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Review Article

SEVERE ACUTE RESPIRATORY SYNDROME

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Abstract

Severe acute respiratory syndrome (SARS) is a form of atypical pneumonia that apparently originated in Guangdong Province of the People's Republic of China in late 2002. This first came to the world's attention in late February 2003, and has since spread worldwide. As of June 23rd 2003, the disease had been reported from 32 countries or regions globally, affecting 8459 people; 805 individuals (9.5 % of the total affected) have died of the disease. A novel coronavirus, the SARS-associated coronavirus (SARS-CoV) has been found in various specimens taken from patients with SARS. Although there has been rapid development of tests to detect SARS Co-V, these tests presently have certain limitations. Definitions of suspected, confirmed and probable cases have been formulated. Measures currently used for the management of patients with SARS include isolation, ribavirin, corticosteroid therapy and mechanical ventilation. Unfortunately, almost 10 % of affected patients succumb to their illness, underlying the need for developing more effective therapy. It remains to be seen how long it will take to bring this epidemic under control.

Key words: *SARS, Coronavirus, epidemic, China*

Severe acute respiratory syndrome (SARS) is the name given to cases of a severe atypical pneumonia that have been occurring since February 1, 2003.[1] The United States Centers for Disease Control and Prevention (CDC) released an interim case definition of SARS on March 22, 2003. This was subsequently updated on April 29, 2003[2] (Table 1).

Table 1 : Updated CDC interim surveillance case definition for severe acute respiratory syndrome (SARS)

Clinical criteria

Asymptomatic or mild respiratory illness

Moderate respiratory illness

- Temperature of > 100.4º F (> 38º C), and
- One or more clinical findings of respiratory illness (eg. cough, shortness of breath, difficulty breathing, or hypoxia) and radiographic evidence of pneumonia, or respiratory distress syndrome, or 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-CoV in specimens obtained during acute illness or > 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 primers, or
- Isolation of SARS -CoV

Negative : Absence of antibody to SARS - CoV in convalescent serum obtained > 21 days after symptom onset

Undetermined: Laboratory testing either not performed or incomplete

Case classification

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

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

SARS-CoV - SARS-associated coronavirus
RT-PCR - reverse transcription polymerase chain reaction

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Background

Guangdong Province in southern China, an agricultural area with a population of 75 million, has thousands of farms with large and small animals, a subtropical climate, and a rainfall of about 2 months / year.[3] In November 2002, a businessman from the city of Foshan in this province may have been the first victim of SARS.[3] However, this first patient and many others did not come to international attention until February 2003, when a physician from Guangdong Province, who had apparently cared for afflicted patients in the Province, became ill while staying in room 911 on the 9th floor of a hotel (Hotel M) in Hong Kong.[4] Some 16 visitors and guests, including at least seven who stayed in rooms on the 9h floor, became infected through contact, in ways that remain mysterious, with this doctor.[5,6] These hotel guests subsequently became the index patients who transported the disease to Vietnam, Singapore, Canada, Ireland and the United States of America (USA).[4]

On March 12, 2003, the World Health Organization (WHO) issued a global alert on this particularly virulent form of atypical pneumonia after the Department of Health in Hong Kong reported the outbreak of pneumonia in one of its public hospitals. At about the same time, WHO received reports of the syndrome from Asian countries such as China, Singapore, Vietnam, Thailand, Indonesia, Taiwan and the Philippines, as well as from countries in other continents including Canada, the USA and Germany.[7]

Table 2 : Cumulative Number of Reported Probable Cases of Severe Acute Respiratory Syndrome[8] (Time Period : Nov. 1, 2002 to June 23, 2003, 16.00 GMT + 2)

