Severe Acute Respiratory Syndrome (SARS)

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DEFINITION

Severe acute respiratory syndrome is an infectious disease in humans that was first recognised in south East Asia in late February 2003. given the disturbing features associated with the disease, which include poorly defined pathogenesis, absence of laboratory diagnostic testing, and failure of known antimicrobial treatments, its emergence prompted the world health organization to issue the first global health alert for over a decade.

WHO Case Definition

As defined by the World Health Organization (WHO), a suspected case is classified as being disease in a person with a documented fever (temperature >38 C), lower respiratory tract symptoms, and contact with a person believed to have had SARS or a history of travel to a geographic area where there has been documented transmission of the illness.

A suspected case with 1) chest radiographic findings of pneumonia, 2) acute respiratory distress syndrome, or 3) an unexplained respiratory illness resulting in death with autopsy findings consistent with the pathology of ARDS without an identifiable cause is considered a probable case.

Suspect case

1. A person presenting after 1 November 2002¹ with history of:
   • High fever (>38 C)
   • Cough or breathing difficulty
   AND one or more of the following exposures during the 10 days prior to onset of symptoms:

   • Close contact² with a person who is a suspect or probable case of SARS;
   • History of travel, to an area with recent local transmission of SARS
   • Residing in an area with recent local transmission of SARS

2. A person with an unexplained acute respiratory illness resulting in death after 1 November 2002¹, but on whom no autopsy has been performed

And one or more of the following exposures during to 10 days prior to onset of symptoms:

²
• **Close contact**\(^2\) with a person who is a suspect or probable case of SARS;

• History of travel to an area with recent local transmission of SARS

• Residing in an area with recent local transmission of SARS

1 The surveillance period begins on 1 November 2002 to capture cases of atypical pneumonia in China now recognized as SARS. International transmission of SARS was first reported in March 2003 for cases with onset in February 2003.

2 Close contact: having cared for, lived with, or had direct contact with respiratory secretions or body fluids of a suspect or probable case of SARS.

**Probable case**

1. A suspect case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR).

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

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

**Exclusion criteria**

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

The incubation period for SARS is two-seven days, though in some rare cases it has been as long as 14 days.

The illness usually begins with a fever (measured temperature greater than 100.4°F [≥38.0°C]). The fever is sometimes associated with chills or other symptoms, including headache, general feeling of discomfort, and body aches. Some people also experience mild respiratory symptoms at the outset. Diarrhea is seen in approximately 10 percent to 20 percent of patients. After 2 to 7 days, SARS patients may develop a dry, nonproductive cough that might be accompanied by or progress to the point where insufficient oxygen is getting to the blood. In 10% to 20% of cases, patients will require mechanical ventilation. Most patients develop pneumonia.

Typical laboratory findings include lymphopaenia (reduced lymphocyte numbers) and mildly elevated aminotransferase levels (indicating liver damage). Death may result from progressive respiratory failure due to alveolar damage. The typical clinical course of SARS involves an improvement in symptoms during the first week of infection, followed by a worsening during the second week. Studies indicate that this worsening may be related to patient's immune responses rather than uncontrolled viral replication.

CAUSES

SARS is caused by a previously unrecognized coronavirus, called SARS-associated coronavirus (SARS-CoV). It is possible that other infectious agents might have a role in some cases of SARS. Researchers in Hong Kong, the United States, and Germany first identified novel coronavirus.

Virology

The coronaviruses (order Nidovirales, family Coronaviridae, genus Coronavirus) are members of a family of large, enveloped, positive-sense single-stranded RNA viruses that replicate in the cytoplasm of animal host cells (Siddell).

Coronaviruses are a group of viruses that have a halo or crown-like (corona) appearance when viewed under an electron microscope. These viruses are a common cause of mild to moderate upper-respiratory illness in humans and are associated with respiratory, gastrointestinal, liver and neurologic disease in animals. Coronaviruses can survive in the environment for as long as three hours.

CDC scientists were able to isolate a virus from the tissues of two patients who had SARS and then used several laboratory methods to characterize the agent. Examination by electron microscopy revealed that the virus had the distinctive shape and appearance of coronaviruses. Tests of serum specimens from patients with SARS showed that the patients appeared to have recently been infected with this coronavirus. Other tests demonstrated that coronavirus was present in a variety of clinical specimens from patients, including nose and throat swabs. In addition, genetic analysis suggests that this new virus belongs to the family of coronaviruses but differs from previously identified coronaviruses.
**Morphology**

Negative-stain transmission electron microscopy of patient samples and of cell culture supernatants reveals pleomorphic, enveloped coronavirus-like particles with diameters of between 60 and 130 nm.

Examination of infected cells by thin-section electron microscopy shows coronavirus-like particles within cytoplasmic membrane-bound vacuoles and the cisternae of the rough endoplasmic reticulum. Extracellular particles accumulate in large clusters, and are frequently seen lining the surface of the plasma membrane.

![Electron micrograph of coronavirus-like particles](image)

*Figure:* Electron micrograph of coronavirus-like particles in cell culture, supernatant after ultracentrifugation and negative staining with uranyl acetate.

**Organization**

The SARS-CoV genome contains five major open reading frames (ORFs) that encode the replicase polyprotein; the spike (S), envelope (E), and membrane (M) glycoproteins; and the nucleocapsid protein (N).

The main function of the S protein is to bind to species-specific host cell receptors and to trigger a fusion event between the viral envelope and a cellular membrane. Much of the species specificity of the initial infection depends upon specific receptor interactions. In addition, the spike protein has been shown to be a virulence factor in many different coronaviruses. Finally, the S protein is the principal viral antigen that elicits neutralizing antibody on behalf of the host.

The M protein is the major component of the virion envelope. It is the major
determinant of virion morphogenesis, selecting S protein for incorporation into virions during viral assembly. There is evidence that suggests that the M protein also selects the genome for incorporation into the virion.

One remarkable feature about coronavirus RNA synthesis is the very high rate of RNA-RNA recombination.

\[\text{Figure: Structure of SARS-associated coronavirus (SARS-CoV).}\]

**Stability and Resistance**

Test to evaluate the stability of SARS-CoV and its resistance against various environmental factors and disinfectants.

The tests show that the virus is stable in feces and urine at room temperature for at least 1-2 days. The stability seems to be higher in stools from patients with diarrhea (the pH of which is higher than that of normal stool).

In supernatants of infected cell cultures, there is only a minimal reduction in the concentration of the virus after 21 days at 4°C and -80°C. After 48 hours at room temperature, the concentration of the virus is reduced by one log only, indicating that the virus is more stable than the other known human coronaviruses under these conditions. However, heating to 56°C inactivates SARS-CoV relatively quickly. Furthermore, the agent loses its infectivity after exposure to different commonly used disinfectants and fixatives.

