological and reverse-transcriptase PCR specific for this virus, 45 out of 50 patients with SARS (but no control group) had evidence of infection with this virus, which might be the primary agent associated with the disease.

[published online on 8 April 2003] [Lancet 396(9366); 1319-25]

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- ◆ Clinical Features

Patients who were household contacts of other infected cases, and who was of older age, had lymphopenia and liver dysfunction, were associated with severe disease.

[published online on 8 April 2003] [Lancet 396(9366); 1319-25]

10 April 2003 (Thu)

Peer-reviewed journals

- ◆ Causative agent

A novel coronavirus was identified in patients with SARS. Genetic characterisation indicated that the virus is only distantly related to known coronavirus (identical in 50 - 60% of the nucleotide sequence). High concentration of viral RNA of up to 100 million molecules per ml were found in sputum. Viral RNA was also detected at extremely low concentration in plasma during the acute phase and in faeces during the late convalescent phase.

[published at www.nejm.org on 10 April 2003] [NEJM 348(20);1967-76]

11 April 2003 (Fri)

World Health Organization

- ◆ Clinical features

The global case-fatality rate for probable SARS is 4%. Higher case-fatality rate appears to be linked to older age, who frequently have underlying chronic disease. Children appear to be less likely to present with SARS than adults. *[SARS information]*

- ◆ Management of contacts

Management of contacts of probable SARS cases

- Give information on clinical picture, transmission, etc. of SARS to the contact
- Place under active surveillance for 10 days and recommend voluntary home isolation
- Ensure contact is visited or telephoned daily by a member of the public health care team.
- Record temperature daily
- If the contact develops disease symptoms, the contact should be investigated locally at an appropriate health care facility

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- The most consistent first symptom that is likely to appear is fever

Management of contacts of suspect SARS cases

- Give information on clinical picture, transmission, etc. of SARS to the contact
- Place under passive surveillance for 10 days
- If the contact develops any symptoms, the contact should self-report via the telephone to the public health authority
- Contact is free to continue with usual activities
- The most consistent first symptom that is likely to appear is fever

[SARS information]

12 April 2003 (Sat)

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Isolation and precautions

The duration of time before or after onset of symptoms during which a patient with SARS can transmit the disease to others is unknown. SARS patients should limit interactions outside the home and should not go to work, school, out-of-home childcare, or other public areas until 10 days after the resolution of fever, provided respiratory symptoms are absent or improving. *[Interim guidelines on infection control precautions for patients with suspected SARS and close contacts in household]*

- ◆ Management of contacts

The close contacts of SARS patients should be vigilant of the development of fever or respiratory symptoms. In the absence of fever or respiratory symptoms, household members of other close contacts of SARS patients need not limit their activities outside home. *[Interim guidelines on infection control precautions for patients with suspected SARS and close contacts in household]*

13 April 2003 (Sun)

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Management of contacts

Persons who may have been exposed to SARS should be vigilant for fever or respiratory symptoms over the 10 days following

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exposure; those who develop fever or respiratory symptoms should limit interactions outside the home and should not go to work, school, out-of-home childcare, church or other public areas. Symptomatic persons should use infection control precautions to minimise the potential for transmission and should seek healthcare evaluation. Healthcare workers should be informed of the possible exposure in advance of the evaluation.

If symptoms do not progress to meet the suspect SARS case definition within 72 hours after first symptoms onset, the person may be allowed to return to work, school, out-of-home childcare, church or other public areas, and infection control precautions can be discontinued. *[Interim domestic guidance on persons who may have been exposed to patients with suspected SARS]*

14 April 2003 (Mon)

Centers for Disease Control and Prevention, Atlanta, USA

◆ Causative agent

The CDC has sequenced the genome for the coronavirus believed to be responsible for the global epidemic of SARS. The CDC's sequence is nearly identical to that determined by a Canadian laboratory late last week. The significant difference is that the CDC-determined sequence has 15 additional nucleotides, which provides the important beginning of the sequence. The new sequence has 29 727 nucleotides, which places well within the typical RNA boundaries for coronaviruses. The entire nucleotide sequence of the virus and the protein analysis phylogenetic tree is available on the CDC website. *[Press release]*