Country / Region	Cumulative Number of Cases	No. of Deaths	No. who Recovered	Date last probable case reported
Australia	5	0	5	12 May 2003
Brazil	3	0	2	9 June 2003
Canada	246	35	182	20 June 2003
China	5326	347	4895	11 June 2003
China, Hong Kong (Special Administrative Region)	1755	296	1411	11 June 2003
China, Macao (Special Administrative Region)	1	0	1	21 May 2003
China, Taiwan	692	84	486	19 June 2003
Colombia	1	0	1	5 May 2003
Finland	1	0	1	7 May 2003
France	7	0	6	9 May 2003
Germany	10	0	9	4 June 2003
INDIA	3	0	3	13 May 2003
Indonesia	2	0	2	23 April 2003
Italy	9	0	9	29 April 2003
Kuwait	1	0	1	9 April 2003
Malaysia	5	2	3	20 May 2003
Mongolia	9	0	9	6 May 2003
New Zealand	1	0	1	30 April 2003
Philippines	14	2	12	15 May 2003
Republic of Ireland	1	0	1	21 March 2003
Republic of Korea	3	0	3	14 May 2003
Romania	1	0	1	27 March 2003
Russian Federation	1	0	0	31 May 2003
Singapore	206	31	170	18 May 2003
South Africa	1	1	0	9 April 2003
Spain	1	0	1	2 April 2003
Sweden	3	0	3	18 April 2003
Switzerland	1	0	1	17 March 2003
Thailand	9	2	7	7 June 2003
United Kingdom	4	0	4	29 April 2003
United States	74	0	36	17 June 2003
Vietnam	63	5	58	14 April 2003
Total	**8459**	**805**	**7324**	

As of June 23rd, 2003, there had been 8459 cases and 805 deaths (a death rate of 9.5%) reported in 32 countries or regions of the world (Table 2).[8]

Epidemiology

SARS can be contracted through close contact with patients, especially by family members and health care workers. Close contact is defined as having cared for or lived with a person known to have SARS or having a high likelihood of direct contact with respiratory secretions or body fluids, or both, of a patient known to have SARS. Examples of close contact include kissing or embracing, sharing eating or drinking utensils, close conversation (<3 ft or <1 m), physical examination, and any direct physical contact between people. Close contact does not include activities such as walking by a person or sitting across a waiting room or office for a brief period of time.[1,2]

Although large-droplet transmission seems to be important in the spread of SARS, implying a requirement for intimate contact with a patient, the unusually rapid transmission suggests that airborne transmission through droplet nuclei (<10 μm in diameter) can occur.[3] Such droplet nuclei, which are key in the transmission of influenza, measles and tuberculosis, allow the organisms to reach directly the alveoli of the lungs of contacts. Alternatively, viral contamination of the water supply or fomites might be important in some locales.[3]

Microbiology of SARS: The SARS-associated coronavirus (SARS-CoV)

Coronaviruses, which are single-stranded RNA viruses (salient characteristics outlined in Table 3),[9] are ubiquitous and can be identified on electron microscopy by the presence of a corona of large, distinctive spikes in the envelope (Figure). The message-sense RNA genome and the viral nucleocapsid phosphoprotein form a helical nucleocapsid. Although human coronaviruses cause up to 30 percent of colds, they rarely cause lower respiratory tract disease. In contrast, coronaviruses are known to cause illnesses in many animals, including pigs, cattle, dogs, cats and chickens, and may cause devastating epizootics of respiratory or enteric disease in livestock and poultry.[9,10] In the SARS outbreak, the aetiological agent was quickly suspected to be a virus. By March 2003, three groups of workers, one each in Hong Kong, the USA and Germany, were able to identify a novel coronavirus in patients with SARS.[11-13]

Table 3 : Important properties of coronaviruses[9]

Virion	:	Spherical, 80-160 nm in diameter, helical nucleocapsid
Genome	:	Single-stranded RNA, linear, nonsegmented, positive-sense, 27-30 kb, MW 5-6 million, capped and polyadenylated, infectious.
Proteins	:	Two glycoproteins and one phosphoprotein. Some viruses contain a third glycoprotein (hemagglutinin esterase).
Envelope	:	Contains large, widely spaced, club- or petal-shaped spikes.
Replication	:	Cytoplasm; particles mature by budding into endoplasmic reticulum and Golgi.