**Natural Host**
Several coronaviruses that were closely related genetically to the SARS coronavirus in animals taken from a southern Chinese market that was selling wild animals for human consumption. Found that the virus in masked palm civets (Paguma larvata, a cat-like mammal) as well as some other species. All six of the civets included in the study were found to harbor SARS coronavirus, which was isolated in cell culture or detected by a PCR molecular technique. Serum from these animals also inhibited the growth of SARS coronavirus isolated from humans. Vice versa, human serum from SARS patients inhibited the growth of SARS isolates from these animals. Sequencing of viruses isolated from these animals demonstrated that, with the exception of a small additional sequence, the viruses are identical to the human SARS virus

Figure: A healthy masked palm civets (Paguma larvata) Chinese wild animal for human consumption.
DIAGNOSIS

Identifying hospitalized patients with SARS is difficult, especially when no epidemiological link has been recognized and the presentation of symptoms is non-specific. Patients with SARS might develop symptoms common to hospitalized patients (e.g., fever or prodromal symptoms of headache, malaise, and myalgia), and diagnostic testing to detect cases is limited.

1. Chest X-ray films

Chest X-ray findings typically begin with a small, unilateral, patchy shadowing, and progress over 1-2 days to become bilateral and generalized, with interstitial or confluent infiltrates. Air-space opacities eventually develop during the course of the disease. In patients who deteriorate clinically, the air-space opacities may increase in size, extent, and severity.

2. Chest CT

Typical findings on CT demonstrate patchy areas of consolidation primarily in a peripheral location. Patients may progress to diffuse involvement of all five lobes with both ground-glass attenuation and air-space consolidation. Focal areas of sparing are common. These findings are characteristic of acute respiratory distress syndrome and correlate with the histological finding of diffuse alveolar damage. Axial CT illustrations of the upper (top figure) and lower (bottom figure) lobes of lung show consolidation, ground-glass attenuation, and focal areas of sparing characteristic of DAD.
Chest Plain Film

The extent of radiographic findings in patients with SARS is variable. The majority of patients (78%) have abnormal radiographs at the time of presentation. Approximately half demonstrate a focal, unilateral area of consolidation. The remainder demonstrates more extensive disease. All patients eventually develop an abnormal chest radiograph. These findings are consistent with a bronchopneumonia. The chest radiograph in the patient with SARS demonstrates focal areas of consolidation in the left lower lobe and right suprahilar area.
Chest radiograph obtained 5 days after admission reveals progression of consolidation and decreased lung volumes. The patient required supplemental oxygen at this time.

**Specimens**

- Figure: Homogeneous appearing hyaline membranes (arrow) line edematous alveolar walls

- Figure: Hyaline membranes line alveolar walls and a fibrin microthrombus is present within the lumen of a small vessel (arrow)

In order to make an early and sensitive diagnosis, it is therefore necessary to use highly sensitive tests that are able to detect the low levels of viral genome present during the first days of illness.

**LABORATORY TESTS**

Samples from suspected and probable SARS cases have been tested for SARS-CoV. Various molecular (PCR-based) assays have been developed by different groups around the world, and although one such assay is available commercially, results of these
tests should still not be used to rule out a suspected case of SARS,

In many viral diseases, virus shedding is greatest during the early symptomatic phase, i.e. around, and immediately following the onset of symptoms. Unfortunately, virus excretion is comparatively low during the initial phase of SARS. It peaks in respiratory specimens and in stools at around day 10 after the onset of the clinical illness. In order to make an early diagnosis, it is therefore necessary to use highly sensitive tests that are able to detect the low levels of viral genome present during the first days of illness.

Because presently available tests are not generally able to detect the small amounts of SARS coronavirus (SARS-CoV) initially shed, they do not yet play a role in patient management and case control, as SARS patients may be capable of infecting others during the initial phase and therefore need to be reliably detected and quickly isolated

The results of the first clinical studies on SARS are now available and able to shed light on the clinical usefulness of various tests on different patient samples at different time points. In one series, IgG seroconversion was documented in 93% of patients at a mean of 20 days; about 50% of patients had seroconverted at around 15 days after the onset of symptoms

**Molecular tests**

SARS-CoV-specific RNA can be detected in various clinical specimens such as blood, stool, respiratory secretions or body tissues by the polymerase chain reaction (PCR). A RT-PCR test kit containing primers and positive and negative controls, developed by the Bernhard Nocht Institute. An inactivated standard preparation is also available for diagnostic purposes through the European Network for Imported Viral Infections (ENIVD). ENIVD is also preparing an international external quality assessment scheme for SARS-CoV assays.

A valid positive PCR result indicates that there is genetic material (RNA) from the SARS-CoV in the sample. It does not mean, however, that the virus present is infectious, or that it is present in a large enough quantity to infect another person.

Negative PCR results do not exclude SARS. Besides the possibility of obtaining incorrect, false-negative test results (e.g. through lack of sensitivity), specimens may not have been collected at a time when the virus or its genetic material was present.

<table>
<thead>
<tr>
<th>Detection method</th>
<th>Clinical material/specimen</th>
<th>Technical details</th>
<th>Diagnostic significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus detection</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Viral isolation on cell culture</td>
<td>Respiratory tract samples: sputum, BAL</td>
<td>Suitable cell lines: Vero; biosafety level 3 facility required</td>
<td>Indicates presence of infectious virus; negative result does not preclude SARS!</td>
</tr>
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<td>--------------------------------</td>
<td>----------------------------------------</td>
<td>---------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Polymerase chain reaction (PCR)</td>
<td>Respiratory tract samples: sputum, BAL, throat swab, throat washing, stool</td>
<td>Different primer sequences and protocols available from the WHO website *</td>
<td>Indicates presence of viral genome, not necessarily of infectious virus; negative result does not preclude SARS! *</td>
</tr>
</tbody>
</table>

**Antibody detection**

<table>
<thead>
<tr>
<th>Immunofluorescence assay (IFA)</th>
<th>Serum</th>
<th>For detection of specific IgG or IgM antibodies or both</th>
<th>IgM IFA usually positive from day 10 after the onset of symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme-linked immunosorbent assay (ELISA)</td>
<td>Serum</td>
<td>May be designed to detect specific IgG or IgM antibodies or both</td>
<td>Usually positive from day 21 after the onset of symptoms</td>
</tr>
<tr>
<td>Neutralization test (NT)</td>
<td>Serum</td>
<td>Requires BSL-3 facility (&quot;live&quot; virus)</td>
<td>Under investigation; study use only</td>
</tr>
</tbody>
</table>