World Health Organization

◆ Causative agent

Canadian scientists have completed full sequencing of the genome of the SARS virus. *[Situation updates]*

◆ Clinical Features

Incubation period: most cases 2 to 10 days (up to 13 days reported) *[Interim guidelines for national SARS preparedness]*

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◆ Diagnosis

A PCR test, developed by the US Centers for Disease Control and Prevention, has been shown to be ten times more sensitive than previous PCR tests for SARS. *[Situation updates]*

◆ Isolation and precautions

Usual ward procedures alone are inadequate to prevent transmission in hospitals; prompt isolation and strict barrier nursing is required. Guidelines on use of PPE, triage and isolation are provided. *[Interim guidelines for national SARS preparedness]*

◆ Management of contacts

If symptoms do not progress to meet the suspect SARS case definition within 72 hours after first symptoms onset, the person may be allowed to return to work, school, out-of-home childcare, church or other public areas, and infection control precautions can be discontinued. *[Interim guidelines for national SARS preparedness]*

◆ Transmission

There may be low risk of transmission in the prodromal phase. *[Interim guidelines for national SARS preparedness]*

◆ Treatment

Maintain oxygenation - intubate and ventilate as required.

Antibiotic therapy on admission that will cover the common causative organisms in acquired pneumonia (including atypical pneumonia). Prophylactic antibiotics should also be used to prevent secondary bacterial infection.

In severe cases, corticosteroids and ribavirin (antiviral medication) have been used, however, there is no evidence to support their general or routine use at this stage. *[Interim guidelines for national SARS preparedness]*

16 April 2003 (Wed)

World Health Organization

◆ Causative agent

Scientists agreed that a new pathogen, a member of the coronavirus

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family never before seen in humans, is the cause of SARS (based on Koch's postulates). The new coronavirus has been named by WHO and member laboratories as "SARS virus". *[Situation updates]*

Peer-reviewed journals

- ◆ Psychological aspects

Patients with SARS reported fear, loneliness, boredom and anger, and they worried about the effects of quarantine and contagion on family members and friends. They experienced anxiety about fever and the effects of insomnia. Staff were adversely affected by fear of contagion and of infecting family, friends and colleagues. Caring for health care workers as patients and colleagues was emotionally difficult. Uncertainty and stigmatisation were prominent themes for both staff and patients. The hospital response required clear communication, sensitivity to individual response to stress, collaboration between disciplines, authoritative leadership and provision of relevant support. The emotional and behavioural reactions of patients and staff are understood to be a normal, adaptive response to stress in the face of an overwhelming event. *[published at www.cmaj.ca on 16 April 2003] [Canadian Medical Association Journal (CMAJ) 168(10); 1245-51]*

World Health Organization

- ◆ Transmission

The knowledge on how the virus is being excreted, by which excretor and secretor, and for how long is still incomplete. *[Press briefing]*

17 April 2003 (Thu)

World Health Organization

- ◆ Clinical features

The Amoy Gardens outbreak in Hong Kong had an unusual feature of a high proportion of cases presenting with diarrhoea, estimated at about 60%. In most other outbreaks, diarrhoea has typically been seen in only 2% to 7% of cases. *[Situation updates]*

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Peer-reviewed journals

◆ Isolation and precautions

In Ontario, all hospital staff, volunteers and visitors were screened using a standard questionnaire and when indicated, body temperature check. *[published at www.cmaj.ca on 17 April 2003] [CMAJ 168(10); 1294-5]*

◆ Treatment

Discussed the clinical course and successful treatment with convalescent plasma for a case of SARS.