Ksiazek and coworkers[12] performed studies in 19 patients with well-defined direct or indirect epidemiologic links either to the outbreak in Hong Kong or to Guangdong Province. They were able to recover a coronavirus in Vero E6 cells, a finding they deemed surprising since, hitherto, the only human or animal coronavirus shown to grow in this cell line was the porcine epidemic diarrhoea virus (which is, however, genetically distinct from and unlikely to be the parent virus to SARS-CoV). The virus was found in multiple specimens, including lung and kidney tissue extracts by virus isolation or reverse-transcription polymerase chain reaction (RT-PCR), in bronchoalveolar-lavage specimens by electron microscopy and PCR, and in sputum or upper respiratory tract swab, aspirate or wash specimens by RT-PCR or virus isolation. There was no evidence of other respiratory pathogens, including human metapneumovirus, on testing by RT-PCR in all the coronavirus -positive patients, except for a rhinovirus in one patient. The authors[12] contended that the relation between this novel coronavirus and the disease was strengthened by the detection of virus in lung tissue and a bronchoalveolar-lavage specimen, thus placing the virus at the site of diseased tissue. However, they also recognized the shortcomings of their study, which included the inability to demonstrate coronavirus antigens in patient tissues by histologic and immunohistochemical methods, or to demonstrate a direct involvement in the pathologic process, or to demonstrate SARS-CoV infection in all suspected patients with SARS. They proposed that their first isolate be named the Urbani strain of the SARS-associated

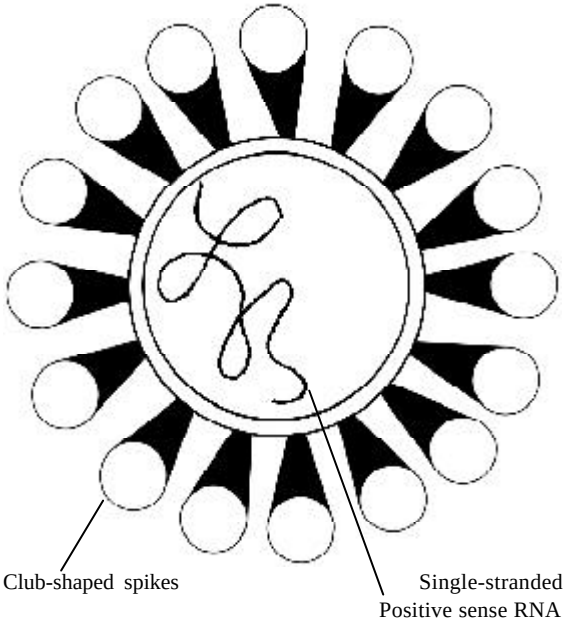

Figure : Schematic representation of a coronavirus

coronavirus, after Dr. Carlo Urbani, who first recognized the severe, atypical nature of the disease and who subsequently died of the infection.

Drosten and associates [13] were also able to identify a novel coronavirus in patients with SARS. The virus was isolated in cell culture using Vero cells, and a sequence 300 nucleotides in length was obtained by a PCR-based random amplification procedure; genetic characterization indicated that this virus was identical in only 50 to 60 percent of the nucleotide sequence to known coronaviruses. Using this sequence, conventional and real-time PCR assays were established for specific and sensitive detection of the virus; the virus was detected in a variety of clinical specimens from patients with SARS, but not in controls. Viral RNA was found at high concentrations (upto 100 million molecules per millilitre) in sputum, and at extremely low concentrations in plasma during the acute phase and in faeces during the late convalescent phase.

The three groups of workers in Hong Kong, the USA and Germany[11-13] were cautious in stressing only the association of a unique coronavirus with SARS, without categorically stating that this virus was the cause of the disease. However, in late May 2003, Fouchier and associates [14] published a brief communication, unequivocally stating that Koch's postulates had been fulfilled for the SARS virus. In their experiments, inoculation of cynomolgus macaques (*Macaca fascicularis)* with SARS-CoV from cell cultures caused lower respiratory tract disease.