Table: Available diagnostic tests for the SARS-associated coronavirus

**Virus isolation**

The presence of the infectious virus can be detected by inoculating suitable cell cultures (e.g., Vero cells) with patient specimens (such as respiratory secretions, blood or stool) and propagating the virus in vitro. Once isolated, the virus must be identified as SARS-CoV using further tests. Cell culture is a very demanding test, but currently (with the exception of animal trials) the only means to show the existence of a live virus. Positive cell culture results indicate the presence of live SARS-CoV in the sample tested. Negative cell culture results do not exclude SARS.
Antibody detection

Various methods provide a means for the detection of antibodies produced in response to infection with SARS-CoV. Different types of antibodies (IgM and IgG) appear and change in level during the course of infection. They can be undetectable in the early stages of infection. IgG usually remains detectable after resolution of the illness. The following test formats are being developed:

- Enzyme-linked immunoabsorbent assay (ELISA): a test which detects a mixture of IgM and IgG antibodies in the serum of SARS patients and reliably yields positive results at around day 21 after the onset of illness.

- Immunofluorescence assay (IFA): This requires the use of SARS-CoV-infected cells fixed on a microscope slide; patient antibodies bind to viral antigens and are in turn detected by immunofluorescent-labelled secondary antibodies against human IgG or IgM or both, using an immunofluorescence microscope. IFA typically yields a positive result after about day 10 after the onset of illness. Results may be quantified by using serial titrations of patient sera. A SARS-CoV IFA manufactured by Euroimmun AG is now available commercially for the detection of IgG and IgM antibodies against SARS-CoV.

- Neutralization test (NT): This test assesses and quantifies, by means of titration, the ability of patient sera to neutralize the infectivity of SARS-CoV on cell culture. NT is therefore likely to be the best correlate of immunity. However, due to the use of the infectious virus it is limited to institutions with BSL-3 facilities.

Interpretation

Positive antibody test results indicate previous infection with SARS-CoV. Seroconversion from negative to positive or a four-fold rise in the antibody titer from acute to convalescent serum indicates a recent infection. A negative antibody test result later than 21 days after the onset of illness is likely to indicate that no infection with SARS-CoV has taken place. There seems to be no background seroprevalence against SARS-CoV in the control populations screened so far. Antibody testing allows the indirect diagnosis of SARS-CoV infection and is unsuitable during the acute illness; it has the advantage of being rather independent of the sample type and timing, in contrast to other virus detection methods.

SPREAD OF SARS

SARS is believed to have originated as early as November 2002 in the Guangdong province of southern China. The disease spread rapidly to Hong Kong, Singapore, Thailand, Vietnam, Canada, and the US mainly by international travellers and aided by the "super spreader" phenomenon, where a few patients infect many through casual contact or environmental contamination.

The principal way SARS appears to be spread is through droplet transmission; namely, when someone sick with SARS coughs or sneezes droplets into the air and someone else breathes them in. It is possible that SARS can be transmitted more broadly
through the air or from objects that have become contaminated.

It is possible that SARS could be spread when a person touches a contaminated object or surface.

**Droplet transmission**

Droplet transmission refers to the spread of viruses contained in relatively large respiratory droplets that people project when they cough or sneeze. Because of their large size, droplets travel only a short distance (usually 3 feet or less) before they settle. Droplet transmission can occur either directly when droplets are inhaled by another person, or indirectly when droplets land on an object or surface (such as a doorknob or telephone) that are then touched by another individual. Common-cold viruses (like rhinovirus) are typically spread by droplets.

**Airborne transmission**

Airborne transmission means the that the virus is spread by very small respiratory aerosol particles or dust, which can be breathed in by people. Small aerosol particles can remain in the air and travel over a greater distance than larger respiratory droplets. Examples of viruses spread by the airborne route are influenza and measles viruses.

Cases of SARS continue to be reported primarily among people who have had direct close contact with an infected person, such as those sharing a household with a SARS patient and health-care workers who did not use infection control procedures while caring for a SARS patient.

**SARS conspiracy theory**

The SARS conspiracy theory began to emerge during the Severe Acute Respiratory Syndrome (SARS) outbreak in China in the spring of 2003, when Sergei Kolesnikov, a Russian scientist and a member of the Russian Academy of Medical Sciences, first publicized his claim that the SARS coronavirus is a synthesis of measles and mumps. This compound cannot be formed in the natural world and thus, according to him, the SARS virus must have been produced under laboratory conditions. Earlier, another Russian scientist, Nikolai Filatov, head of Moscow's epidemiological services, had commented that the SARS virus was probably man-made.

Many Chinese believed that the SARS virus could be a biological weapon manufactured by the United States, who perceived China's rise as a potential threat to its dominance and superiority in the world. The failure to find the source of the SARS virus further convinced these people and many more that SARS was artificially synthesised and spread by some individuals and even governments. However, a great deal of very convincing circumstantial evidence suggests that the SARS virus crossed over to humans from civet cats, a type of animal that is often killed and eaten in Guangdong, where SARS was first discovered. Some people in Taiwan and the United States have also expressed doubts and speculated that SARS could be a biological weapon developed by
mainland China.

Supporters of the conspiracy theory suggest that SARS caused the most serious harm in mainland China, Hong Kong, Taiwan and Singapore, regions where most Chinese reside, while the United States, Europe and Japan were not much affected. Canada suffered 40 deaths. Conspiracists further point out that SARS has an average mortality rate of around 10% around the world, but no one died in the United States from SARS, despite the fact that there were 71 reported cases. The United States government has officially denied that it has any relationship to the development and spread of the SARS virus.

In October 2003, Tong Zeng, a Chinese lawyer and a volunteer in a 1998 Chinese-American medical cooperation program, published a book that again speculated that SARS could be a biological weapon developed by the United States against China. In the book, Tong disclosed that in the 1990s, many American research groups collected thousands of blood and DNA samples and specimens of mainland Chinese (including 5000 DNA samples from twins) through numerous joint research projects carried out in China. These samples were then sent back to the United States for further research, and could be used in developing biological weapons targeting Chinese. These samples came from 22 provinces in China, all of which were hit by SARS in 2003. Only provinces like Yunnan, Guizhou, Hainan, Tibet and Xinjiang were left out, and all these provinces suffered less severely during the SARS outbreak. The author suspects that Japan is also involved, as many Japanese factories in Guangdong in the 1990s made it compulsory for all workers to have blood tests in the factory annually, rather than asking workers to go to local hospitals for blood tests and a proper physical examination. However Tong Zeng admits that these are only speculations, and he does not have any concrete proof from the study of the virus's genetic sequence.