[published at www.hkmj.org.hk on 17 April 2003] [Hong Kong Medical Journal (HKMJ) 9(3);199-201]

18 April 2003 (Fri)

Peer-reviewed journals

◆ Diagnosis

It was reported that the real-time quantitative PCR assay was positive in 79% of SARS cases and negative in 98% of control with and without viral infections. The test can be completed in 3-4 hours. *[Published at www.clinchem.org on 18 April 2003] [Clinical Chemistry 49 (6); 953 – 955]*

World Health Organization

◆ Transmission

Defective U-traps in bathrooms, an amplifying effect of bathroom exhaust fans, a cracked sewer vent pipe serving Amoy Gardens Block E, and an aerodynamic effect in a lightwell to which bathroom windows opened are thought to have been involved in the rapid spread of SARS to residents. The study found no epidemiological or laboratory evidence that the SARS virus was transmitted by air, water, or infected dust aerosols. *[Situation updates]*

19 April 2003 (Sat)

World Health Organization

◆ Clinical features

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Around 20% of the cases related to the Amoy Gardens outbreak require intensive care, compared with 10% seen in non-Amoy cases. Some deaths are now occurring in younger, previously healthy persons as well as in the elderly and persons with underlying disease. Speculation centres on whether these cases represent infection with high virus loads, as might occur following exposure to a concentrated environmental source, or whether the virus may have mutated into a more virulent form. *[Situation updates]*

23 April 2003 (Wed)

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Transmission

It is uncertain how long the SARS Coronavirus can survive in the environment. In one preliminary study, researchers in Hong Kong found that both dried and liquid samples of the virus survived as long as 24 hours in the environment. *[Frequently Asked Questions]*

24 April 2003 (Thu)

World Health Organization

- ◆ Isolation and precautions

Strict adherence to the barrier nursing of patients with SARS, using precautions of airborne, droplet and contact transmission. *[Hospital Infection Control Guidance for SARS]*

25 April 2003 (Fri)

Peer-reviewed journals

- ◆ Isolation and precautions

Report of measures taken by a community hospital in Ontario that brought SARS under control in 8 days, including the following:-

Infection control measures

- 10-day mass voluntary quarantine of over 500 staff, patients and visitors
- Completion of SARS screening questionnaire before entering hospital
- Measurement of oral temperature upon entering and exiting hospital

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- Wearing of gowns, gloves and N95 masks by all staff and visitors to hospital
- Stringent handwashing in all hospital areas
- Use of eye protection in patient care areas
- Wearing of double gowns, double gloves, and hair and shoe covers in high-risk areas (emergency department, ICU and SARS unit)
- Elimination of nebulised medication
- Moratorium on non-invasive ventilation

Organisational intervention

- Closing of emergency department
- Suspension of elective surgery
- Prevention of inter-facility patient transfer
- Cancellation of ambulatory clinics
- Cancellation of outpatient diagnostic procedures
- Prevention of hospital staff from working at other institutions
- Restriction of hospital visitors

Development of SARS assessment and treatment unit

- Dedicated 15-bed unit in a separate ward
- Single rooms
- Rooms retrofitted with externally exhaust HEPA filters
- 2 hospital-based internalists/intensivists for 24-hour patient care
- Full hemodynamic monitoring and ventilation support for critically ill patients with SARS

[published at www.cmaj.ca on 25 April 2003] [CMAJ 168(10); 1415-20]

29 April 2003 (Tue)

Centers for Disease Control and Prevention, Atlanta, USA

◆ Case definition

Probable case: meets the clinical criteria for severe respiratory illness of unknown aetiology with onset since 1 February 2003, and epidemiologic criteria; laboratory criteria confirmed, negative, or undetermined

Suspect case: meets the clinical criteria for moderate respiratory illness of unknown aetiology with onset since 1 February 2003, and epidemiologic criteria; laboratory criteria confirmed, negative, or undetermined

April

Clinical criteria

- Asymptomatic or mild respiratory illness
- Moderate respiratory illness
 - temperature > 38°C, AND
 - one or more clinical findings of respiratory illness (eg cough, shortness of breath, difficulty breathing, or hypoxia)
- Severe respiratory illness
 - temperature > 38°C, AND
 - one or more clinical findings of respiratory illness (eg cough, shortness of breath, difficulty breathing, or hypoxia)
 - autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause

Epidemiologic criteria

- travel (including transit in an airport) within 10 days of onset of symptoms to an area with current or recently documented or suspected community transmission of SARS, or
- close contact within 10 days of onset of symptoms with a person known or suspected to have SARS infection