Morphologically, SARS-CoV appears to exhibit most characteristics of coronaviruses, including the spikes (oligomers of the spike (S) glycoprotein) which bind to receptors on host cells and fuse the viral envelope with host cell membranes, but does not possess the hemagglutinin-acetylesterase glycoprotein that binds to sugar moieties on cell membranes.[10] Genetically, however, the SARS-CoV appears distinct from other coronaviruses. Sequencing of the 29,571 base genome of the Tor2 isolate of this virus revealed that this is only moderately related to other known coronaviruses, and does not closely resemble any of the three previously known groups of coronaviruses.[15]

Ruan *et al*[16] sequenced the entire SARS viral genome of cultured isolates from an index case presenting in Singapore, from three primary contacts and from one secondary contact; these sequences were compared with isolates from Canada, Hong Kong, Hanoi, Guangzhou, and Beijing. A total of 129 sequence variations was identified among the 14 isolates, with 16 recurrent variant sequences. Common variant sequences at four loci were found to define two distinct genotypes of the SARS virus: one genotype was linked with infections originating in Hotel M in Hong Kong, while the second genotype encompassed isolates from Hong Kong, Guangzhou and Beijing with no association with Hotel M. Other common sequence variants further distinguished the geographical origins of the isolates, especially between Singapore and Beijing. These workers hypothesized that although the SARS epidemic is of recent onset, genetic signatures are emerging which partition the global viral isolates into groups on the basis of contact source history and geography. These signatures can be used to trace sources of infection. In addition, a common variant associated with a non-conservative aminoacid change in the S1 region of the spike protein is believed to suggest that immunological pressures might be starting to influence the evolution of the SARS virus in human populations.

Genetic changes are known to occur frequently in coronaviruses.[9] The unique RNA-dependent RNA polymerase of coronaviruses often switches template strands during replication, causing RNA recombination when a cell is infected with several coronaviruses; this error-prone polymerase also generates point mutations and large deletions or insertions of foreign RNA into the viral genome.[10] Because of this, it is tempting to suggest that SARS-CoV could have arisen as a mutant of a human coronavirus that acquired new virulence factors, as a mutant of an animal coronavirus that can infect human cells, or as a recombinant of two human coronaviruses or a human coronavirus and an animal coronavirus. The apparent lack of antibody in all serum

specimens except those from patients with SARS[11] suggests that this virus has not previously circulated, or has not circulated widely, in humans, and is further evidence of the association between this novel coronavirus and SARS. Since the nucleotide sequence of the SARS-CoV genome differs substantially from sequences of all known coronaviruses,[15] SARS-CoV is probably neither a mutant of any known coronavirus nor a recombinant of known coronaviruses.[10] It is a previously unknown coronavirus, probably from a nonhuman host, that somehow acquired the ability to infect humans.[10] The detection of SARS-CoV in faecal and serum samples from patients, as well as in respiratory specimens, suggests that this virus, like many animal coronaviruses, may be spread both by faecal contamination and by respiratory droplets.[10]

Clinical Features

After an incubation period of 2-7 days, the illness begins with a prodrome of fever (temperature >38ºC), usually associated with chills, rigors and other symptoms, such as severe headache, dizziness, malaise and myalgia (Table 1). Onset of fever is abrupt and the temperature is usually high, typically with chills and rigors.[17] A measured documented temperature of >38ºC is preferred. However, clinical judgement should be used when evaluating patients for whom a measured temperature of >38ºC has not been documented.[1,2] Factors that might be considered when classifying patients who do not strictly meet the clinical criteria for this case definition include patient self-report of fever, use of antipyretics, presence of immunocompromising conditions or therapies, lack of access to health care or inability to obtain a measured temperature.[1,2]

After 3-7 days of prodromal symptoms, a lower respiratory phase begins with onset of dry, non-productive cough or dyspnoea, which may be accompanied by or progress to hypoxaemia. In some instances, a patient may rapidly deteriorate, with low oxygen saturation and acute respiratory distress requiring intubation and mechanical ventilation.[17] Between 10% and 20% of patients have required ventilation. Rash and neurological or gastrointestinal features are usually absent, but some patients develop diarrhoea during the febrile prodrome.[17] Zhang[18] has described lesions of the digestive system occurring in patients with SARS, pointing out that the spread of SARS from one individual to many tenants at Amoy Gardens in Hong Kong was believed to be by the faecal route.