Some scientists acknowledge the possibility that the SARS virus was man-made, and some have also noticed there is genetic material in the SARS DNA sequence that does not match any previously known virus, implying it could be man-made. Notably, an expert from the Centre for Disease Control and Prevention of China, Hou Yunde, who initially denied that SARS could be man-made, later admitted in a SARS seminar held by the Chinese Ministry of Health in December 2003 that it was possible.
EPIDEMIOLOGY

Introduction

Severe acute respiratory syndrome (SARS) is a new infectious disease, which was first recognized in 2003 February 28, when cases of an atypical pneumonia of unknown cause began appearing among staff at a hospital in the Vietnam French Hospital of Hanoi. Within two weeks, similar outbreaks occurred in various hospitals in Hong Kong, Singapore and Toronto.

After the disease had moved out of southern China, Hanoi, Hong Kong, Singapore, and Toronto became the initial "hot zones" of SARS, characterized by rapid increases in the number of cases, especially in healthcare workers and their close contacts. In these areas, SARS first took root in hospital settings, where staff, unaware that a new disease had surfaced, exposed themselves to the infectious agent without barrier protection. All of these initial outbreaks were subsequently characterized by chains of secondary transmission outside the healthcare environment.

The number of worldwide cases exceeded 4000 on 2003 April 23 and then rapidly soared to 5000 on 2003 April 28, 6000 on 2003 May 2, and 7000 on 2003 May 8, when cases were reported from 30 countries. During the peak of the global outbreak, near the start of May, more than 200 new cases were being reported each day.

As of July 3, 2003, severe acute respiratory syndrome (SARS) had been diagnosed in more than 8,000 patients. The first SARS epidemic can be summarized as follows (Oxford):

1. The epidemiological observation that SARS was first detected in the Guangdong province in November 2002 and took three months to spread even to the immediately neighboring Hong Kong, despite easy exchange of family members between the two areas, does suggest, fortunately, a virus with a low infectiousness.

2. Outbreaks to date have been restricted to families, often living in high-density accommodation, and to hotels and hospitals. This limited spread is the hallmark of a virus with low communicability.

3. A truly global respiratory virus like influenza rather quickly emerged to infect millions of persons worldwide. Given the remarkable extent of air travel today, the SARS virus is not spreading rapidly, at least to date.

Starting Point

In November 2002, cases of a highly contagious and severe atypical pneumonia were noted in the Guangdong Province of southern China. The condition appeared to be particularly prevalent among healthcare workers and members of their household. Many cases were rapidly fatal. During the first week of February there was growing concern among the public about a mysterious respiratory illness, which apparently had a very high mortality and which caused death within hours.
Global Spread

SARS was carried out of the Guangdong Province on February 21, 2003, when an infected medical doctor spent a single night on the 9th floor of a Hong Kong hotel when he visited his family. He had become unwell a few days earlier and was now seriously ill. He was admitted to a hospital on February 22 and died ten days later.

Before the end of February, guests and visitors to the hotel's ninth floor had seeded outbreaks of cases in the hospital systems of Hong Kong, Vietnam, and Singapore. Simultaneously, the disease began spreading around the world along international air travel routes as guests at the hotel flew home to Toronto and other cities around the world.

SARS, the first severe infectious disease to emerge in the twenty-first century, has taken advantage of opportunities for rapid international spread made possible by the unprecedented volume and speed of air travel. SARS has also shown how, in a closely interconnected and interdependent world, a new and poorly understood infectious disease can adversely affect economic growth, trade, tourism, business and industrial performance, and social stability as well as public health.

Hong Kong

The Hong Kong index patient (the physician from Guangdong) infected 12 other persons who had been staying at the same hotel. Two of these individuals were subsequently responsible for outbreaks in two local hospitals.

Towards the end of March 2003, a further SARS outbreak occurred among residents of Amoy Gardens, Hong Kong, with a total of 320 SARS cases in less than three weeks.

![Epidemic curve, Hong Kong; June 16, 2003.](image)

After the initial phase of exponential growth, the rate of confirmed SARS cases fell to less than 20 per day by April 28, 2003.
By June 16, 1755 cases of SARS had been diagnosed in Hong Kong. 295 patients (16.8%) had died. 1386 patients (79.0%) had recovered. Around 30% of cases occurred in healthcare workers. Among these, nurses were the most exposed category, accounting for about 55% of all infected healthcare workers. 15% were doctors, 27% support staff. Eight medical workers had died by June 2.

On June 23, the WHO removed Hong Kong from its list of areas with recent local transmission of SARS.

**Vietnam**

The outbreak in Vietnam began on February 26, when a 48-year-old Chinese-American businessman was admitted to the French hospital in Hanoi with a 3-day history of high fever, dry cough, myalgia and a mild sore throat. He had previously been in Hong Kong, where he visited an acquaintance staying on the 9th floor of the hotel where the Guangdong physician was a guest.

The outbreak in Vietnam began on February 26, when a 48-year-old Chinese-American businessman was admitted to the French hospital in Hanoi with a 3-day history of high fever, dry cough, myalgia and a mild sore throat. He had previously been in Hong Kong, where he visited an acquaintance staying on the 9th floor of the hotel where the Guangdong physician was a guest.

On April 28, the WHO removed Vietnam from the list of affected areas, making it the first country to successfully contain its SARS outbreak.

**Toronto**

SARS was introduced to Toronto by a woman of Hong Kong descent who had traveled home to visit relatives from February 13 to February 23, 2003. Whilst visiting their son in Hong Kong, she and her husband stayed at Hotel M from February 18 until February 21, at the same time and on the same floor as the Guangdong physician from whom the international outbreak originated. The woman and her husband only stayed in the hotel at night, and spent the days visiting their son. They returned to their apartment in Toronto, which they shared with two other sons, a daughter-in-law, and a five-month-old grandson on February 23, 2003. Two days later, the woman developed fever, anorexia, myalgia, a sore throat, and a mild non-productive cough. She died nine days after the onset of the illness. On March 8 and 9, five out of the six adult family members presented with symptoms of SARS.

To date, 251 cases of SARS have been diagnosed in Canada, most of them in the Toronto area. 43 patients have died.

On July 2, the WHO removed Toronto from its list of areas with recent local transmission.

**China**

Up until mid-April, the Chinese authorities underestimated the magnitude of
the epidemic in Beijing, with only 37 cases having been reported by April 19. In the following two days, the Chinese authorities announced more than 400 new SARS cases.

In May 11, 2003 the epidemic in China seems to be under control. 5,327 cases of SARS have been diagnosed, 349 patients have died.