Laboratory criteria

- Confirmed
 - detection of antibody to SARS Coronavirus (SARS-CoV) in specimens obtained during acute illness or more than 21 days after illness onset, or
 - detection of SARS-CoV RNA by RT-PCR confirmed by a second PCR assay, by using a second aliquot of the specimen and a different set of PCR primers, or
 - isolation of SARS Coronavirus
- Negative
 - absence of antibody to SARS-CoV in convalescent serum obtained more than 21 days after symptom onset
 - Undetermined: laboratory testing either not performed or incomplete

[MMWR 52; D429;1-3]

◆ Clinical Features

No instances of SARS-CoV infection have been detected in persons who are asymptomatic. However, data are insufficient to exclude the possibility of asymptomatic infection with SARS-CoV. [MMWR 52; D429;1-3]

April

Peer-reviewed journals

◆ Clinical Features

First 10 children with SARS managed during the early phase of the epidemic in Hong Kong were prospectively followed up. Two distinct patterns of clinical presentation among them were noted. Teenage patients presented with symptoms of malaise, myalgia, chill, and rigor similar to those of adults, whereas the younger children presented mainly with cough and runny nose, and none had chills, rigor, or myalgia. The clinical course was much milder and shorter among younger patients, and radiological changes were milder and generally resolved more quickly than the teenagers. The children were treated with high dose ribavirin, oral prednisolone, or intravenous methylprednisolone, with no short-term adverse effects. Four teenagers required oxygen therapy and two needed assisted ventilation. None of the younger children required oxygen supplementation. All paediatric patients had clinically important lymphopenia, but it was more severe among the teenagers.

Eight of the ten children had been attending school at the time of presentation. There was no evidence that they spread the infection to their classmates. This finding is in sharp contrast to the experience reported among adults that SARS carries a very high infectivity rate.

[published online on 29 April 2003] [Lancet 396(9370); 1701-3]

Centers for Disease Control and Prevention, Atlanta, USA

◆ Transmission

Data are insufficient to exclude the possibility of asymptomatic infection with SARS-CoV and the possibility that such persons can transmit the virus. *[MMWR 52; D429;1-3]*

May	
1 May 2003 (Thu)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Case definition <p><i>Suspect case</i></p> <p>(1) A person presenting after 1 November 2002 with history of</p> <ul style="list-style-type: none"> ○ high fever (>38°C), AND ○ cough or difficulty breathing, AND ○ one or more of the following exposure during the 10 days prior to onset of symptoms, <ul style="list-style-type: none"> - close contact with a person is a suspect or probable case of SARS, or - history of travel to an area with recent local transmission of SARS - residing in an area with recent local transmission of SARS <p>(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 exposure during the 10 days prior to onset of symptoms</p> <ul style="list-style-type: none"> ○ close contact with a person who is a suspect or probable case of SARS, or ○ history of travel, to an area with recent local transmission of SARS ○ residing in an area with recent local transmission of SARS <p><i>Probable case</i></p> <p>(1) A suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome on chest x-ray.</p> <p>(2) A suspect case of SARS that is positive for SARS coronavirus by one or more assays.</p> <p>(3) A suspect case with autopsy findings consistent with the pathology of respiratory distress syndrome without an identifiable cause.</p> <p><i>WHO continues to advise clinicians that patients should not have their case definition category downgraded while awaiting results of laboratory testing or on the basis of negative results. Negative test results for SARS virus cannot be used to exclude infection in either suspect or probable cases. [Situation updates]</i></p>
2 May 2003 (Fri)	<p>Peer-reviewed journals</p> <ul style="list-style-type: none"> ◆ Clinical Features <p>Age and chronic HBV infection are independent significant risk factors for progression to ARDS on multivariate analysis.</p>

May

[Summary published at WHO webpage on 2 May 2003] [Lancet 361 (9371):1767-72]

- ◆ Transmission

Quantitative RT-PCR of NPA in 14 patients (4 had ARDS and 10 without ARDS) consistently demonstrated a peak viral load on day 10 and a decrease to admission level on day 15.