Radiological features

Chest radiographs often show focal interstitial infiltrates that progress to more generalized patchy infiltrates. In late stages, there can be evidence of consolidation. Wong *et al*[19] found that initial chest radiographs were abnormal in 78.3% of 138 patients and showed air-space opacity; the lower lung zone was involved in 64.8% and the right lung in 75.9%. Peripheral lung involvement was noted in 75% of patients, with unifocal involvement occurring more frequently than multifocal or bilateral involvement.[19] Antonio *et al*[20] have recently reported on their initial experience with thin-section computed tomographic (CT) findings in 24 patients with confirmed SARS; the scans were obtained on average 36.5 days after hospital admission. These workers found that pulmonary fibrosis may develop early in patients with SARS who have been discharged after treatment; patients who were older and who had more severe disease during treatment were more likely to develop thin-section CT findings of fibrosis, such as residual ground-glass opacification and interstitial thickening.[20]

Laboratory tests for the detection of the SARS-associated coronavirus

Non-specific investigations

Suggestive laboratory features include: lymphopaenia, thrombocytopaenia and elevated lactate dehydrogenase levels. Total white blood cell counts are generally normal or decreased. At the peak of the respiratory illness, approximately 50% of patients have leucopaenia and thrombocytopaenia or platelet counts at the lower limit of the normal range.[7] Early in the respiratory phase, elevated creatinine phosphokinase levels (as high as 3000 IU/L) and hepatic transaminases (two to six times the upper limit of normal) have been noted.[7] In most patients, renal function tests are normal.[7] Elevated lactate dehydrogenase has been documented to occur in 87%, hypocalcaemia in 60% and lymphopaenia in 54%.[7]

Specific investigations

a. Molecular tests

An RT-PCR test specific for viral RNA has been found positive within the first 10 days after onset of fever in specimens from some SARS patients.[2] A valid positive PCR result indicates the occurrence of SARS-CoV viral RNA in the sample; however, it does not necessarily mean that the virus present is infectious nor that it is present in a large enough quantity to infect another person.[7] At the same time, negative PCR results do not exclude SARS, since there is the possibility of obtaining false-negative test results as the specimens may not have been collected at a time when the virus

or its genetic material was present.[7] Moreover, the duration of detectable viraemia or viral shedding is unknown,[2] although Peiris *et al* [21] reported that when RT-PCR tests were performed for nasopharyngeal aspirates of patients with SARS, peak viral loads were noted on day 10, while the load at day 15 was lower than at admission.

The SARS-CoV -specific RNA can be detected in various clinical specimens, including serum, faeces, nasal secretions[2] or body tissues[7] by PCR. A number of PCR protocols have been developed by members of the WHO laboratory network.[22]

b. SARS-CoV isolation

The presence of the infectious virus can be detected by inoculating suitable cell culture lines (eg. Vero cells) with patient specimens, and by propagation of the virus. Once isolated the virus must be identified as SARS-CoV using further tests.

c. Detection of antibody

Serologic testing for coronavirus antibody can be performed by using indirect fluorescent antibody (IFA) or enzyme -linked immunosorbent assays (ELISA) that are specific for antibody produced after infection. Although some patients have detectable coronavirus antibody during the acute phase (that is, within 14 days of the onset of the illness), definitive interpretation of negative coronavirus antibody tests is possible only for specimens obtained > 21 days after onset of symptoms.[2] IgG levels are believed to peak at 60 days after the onset of the illness, and to remain detectable even after resolution of the illness, whereas IgM levels peak at about 14 days.[7]