On June 24, Beijing was removed from the list of areas with recent local transmission

**Other Countries**

The number of probable SARS cases reported from other countries over the time period November 1, 2002 to July 31, 2003, is shown in the following table.

<table>
<thead>
<tr>
<th>Country</th>
<th>Cumulative number of case(s)</th>
<th>Number of deaths</th>
<th>Case fatality ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>6</td>
<td>0</td>
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<tr>
<td>Canada</td>
<td>251</td>
<td>43</td>
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<tr>
<td>China</td>
<td>5327</td>
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<td>France</td>
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<tr>
<td>Germany</td>
<td>9</td>
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<tr>
<td>Hong Kong</td>
<td>1755</td>
<td>299</td>
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<tr>
<td>India</td>
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<tr>
<td>Vietnam</td>
<td>63</td>
<td>5</td>
<td>8</td>
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<td><strong>Total</strong></td>
<td><strong>8098</strong></td>
<td><strong>774</strong></td>
<td><strong>9.6</strong></td>
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</tbody>
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Notes:
The cumulative number of cases includes the number of deaths.

**Eradication**

As the number of new cases continues to dwindle, one of the most important questions for the future is whether SARS can be eliminated or eradicated from its new human host. Experience with many other infectious diseases, including smallpox and poliomyelitis, has demonstrated that complete eradication of an infectious disease is possible only when three precise requirements can be met:

1. An effective intervention capable of interrupting transmission - ideally, a vaccine - must be available.
2. Easy-to-use diagnostic tools are needed, with sufficient sensitivity and specificity to detect levels of infection that can lead to transmission of the disease.

3. Finally, infection of humans must be essential to the life-cycle of the causative agent - if the chain of human-to-human transmission is broken, the agent cannot survive. Existence of an animal reservoir greatly complicates eradication, but does not preclude it, provided that interventions exist to break the chain of transmission in the animal species as well.

To achieve eradication at the global level, the control intervention must be safe, simple, and affordable. Current control measures for SARS, including case detection and isolation, tracing and follow-up of contacts, and quarantine, are effective but extremely time-intensive, costly, and socially disruptive. Few, if any, countries can sustain such efforts over time.
SARS TREATMENT

The treatment of coronavirus-associated SARS has been evolving and so far there is no consensus on an optimal regimen. Severe cases of SARS often require hospitalization, especially if breathing problems develop. Patient will be placed in isolation to prevent passing the disease to others.

Treatment strategies for SARS were first developed on theoretical bases and from clinical observations and inferences. Prospective randomized controlled treatment trials were understandably lacking during the first epidemic of this novel disease. The mainstream therapeutic interventions for SARS involve broad-spectrum antibiotics and supportive care, as well as antiviral agents and immunomodulatory therapy. Assisted ventilation in a non-invasive or invasive form would be instituted in SARS patients complicated by respiratory failure.

- Antibiotic therapy
- Antiviral therapy
- Immunomodulatory therapy
- Assisted ventilation
- Standardized treatment protocol
- An Alternative Proposal to Treat SARS
- Alternative medicine
- Inhibitors of SARS Chymotrypsin-Like Cysteine Proteinase
- Other immunomodulators
- Ventilation

**Antibiotic therapy**

Anti-bacterial agents are routinely prescribed for SARS because its presenting features are non-specific and rapid laboratory tests that can reliably diagnose the SARS-CoV virus in the first few days of infection are not yet available. Appropriate empirical antibiotics are thus necessary to cover against common respiratory pathogens as per national or local treatment guidelines for community-acquired or nosocomial pneumonia. Upon exclusion of other pathogens, antibiotic therapy can be withdrawn.

In addition to their antibacterial effects, some antibiotics are known to have immunomodulatory properties, notably the *quinolones and macrolides. Their effect on*
the course of SARS is undetermined.

Antiviral therapy

Various antiviral agents were prescribed empirically from the outset of the epidemic and their use was continued despite lack of evidence about their effectiveness. With the discovery of the SARS-CoV as the etiologic agent, scientific institutions worldwide have been vigorously identifying or developing an efficacious antiviral agent. Intensive in vitro susceptibility tests are underway.

Ribavirin

Ribavirin is an anti-viral drug which is active against a number of DNA and RNA viruses. It is a member of the nucleoside antimetabolite drugs that interfere with duplication of viral genetic material.

Ribavirin is a pro-drug, activated by cellular kinases which change it into the 5' triphosphate nucleotide. In this form it interferes with aspects of RNA metabolism related to viral reproduction.

The prevalence of side effects from ribavirin is dose-related. High doses often result in more adverse effects, such as hemolytic anemia, elevated transaminase levels and bradycardia.

1. Mechanism(s) of Action

Ribavirin's carboxamide group can resemble adenine or guanosine, depending on its rotation, and for this reason when ribavirin is incorporated into RNA, it pairs equally well with either cytosine or uridine, inducing mutations in RNA-dependent replication in RNA viruses. Such hypermutation can be lethal to RNA viruses.

Ribavirin 5' mono- di- and tri-phosphates, in addition, are all inhibitors of certain viral RNA-dependent RNA polymerases which are a feature of RNA viruses.

Neither of these mechanisms explains ribavirin's effect on many DNA viruses, which is more of a mystery. Ribavirin 5'-monophosphate inhibits cellular inosine monophosphate dehydrogenase, thereby depleting intracellular pools of GTP. This mechanism may be useful in explaining the drug's general cytotoxic and anti-DNA replication effect (i.e. its toxicity) as well as some effect on DNA viral replication.

Ribavirin is an inhibitor of some viral RNA guanylyl transferase and (guanine-7N-)-methyl transferase enzymes, and this may contribute to a defective 5'-cap structure of viral mRNA transcripts and therefore inefficient viral translation for certain DNA viruses, such as vaccinia virus (a complex DNA virus). It has been suggested that incorporation of ribavirin into the 5' end of mRNA transcripts would mimic the 7-methyl guanosine endcap of cellular mRNAs, causing poor cellular translation of these. This would be a cell-toxic effect, but it does not seem to be important at therapeutic ribavirin concentrations. Any difference between cellular and viral enzyme handling of ribavirin-containin mRNA transcripts, is a potential mechanism of differential inhibition of ribavirin.
to translation of mRNAs from viruses (including DNA viruses).
Finally, ribavirin is known to enhance host T-cell-mediated immunity against viral infection through helping to switch the host T-cell phenotype from type 2 to type 1. This may explain ribavirin's antiviral activity against some viruses such as hepatitis C, at doses which do not clearly interfere with replication of the virus when used without interferon.