[Summary published at WHO webpage on 2 May 2003] [Lancet 361(9371): 1767-72]

- ◆ Treatment

A prospective study of the clinical, haematological, radiological, and microbiological findings of 75 patients managed with HA's standardised treatment protocol of using ribavirin and corticosteroid. The fever and pneumonia initially responded to treatment. However, patient developed recurrent fever (85.3%) on day 8.9 ± 3.1 (range 4 to 18), watery diarrhoea (73.3%) on day 7.5 ± 2.3 (range 3 to 15), radiological deterioration (80%) on day 7.4 ± 2.2 (range 3 to 13) and respiratory deterioration (45.3%) on day 8.6 ± 3 (range 5 to 19). In 45.3% of patients, marked improvement of initial pulmonary lesions was closely associated with appearance of new radiological lesions at other sites. 20% progressed to ARDS during the third week. The consistent clinical progression, shifting radiological infiltrates and an inverted V viral load profile suggested that deterioration during the second week is not related to uncontrolled viral replication but may rather be related to immunopathological damage.

[Summary published at WHO webpage on 2 May 2003] [Lancet 361 (9371):1767-72]

3 May 2003 (Sat)

Peer-reviewed journals

- ◆ Clinical Features

Fever is a cardinal symptoms but not always so, and is sometimes absent in elderly patients. Some patients have presented with diarrhoea or, at least two cases, with severe acute abdominal pain requiring exploratory laparotomy. *[Lancet 361(9368):1486]*

May	
	<ul style="list-style-type: none"> ◆ Isolation and precautions <p>Multivariate analysis showed that health care staff who wore masks are less likely to get infected (p=0.011). Staff who wore surgical or N95 masks were significantly associated with non-infection, but this was not the case for paper masks. [<i>Lancet 361(9368);1519-20</i>]</p> ◆ Transmission <p>The surgical and N95 masks were both effective in significantly reducing the risk of infection, which together with the finding that 30% of non-infected staff did not use masks supports that transmission is not airborne. [<i>Lancet 361(9368);1519-20</i>]</p>
4 May 2003 (Sun)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Transmission <p>Virus is stable in faeces and urine at room temperature for at least 1 and 2 days respectively. Virus is more stable (up to 4 days) in stool from diarrhoea patients. [<i>First data on stability and resistance of SARS-CoV</i>]</p>
5 May 2003 (Mon)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Transmission <p>The dose of virus needed to cause infection remains unknown. [<i>Situation updates</i>]</p>
6 May 2003 (Tue)	<p>Peer-reviewed journals</p> <ul style="list-style-type: none"> ◆ Clinical Features <p>144 adult patients in the Greater Toronto area were studied. 76% of those treated with ribavirin had haemolysis. 20% were admitted to ICU. Multivariate analysis showed that the presence of diabetes (RR 3.1 95% CI 1.4 to 7.2) or other comorbid conditions (RR 2.5, 95% CI 1.1 to 5.8) were independently associated with poor outcome (death, ICU admission, or mechanical ventilation).</p>

May

[published online on 6 May 2003] [Journal of the American Medical Association (JAMA) 289(21);1-9]

7 May 2003 (Wed)

Peer-reviewed journals

- ◆ Clinical Features

Studied 1425 cases in Hong Kong. The mean incubation period is estimated at 6.4 (95% CI 5.2 - 7.7). The mean time from onset to admission to hospitals varied between 3 and 5 days, with longer times earlier in the epidemic. A non-parametric method yield estimates of 6.8% (4.0-9.6) and 55.0% (45.3-64.7%) respectively for patients aged younger than 60 and patients aged 60 or above. Patients' age was strongly associated with outcome. The time between onset of symptoms and admission to hospital did not alter outcome, but shorter intervals will be important to the wider population by restricting the infectious period before patients are placed in quarantine. [*Lancet* 361(9371):1761-6]

World Health Organization

- ◆ Clinical Features

The case fatality ratio of SARS ranges from 0 to 50% depending on the age group affected, with an overall estimate of case fatality of 14 - 15%. The case fatality ratio is estimated to be less than 1% in persons aged 24 years or younger, 6% in person aged 25 to 44 years, 15% in person aged 45 to 64 years, and greater than 50% in persons aged 65 years and older.