d. Histopathological findings

Nicholls *et al* [23] reported on the histopathological appearance of post-mortem tissue samples from six patients, all of whom had serological evidence of recent infection with SARS-CoV. Diffuse alveolar damage was common but not universal. Morphological changes identified were bronchial epithelial denudation, loss of cilia and squamous metaplasia. Secondary bacterial infection was present in one patient. A giant-cell infiltrate was seen in four patients, with a marked increase in macrophages in the alveoli and the interstitium of the lung. Haemophagocytosis was present in two patients, supporting the contention that cytokine dysregulation accounts, at least partly, for the severity of the clinical disease. Electron microscopy revealed viral particles in the cytoplasm of epithelial cells corresponding to coronavirus.[23]

e. Other diagnostic considerations

In patients with suspected SARS, a work-up for known causes of community-acquired pneumonia should be performed, and specimens should be sent to the appropriate public health laboratory for viral identification and serologic analysis. Peiris *et al* [21] investigated the temporal progression of the clinical, radiological and virological changes in a community outbreak of SARS, following up 75 patients for 3 weeks who were managed with a standard treatment regimen of ribavirin and corticosteroids. Fever and pneumonia were found to initially improve, but 85% of patients developed recurrent fever after a mean of 8.9 days, 73% had watery diarrhoea after 7.5 days, 80% had radiological worsening after 7.4 days, and respiratory symptoms worsened in 45% after 8.6 days. In 45% patients, improvement of initial pulmonary lesions was associated with appearance of new radiological lesions at other sites. Quantitative RT-PCR of nasopharyngeal aspirates in 14 patients showed a peak viral load at day 10, and at day 15 a load lower than at admission. Age and chronic hepatitis B virus infection treated with lamivudine were significant independent risk factors for progression to acute respiratory distress syndrome. SARS-CoV in faeces was seen on RT-PCR in 97% of 67 patients at day 14. Mean time to sero-conversion was 20 days. The authors opined that the consistent clinical progression, shifting radiological infiltrates and inverted V viral load profile suggested that worsening in week 2 is unrelated to uncontrolled viral replication but may be related to immunopathological damage.

Management of suspected SARS

Wenzel and Edmond [3] have provided clear guidelines for the management of patients with suspected SARS :

1. Isolate the patient in a private room (with negative pressure if possible). Health care providers should wear gloves, gowns, masks, eye protection and wash hands carefully after removing gloves. There should also be limits to the number of health care providers caring for the patient, as well as to the number of visitors.

2. Perform diagnostic studies by obtaining specimens to rule out causes of atypical pneumonia as well as for SARS testing. A CT scan of the chest should also be considered

3. Provide treatment for the patient, including supplementary oxygen for hypoxemia

A series of 31 patients with probable SARS in Hong Kong were treated according to a treatment protocol

consisting of antibacterials (levofloxacin 500 mg once daily intravenously/orally *or* clarithromycin 500 mg twice daily orally plus amoxycillin-clavulanic acid 375 mg thrice daily orally if patient was <18 years old, pregnant or suspected to have tuberculosis), and a combination of ribavirin (400 mg 8th hourly intravenously for at least 3 days or till condition became stable, and then increased to 800 mg 8th hourly) and methylprednisolone.[24] One patient recovered with antibacterials alone, 17 showed rapid and sustained responses, and 13 achieved improvement with step-up or pulsed methylprednisolone. Although four patients required short periods of non-invasive ventilation, no patient required intubation or mechanical ventilation. There was no mortality or treatment morbidity in this series.[24]

Prevention and Control of SARS

Patients with SARS and those with atypical pneumonia who have any possible link to the outbreaks should be managed in hospital using isolation and infection control techniques.[1] Attention to hand washing and standard isolation techniques is important. Respiratory precautions should be used if patients need a respirator. Health care workers should wear eye protection during all direct contact with patients. Patients being transported or in ambulatory health care settings should wear a surgical mark. They should also do so when in contact with other people in their homes. It is important to remember that SARS is transmitted through close personal contact and not through exposure in public places.[1]