2. Pharmacokinetic data

- Bioavailability: - 45% oral(without food), about 76% with fatty meal
- Metabolism: - Metabolized to 5’phosphates, de-riboside, and deriboside carboxylic acid
- Half life: -12 days - Multiple Dose; 120-170 hours - Single Dose
- Excretion: -10% fecal, remainder in urine (30% unchanged, remainder metabolites)

Neuraminidase inhibitor

Oseltamivir phosphate is a neuraminidase inhibitor for the treatment of both influenza A and B viruses. It was commonly prescribed together with other forms of therapy to SARS patients in some Chinese centers. Since there is no evidence that this drug has any efficacy against SARS-CoV, it is generally not a recommended treatment apart from in its role as an empirical therapy to cover possible influenza.

Protease inhibitor

Lopinavir-ritonavir co-formulation is a protease inhibitor preparation used to treat human immunodeficiency virus (HIV) infection. It has been used in combination with ribavirin in several Hong Kong hospitals, in the hope that it may inhibit the coronaviral proteases, thus blocking the processing of the viral replicase polyprotein and preventing the replication of viral RNA.

Preliminary results suggest that the addition of lopinavir-ritonavir to the contemporary use of ribavirin and corticosteroids might reduce intubation and mortality rates, especially when administered early. It thus appears worthwhile to conduct controlled studies on this promising class of drugs.

Human interferons

Interferons are a family of cytokines important in the cellular immune response. They are classified into type I (interferon α and β, sharing components of the same receptor) and type II (interferon γ which binds to a separate receptor system) with different antiviral potentials and immunomodulatory activities.

So far, the use of interferons in the treatment of SARS has been limited to interferon α, as reported from China and Canada. The Chinese experiences were mostly
in combining the use of interferons with immunoglobulins or thymosin, from which the efficacy could not be ascertained. Faster recovery was observed anecdotally in the small Canadian series using interferon alfacon-1, also known as consensus interferon.

In vitro testing of recombinant interferons against SARS-CoV was recently carried out in Germany using interferon α-2b, interferon β-1b and interferon α-1b. Interferon β was found to be far more potent than interferon α-1b, and remained effective after viral infection. Although interferon α could also effectively inhibit SARS-CoV replication in cell cultures, its selectivity index was 50-90 times lower than that of interferon β. These in vitro results suggested that interferon β is promising and should be the interferon of choice in future treatment trials.

**Human immunoglobulins**

Human gamma immunoglobulins were used in some hospitals in China and Hong Kong. In particular, an IgM-enriched immunoglobulin product was tried in selected SARS patients who were deteriorating despite treatment. However, as there was often concomitant use of other therapies such as corticosteroids, their effectiveness in SARS remains uncertain.

Convalescent plasma, collected from recovered patients, was also an experimental treatment tried in Hong Kong. It is believed that the neutralizing immunoglobulins in convalescent plasma can curb increases in the viral load. Preliminary experience of its use in a small number of patients suggests some clinical benefits and requires further evaluation.

**Traditional herbal medicine**

In China, traditional herbal medicine has been frequently used in conjunction with Western medicine to treat SARS, and is believed to be effective.

Recently, glycyrrhizin, an active component derived from liquorice roots, was tested against SARS-CoV in vitro. It has previously been used in the treatment of HIV and hepatitis C virus infections, and was found to be relatively non-toxic with infrequent side effects (e.g. hypertension; hypokalemia). In Vero cell cultures, it could inhibit the adsorption, penetration and replication of SARS-CoV, and was most effective when administered both during and after viral adsorption. It has been postulated that the mechanisms are mediated through the nitrous oxide pathway. However, as glycyrrhizin can only act against SARS-CoV at very high concentrations, its clinical dosing and utility remain uncertain. It could perhaps be explored as an adjunct therapy for SARS, or continued as an ingredient or base in herbal preparations.

**Immunomodulatory therapy**

The rationale for using immunomodulatory therapy in SARS is based on the fact that acute infections in general can stimulate the release of proinflammatory cytokines. In SARS, there may be an excessive host response or cytokine dysregulation. This hypothesis may be substantiated from the observation that clinical deterioration can paradoxically occur despite a fall in the viral load as IgG seroconversion takes place, as well as from autopsy findings which demonstrate a prominent increase in alveolar macrophages with hemophagocytosis. A tri-phasic model of pathogenesis comprising viral replicative, immune hyperactive and pulmonary destructive phases was thereafter
proposed. Intuitively, immunomodulatory therapy carefully applied during the hyper-immune phase may be an important treatment component in SARS.

**Corticosteroids**

Corticosteroids have been the mainstay of immunomodulatory therapy for SARS. Their timely use often led to early improvement in terms of subsidence of fever, resolution of radiographic infiltrates and better oxygenation, as described in many Chinese and Hong Kong reports. However, there is much scepticism and controversy about the use of corticosteroids, centering on their effectiveness, adverse immunosuppressive effects and impact on final patient outcomes.

An early Singaporean report on five patients on mechanical ventilation indicated that corticosteroids showed no benefits. A retrospective series of over 320 patients from a regional hospital in Hong Kong concluded that two-thirds progressed after early use of ribavirin and corticosteroids, but only about half of these subsequently responded to pulsed doses of methylprednisolone. A cohort study also noted that about 80% of patients had recurrence of fever and radiological worsening. This contrasted with another paper which described four patient stereotypes for pulsed methylprednisolone therapy, namely the good responder, good responder with early relapse, fair responder and poor responder. The good responders were the most common group. Methylprednisolone was identified as a major independent predictor for mortality.

The inconsistencies of treatment outcomes in SARS (or other illnesses) could be due to differences in the timing, dosing and duration of corticosteroid use. The following points have been emphasized:

1. The timing of initiating corticosteroids should coincide with the onset of a truly excessive immune response, which may be best represented by a combination of clinico-radiographic surrogate criteria. Too early use of corticosteroids may theoretically prolong the viral replicative phase and increase the viral burden, whereas delayed administration may not be able to halt the cytokine storm and prevent immunopathological lung damage.

2. The dosage of corticosteroids should be chosen to sufficiently counterbalance the degree of hyper-immunity. It should be adjusted to individual body weight and disease severity, with the latter reflected by surrogate criteria before the immunological profile of SARS is fully understood.

3. The duration of corticosteroids should be adequate to maintain the optimized immune balance. Too short a course may result in a rebound of cytokine storm with lung damage, whereas protracted usage will put the patient at risk of various corticosteroid complications.