WHO continues to conclude that the current best estimate of the maximum incubation period is 10 days despite the recently published analysis of data from Hong Kong estimates a longer maximum incubation period. [*Situation updates*]

Centers for Disease Control and Prevention, Atlanta, USA

- ◆ Management of contacts

Persons who may have been exposed to SARS should be vigilant for fever or respiratory symptoms over the 10 days following exposure; those who develop fever or respiratory symptoms should

May

limit interactions outside the home and should not go to work, school, out-of-home childcare, church or other public areas. Symptomatic persons should use infection control precautions to minimise the potential for transmission and should seek healthcare evaluation. Healthcare workers should be informed of the possible exposure in advance of the evaluation.

If symptoms improves or resolves within 72 hours after first symptoms onset, the person may be allowed to return to work, school, out-of-home childcare, church or other public areas, and infection control precautions can be discontinued. If symptoms does not progress to meet case definition, but has persistent fever or unresolving respiratory symptoms, continue isolation precautions for an additional 72 hours, then perform clinical evaluation.

If symptoms progress to meet case definition, use isolation precaution until 10 days after resolution of fever. *[Interim domestic guidance on persons who may have been exposed to patients with suspected SARS (update)]*

8 May 2003 (Thu)

Peer-reviewed journals

- ◆ Clinical Features

Common thin-section CT features of SARS are ground-glass opacification and lower lobe and peripheral distribution. (Observations based on 74 patients.)

[published online in Radiology on 8 May 2003]

9 May 2003 (Fri)

Peer-reviewed journals

- ◆ Causative agent

The entire viral genome of 14 specimens from Singapore, Hong Kong, Canada, Beijing and Hanoi were sequenced. Genetic signatures are emerging that partition the world wide SARS viral isolates into groups on the basis of contact-source history and geography. These signatures can be used to trace sources of infection.

May

A common variant associated with a non-conservative aminoacid change in the S1 region of the spike protein suggests that immunological pressures might be starting to influence the evolution of the virus in human population. However, the mutation may only represent adaptation to Vero cells during propagation before sequencing.

[published online on 9 May 2003] [Lancet 361(9371):1779-85]

- ◆ Diagnosis

Cumulative percentage of patients with IgG seroconversion was reported at a mean of 20 (5.1) days.

[published online on 9 May 2003] [Lancet 361(9371):1767-72]

- ◆ Transmission

Viral positivity rate based on 20 patients on day 10, 13, 16, 19, 21 after symptoms onset are respectively -

NPA - 95, 90, 90, 75, 47

Stool - 100, 100, 95, 80, 67

Urine - 50, 45, 35, 30, 21

[published online on 9 May 2003] [Lancet 361(9371):1767-72]

10 May 2003 (Sat)

Peer-reviewed journals

- ◆ Treatment

Reported a standard treatment protocol for SARS adult patients. A series of 31 patients were treated according to the protocol consisting of antibacterial and a combination of ribavirin and methylprednisolone. Through the experience with the first 11 patients, the standard dose regime was finalised, including pulse methylprednisolone. One patient recovered on antibacterial treatment alone, 17 showed rapid and sustained response, and 13 achieved improvement with step-up or pulse methylprednisolone. Four patients required short period of non-invasive ventilation. No patient required intubation or mechanical ventilation. There was no mortality or treatment morbidity in this series. *[Lancet 361(9369):1615-7]*

May	
13 May 2003 (Tue)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Transmission <p>Cases do not appear to be infectious before the onset of symptoms. Infectiousness probably only starts with the onset of respiratory symptoms and appears to be low until the case becomes very sick. <i>[Interim guidelines for national SARS preparedness (update)]</i></p> <p>Peer-reviewed journal</p> <ul style="list-style-type: none"> ◆ Treatment <p>The viral main proteinase(3CL^{pro}) controlling the activities of the coronavirus replication complex represents an attractive target for therapy. The structures reveal a remarkable degree of conservation of the substrate-binding sites, which is further supported by recombinant SARS-CoV M^{pro}-mediated cleavage of a TGEV M^{pro} substrate. Molecular modelling suggests that available rhinovirus 3C^{pro} inhibitors may be modified to make them useful for SARS therapy.</p> <p><i>[published online on 13 May 2003] [Science 300(5626);1763-7]</i></p>
15 May 2003 (Thu)	<p>World Health Organization</p> <ul style="list-style-type: none"> ◆ Isolation and precautions <p>Deferral of blood donations from donors who are symptomatic or a close contact of a case. Blood transfusion services are to ask blood donors who have donated blood to report if diagnosed as suspect or probable SARS case within 1 month after blood donation; and the services are to recall the blood products still not transfused, and to follow up the recipients who have received blood/blood products from donors fulfilling the probable case definition of SARS within 1 month after blood donation. <i>[WHO recommendations on SARS and blood safety]</i></p>
16 May 2003 (Fri)	<p>Peer-reviewed journals</p> <ul style="list-style-type: none"> ◆ Clinical Features