Hospital workers are at the forefront of the global response to SARS. Unfortunately, they are also at considerable risk of contracting SARS when there is an opportunity for unprotected exposure.[5,6] Constant vigilance is required in the screening of hospital staff, patients and visitors to prevent the future introduction of this disease into hospitals. Dwosh *et al* [25] described interventions used to contain an outbreak of SARS at a community hospital in Ontario, Canada. These were basically of three types, namely, infection control measures, organizational interventions and the development of a SARS Assessment and Treatment Unit. The infection control measures consisted of the following:

- 10 - day voluntary home quarantine for staff, patients and visitors.
- Completion of SARS screening questionnaire before entering hospital
- Measurement of oral temperature upon entering and exiting hospital
- Wearing of gowns, gloves and N9S masks by all staff and visitors to hospital
- Stringent hand washing 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 nebulized medications
- Moratorium on non-invasive ventilation.

Organizational interventions consisted of:

- Closing of the emergency department
- Suspension of elective surgery
- Prevention of patient transfers between facilities
- Cancellation of out patient diagnostic procedures
- Prevention of hospital staff from working at other institutions
- Restriction of hospital visitors.

A SARS assessment and treatment unit was also developed. This consisted of a dedicated unit on a separate ward, single rooms, rooms retrofitted with externally exhausted HEPA filters, 2-hospital-based internists / intensivists for 24 hour patient care, and full haemodynamic monitoring and ventilator support for critically ill patients with SARS.[25] This paper clearly illustrates how the rigorous application of respiratory isolation and barrier precautions is an effective means of controlling the spread of this disease in the hospital setting. However, these authors stress the need for public health efforts focused on identifying the close contacts of new patients as a prerequisite to limit the spread of SARS from the hospital setting to the community; they also opine that the study of the utility of mass voluntary quarantine measures in the management of future SARS outbreaks is warranted.[25]

Future perspective in the study of SARS

Knowledge about the natural history, diagnosis and treatment of SARS grows each week. In retrospect, it appears that many of the treatments commonly used in acute management of respiratory disease, for example non-invasive positive pressure ventilation (NIPPV) and the use of nebulized medications, may have actually facilitated the transmission of the SARS-CoV. The use of NIPPV and nebulized medications should be avoided in SARS patients.[25]

Serologic tests of wild and domestic animals and birds in the region where the outbreak first appeared may identify the usual host.[10] Comparison of isolates of SARS-CoV from infected patients and from the natural host may reveal how the virus 'jumped' to humans, and

may also shed light on whether the virus, by so doing, has lost the ability to infect its original host.[10] Such information would be of tremendous value since, if there is no animal reservoir, there will be a better chance of eliminating the virus from humans.

There are potential targets for the development of new drugs against coronaviruses; these include protease inhibitors to prevent processing of the RNA polymerase or cleavage of the viral S glycoprotein, inhibitors of coronavirus acetylesterase activity to limit viral replication, and inhibitors of membrane fusion to block viral entry.[10] Antibodies against the viral S glycoprotein or the unidentified receptor for the SARS-CoV might also block entry of the virus.[10] It is prudent to develop safe, effective drugs and vaccines against the SARS-CoV as quickly as possible, in case the outbreak cannot be contained.[10] The development of drugs and vaccines for SARS will also provide new strategies for the prevention and treatment of other coronavirus diseases of animals and humans.

Conclusions

Although the battle against SARS appears to be approaching victory, there is no room for complacency. Just when it was believed that Toronto could be declared as SARS-free in early June 2003, the sudden emergence of a cluster of cases set back the efforts of the Canadian health care authorities. Thus, what may appear to be eradication of the disease in various locales may only be temporary lulls in the ongoing struggle against SARS. Among Asian countries, India appears to have been relatively fortunate to have been spared the disease in its full-blown epidemic form, an interesting aspect that warrants further study. However, there is no room for complacency, and all possible hygienic precautions should be followed as a routine to ensure that the disease never rears its head in the Indian subcontinent.

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