As superimposing infections add to the morbidity and mortality and offset the beneficial effects of corticosteroids in SARS, it is of vital importance that strict control of hyperglycemia during corticosteroid administration is implemented to reduce the chance of septic complications and measures are taken to prevent ventilator-associated pneumonia. Successful control of superimposing infections also demands a judicious use of empirical and culture-directed antimicrobials.
Other immunomodulators

Thymosin alpha 1 is used in the treatment of chronic viral hepatitis B and C, and has also been administered to SARS patients in some Chinese hospitals. It is a relatively safe product and may augment T-cell function. The role and effectiveness of this agent in SARS has not yet been determined. Other immunomodulatory agents in anecdotal use included tumor necrosis factor blocking agents, namely etanercept and infliximab, and some other compounds like cyclophosphamide, azathioprine, cyclosporin and thalidomide.

Assisted ventilation

Despite treatment efforts, some SARS patients still develop acute hypoxemic respiratory failure. According to the current literature, 20-30% of SARS warranted admission into intensive care units, and 10-20% eventually required intubation and mechanical ventilation.

The initial management of SARS-related respiratory failure is oxygen supplementation. If the oxygen saturation remains low or dyspnea persists, assisted ventilation, either through non-invasive or invasive means, has to be considered.

Non-invasive ventilation

Non-invasive ventilation (NIV) is instituted via a face or nasal mask, as distinguished from invasive ventilation which necessitates endotracheal intubation. It is a valuable treatment for acute respiratory failure of various causes, and can avoid complications associated with intubation and invasive ventilation. Its application in SARS may be of particular benefit since SARS patients are frequently treated with high dose corticosteroids, which predispose them to infections including ventilator-associated pneumonia.

NIV can be given using a Continuous Positive Airway Pressure (CPAP) of 4-10 cm H2O or bi-level pressure support with an inspiratory positive airway pressure (IPAP) of <10 cm H2O and an expiratory positive airway pressure (EPAP) of 4-6 cm H2O. Contrary to the scenarios for non-SARS-related acute respiratory distress syndrome, higher pressures were generally not necessary and should be avoided whenever possible, because not only was there usually no additional clinical improvement observed, but it can also add to the risk of pneumothorax and pneumomediastinum. The latter conditions are known complications of SARS, even without assisted positive pressure ventilation.

Invasive mechanical ventilation

Patients with SARS-related respiratory failure who continue to deteriorate while on NIV, or in whom NIV is contraindicated, should be promptly intubated and mechanically ventilated. The actual endotracheal intubation procedure bears a high infective risk and healthcare workers must strictly adhere to all infection control measures. To minimize the risk, the procedure is best performed by highly skilled personnel using rapid sequence induction. Other approaches like a "modified awake" intubation technique and elective intubation upon recognizing signs of imminent need for airway management have been recommended.
Most centers used ventilation method and settings with reference to the strategies for acute respiratory distress syndrome (ARDS). Both pressure and volume control ventilation can be employed. The tidal volume should be kept low at 5-6 ml per Kg of the predicted body weight, and plateau pressures be kept less than 30 cm H₂O. Positive end-expiratory pressure (PEEP) should also be titrated to as low as possible to maintain the oxygenation, since a high rate (34%) of barotraumas have been reported. Mechanically ventilated patients should be adequately sedated and a short-term neuromuscular blockade may be required for permissive hypercapnia.

**Standardized treatment protocol**

- A standardized treatment protocol for adult SARS in Hong Kong

1. Antibacterial treatment
   - Start levofloxacin 500 mg once daily intravenously or orally
   - Or clarithromycin 500 mg twice daily orally plus amoxicillin and clavulanic acid 375 mg three times daily orally if patient <18 years, pregnant, or suspected to have tuberculosis

2. Ribavirin and methylprednisolone
   *Add combination treatment with ribavirin and methylprednisolone when:*

   🌡️ Extensive or bilateral chest radiographic involvement
   🌡️ Or persistent chest radiographic involvement and persistent high fever for 2 days
   🌡️ Or clinical, chest radiographic, or laboratory findings suggestive of worsening
   🌡️ Or oxygen saturation <95% in room air

**Standard corticosteroid regimen for 21 days**

- Methylprednisolone 1 mg/kg every 8 h (3 mg/kg daily) intravenously for 5 days
• Then methylprednisolone 1 mg/kg every 12 h (2 mg/kg daily) intravenously for 5 days

• Then prednisolone 0.5 mg/kg twice daily (1 mg/kg daily) orally for 5 days

• Then prednisolone 0.5 mg/kg daily orally for 3 days

• Then prednisolone 0.25 mg/kg daily orally for 3 days

• Then off

**Ribavirin regimen for 10-14 days**

• Ribavirin 400 mg every 8 h (1200 mg daily) intravenously for at least 3 days (or until condition becomes stable)

• Then ribavirin 1200 mg twice daily (2400 mg daily) orally

• Pulsed methylprednisolone

  • Give pulsed methylprednisolone if clinical condition, chest radiograph, or oxygen saturation worsens (at least two of these), and lymphopenia persists

  • Give as methylprednisolone 500 mg twice daily intravenously for 2 days, then back to standard corticosteroid regimen

• Ventilation

  • Consider non-invasive ventilation or mechanical ventilation if oxygen saturation <96% while on >6 L per min oxygen or if patient complains of increasing shortness of breath

• A treatment regimen for SARS in Guangzhou, China

  ○ Levofloxacin 200 mg twice daily plus azithromycin 600 mg daily intravenously.

  ○ Recombinant interferon a 3,000,000 U daily intramuscularly (for 75% of their cases).
○ If patients failed to respond (continuing high fever), with pulmonary infiltrates involving more than one pulmonary segment, or an expanding area of consolidation was observed, they were treated with high-dose methylprednisolone for 5-14 days (160-1000 mg daily depending on symptoms and X-ray results: 160 mg daily if one lobe was involved; 320 mg daily if >1 lobe; 25% needed an increase in dosage from 160 to 320-720 mg daily to maintain respiratory physiological parameters and to control temperature).

○ Oxygen 3-5 L per min was given by mask if SaO2 <95% or, if patients felt short of breath, non-invasive continuous positive airway pressure (CPAP) ventilation was used.

○ If CPAP failed (SaO2 <90%), mechanical ventilation was used.

○ Immunoglobulins, thymic peptides or recombinant human thymus proteins were given to some critically ill patients.

**An Alternative Proposal to Treat SARS**

The fact that most of the current victims that have died of SARS are those that have preexisting chronic illnesses, shows that the reserves in their defense system is an important variable in the outcome.

According to most proponents of vitamin C in its role of fighting infection, a low dosage of it is not useful at all. There is a critical threshold for this supplement to be effective. For the current prevention of SARS, one should maximize their level of vitamin C intake by a method called "titrating to bowel tolerance" to give optimal protection. The maximum protection from oral doses of vitamin C is obtained at a point just short of diarrhea.