May

According to a study on the postmortem tissue samples from six patients died from SARS, the disease is associated with epithelial-cell proliferation and an increase in macrophages in the lung. The presence of haemophagocytosis supports the contention that cytokine dysregulation may account, at least partly, for the severity of the clinical disease.

[published online on 16 May 2003] [Lancet 361(9371):1773-8]

Centers for Disease Control and Prevention, Atlanta, USA

◆ Transmission

The spread of SARS to protected health care staff in Canada may be due to –

- the use of N95-equivalent respirators that are not approved by the National Institute for Occupational Safety and Health (NIOSH) when rated at N95 or greater level of protection.
- fit-testing was not performed
- use of BiPAP

[MMWR 52 (19) 433-6]

World Health Organization

◆ Transmission

Data indicated that SARS virus in sterilised stool can survive for 36 hours on a plastered wall or a formica surface, for 72 hours on a plastic or stainless steel surface, and for 96 hours on a glass slide.

[Situation updates]

17 May 2003 (Sat)

Peer-reviewed journals

◆ Clinical Features

Reported 4 patients with chronic comorbidities who have not had the characteristic fever of over 38°C on admission, raising questions about the sensitivity of temperature monitoring as a screening tool.

[Lancet 361(9370);1740]

May

20 May 2003 (Tue)

Peer-reviewed journals

- ◆ Clinical Features

More distinctive radiographic findings of SARS are predominant peripheral location; common progression pattern from unilateral focal air-space opacity to unilateral multifocal or bilateral involvement during treatment; and lack of cavitations, lymphadenopathy, and pleural effusion . (*Observations based on 24 patients.*)

[published online in Radiology on 20 May 2003]

23 May 2003 (Fri)

World Health Organization

- ◆ Causative agent

A study detected several coronaviruses closely related genetically to the SARS coronavirus in two of the animal species tested (masked palm civet and raccoon-dog) . The study also found that one additional species (Chinese ferret badger) elicited antibodies against the SARS coronavirus. Sequencing of viruses isolated from these animals demonstrated that, with the exception of a small additional sequence, the viruses are identical with the human SARS virus. At present, no evidence exists to suggest that these wild animal species play a significant role in the epidemiology of SARS outbreaks. However, it cannot be ruled out that these animals might have been a source of human infection. *[Situation updates]*

Peer-reviewed journals

- ◆ Transmission

With the use of detailed epidemiological data from Singapore and epidemic curves from other settings (including Hong Kong), the reproductive number for SARS in the absence of interventions and in the presence of control efforts were estimated. It was estimated that every single infectious case of SARS will infect about three secondary cases in a population that had not yet instituted control measures. Public health efforts to reduce transmission are expected to have a substantial impact on reducing the size of the epidemic.

[published online on 23 May 2003] [Science 300(5627);1966-70]

May

◆ Transmission

Using the epidemiological data of 1512 cases from Hong Kong, it was shown that the aetiological agent of SARS is moderately transmissible. Excluding super-spreading event, it was estimated that 2.7 secondary infections were generated per case on average at the start of the epidemic, with a substantial contribution from hospital transmission. Transmission rates fell during the epidemic, primarily as a result of reductions in population contact rates and improved hospital infection control, but also because of more rapid hospital attendance by symptomatic individuals. Restrictions on longer range population movement were shown to be a potentially useful additional control measure in some contexts. [*Science* 300(5627);1961-6]