One can start with three grams a day (3 x 1 gram), and gradually increase by one gram a day until the point of causing slight diarrhea, then, it can be stepped back one notch. Since the absorption mechanism in the gut and kidney can reach a saturation point, it is better to take multiple doses throughout the day than one large dose.

Some people may even require a dosage of 200 grams a day before exhibiting bowel intolerance. This means the body is actually using it and needs it. It is not in excess, so it is doing its job of protecting your body. When it is accessible, the buffered form of vitamin C can prevent gastric irritation when vitamin C is taken in a high dose.

Since vitamin C is water soluble, there is no accumulated toxicity in the body, for the body can easily excrete any excess. Concerns by critics of some theoretical side effects such as kidney stones have not been substantiated by clinical observations.

The oral approach is suitable for prevention in the general public and for those who have come in contact with someone infected with SARS. Those who have already contracted the illness would benefit from a much higher dosage through intravenous infusion of vitamin C. This can serve as a concurrent treatment to enhance whatever antibiotics or medications that orthodox medication can offer.
Vitamin C has many mechanics of action that qualifies it as a possible antidote for the present SARS epidemic:

- Vitamin C is an important ingredient for the synthesis of collagen, a glue like material that holds cells together. Collagen reinforces the physical barrier against germs attacking from the outside.

- Vitamin C is essential for the activity of the white blood cells, the phagocytosis activities of neutrophils, the production of Interferon (an antiviral substance) and antibodies, and the action of the B and T lymphocytes.

- During illness, there is a rapid consumption and therefore depletion of the level of vitamin C in the body. Tissue depletions, followed by general depletion, lead to the rapid breakdown of the body’s defense systems. Complications ensue.

- The replication of the virus and the body fighting it involve the release of free radicals. Free radicals of the potent toxins ultimately cause symptoms and damage to the body. Vitamin C is well known to be a strong antibiotic, capable of neutralizing free radicals.
PREVENTION 9

In the absence of a vaccine, the most effective way to control a new viral disease such as SARS is to break the chain of transmission from infected to healthy persons. In almost all documented cases, SARS is spread through close face-to-face contact with infected droplets when a patient sneezes or coughs.

It is best to avoid travelling to places affected by SARS unless absolutely necessary. Frequent washing of hands will help minimise the risk of infection. Though wearing a mask helps reduce inhalation of droplets spread in the air due to sneezing or coughing, it may not be of much use in public areas.

Infection Control in Healthcare Settings

Hospital workers remain on the front lines in the global response to SARS. They are at considerable risk of contracting SARS when there is an opportunity for unprotected exposure. In order to protect healthcare workers and to prevent disease dissemination, strict infection control measures and public education are essential.

In the SARS hospitals, all healthcare workers should have mandatory body temperature recording twice daily. In non-SARS hospitals, in order to minimize patient contact and deal with the potential increased workload from the SARS hospital, all elective surgery is cancelled, as are most outpatient clinics. In order to protect themselves, staff are required to wear an N95 mask, gloves and gown when in contact with all patients. Every attempt is made to streamline workflow to minimize the number of staff in contact with a patient and the time spent with a patient. Because of the potential risk of an individual healthcare worker contaminating a whole department of colleagues, medical units have been divided into small teams who do not have any contact with the other team. Some departments have mandated that one team must be at home to ensure that if another team is quarantined because of exposure, there will still be a clean team available to continue emergency work.

Protective Measures

Droplet infection seems to be the primary route of spread for the SARS virus in the healthcare setting. In a case control study in five Hong Kong hospitals, with 241 non-infected and 13 infected staff with documented exposures to 11 index patients, no infection was observed among 69 healthcare workers who reported the use of mask, gloves, gowns, and hand washing. N95 masks provided the best protection for exposed healthcare workers, whereas paper masks did not significantly reduce the risk of infection.

Table: shows a summary of precautions for droplet infection. The implementation of aggressive infection control measures was effective in preventing the further transmission of SARS.

- Patients should wear N-95 masks once symptoms develop and be placed immediately in isolation facilities with negative pressure.
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<tbody>
<tr>
<td></td>
<td>Healthcare workers should wear similar masks together with head cover, goggles, gowns, and gloves when caring for these patients.</td>
</tr>
<tr>
<td></td>
<td>Daily and terminal disinfection should be thorough, with careful washing and disinfection of the bed, handrails, bedside tables, floor, and equipment with hypo chlorite solution (1000 ppm).</td>
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<td></td>
<td>For intubated patients, the use of a closed suction system is essential to avoid air leakage and enhanced disease transmission.</td>
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As the SARS virus may be viable in the environment for several days, precautionary measures, including rigorous disinfection and hygiene procedures should provide the highest standard of protection.

**Hand washing**

It is essential to wash hands before touching faces or eyes.

**Gloves**

Health Canada advises double gloving when attending a suspected SARS patient. Hands must be washed after de-gloving.

**Face Masks**

The N95 respirator/mask has filter efficiency level of 95% or greater against particulate aerosols free of oil when tested against a 0.3-micron particle. It is fluid resistant, disposable and may be worn in surgery. The "N" means "Not resistant to oil". The "95" refers to a 95% filter efficiency. The following points have to be kept in mind:

- An occlusive fit and a clean shave for men provide the best protection for the healthcare worker.
- Masks should be tested for fit according to the manufacturer's recommendations. In addition, masks should be fit-checked each time the mask is put on. To check the mask, the wearer takes a quick, forceful inspiration to determine if the mask seals tightly to the face.
- For instructions on how best to use the N95 mask or equivalent, refer to the handout provided by the manufacturer, or follow your provincial regulations.
- There are no published data on the length of time the mask is effective for the wearer. Health Canada recommends masks should be changed if they become wet, interfere with breathing, are damaged or visibly soiled.
- A respirator (mask) which has been exposed to a probable SARS case is considered contaminated and should be discarded.
- When discarding the mask: Wash hands prior to handling the mask. Carefully remove the mask using the straps. Discard. Wash hands after handling the mask.
• If re-using the mask: Place in a clean, dry location such as a paper bag. Do not mark the mask with a pen or marker. The name of the owner should be written on the outside of the paper bag to identify the mask. Hands should be washed after handling the mask.

Even for doctors in the community, it is advisable to wear a N95 mask when seeing any patient with respiratory symptoms

**Additional protection**

Theatre caps may reduce the risk of staff potentially contaminating their hands by touching their hair. The nature of the novel coronavirus is such that mucous membrane and eye spread is likely and therefore disposable fluid-resistant long sleeved gowns, goggles and disposable full-face shields are recommended for frontline medical staff at risk of exposure to SARS.
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