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A critical review on severe acute respiratory syndrome (SARS)

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Abstract
Severe acute respiratory syndrome (SARS) is a newly emerged infectious disease with a significant morbidity and mortality. On 11 February 2003, the Program for Monitoring Emerging Diseases reported that, since November 2002, an unidentified agent had caused some 300 cases of pneumonia in persons in the south of China. On 12 March 2003, the World Health Organization (WHO) issued a global alert regarding these and similar cases in Hong Kong and Vietnam. This clinical syndrome subsequently became known as "severe acute respiratory syndrome" (SARS). Since then, 8098 people in 37 countries have had probable SARS diagnosed, 774 of whom have died, yielding a global case-fatality rate of average 10%. On 5 July 2003, the WHO reported that the last known human chain of transmission of SARS had been broken.
A newly discovered coronavirus (SARS-CoV) has been identified as the cause of SARS. SARS-CoV–like viruses have been detected in Himalayan palm civets and a raccoon-dog in a market in southern China, suggesting that the origin of SARS-CoV may have been from these or other wild animals. Given the possibility that human or animal reservoirs of SARS-CoV may still exist and that SARS may have a seasonal predilection, there is concern that SARS may return in upcoming respiratory seasons. WHO guidelines emphasize the need for all countries to remain vigilant and to maintain their capacity to detect and respond to the potential reemergence of SARS.

Keywords: severe acute respiratory syndrome (sars), sars-cov, epidemic, virus, emerging diseases, etc.

Introduction
In 1992, the Institute of Medicine (IOM) published a report [1] on the increasing public health challenges created by emerging infections. Described as a "wake up call" on the risks of infectious diseases, the report sought to reverse the trend toward complacency that had developed in the last half of the 20th century following years of significant medical and scientific advances. In March 2003, the IOM published an update [2] to this report, expanding on these challenges and highlighting the need for more global recognition and response to the threats posed by infectious diseases. The new report, Microbial Threats to Health: Emergence, Detection, and Response, describes many factors that alone or in combination can lead to the emergence of infectious diseases and provides recommendations to reduce their impact on public health worldwide.
In the last few years, new and re-emerging pathogens have surfaced at alarming rates. Recent examples include West Nile virus, monkey-pox, and the intentional anthrax attacks in the United States along with the emergence of severe acute respiratory syndrome (SARS) and the continued threats of influenza on a global level. These events have resulted in renewed interest in infectious diseases on the part of the media, policy makers, and the public. They have also clearly shown how infectious disease outbreaks can impact national security and the global economy. The rapid spread of illnesses across national boundaries has also served to highlight the widespread implications that can result from local outbreaks and the importance of rapid response efforts to contain them.

Aims and Object
- Reinforce basic infection control practices in healthcare facilities and among healthcare personnel.
- Ensure early recognition and prevention of transmission of SARS-CoV and other respiratory viruses at the initial encounter with a healthcare setting.
- In the absence of SARS-CoV transmission in the world, implement screening to detect the re-emergence of SARS-CoV, and ensure appropriate triage and management of patients with possible SARS-CoV disease.
- In the presence of person-to-person transmission of SARS-CoV in the world, ensure the prompt identification and appropriate management of patients with possible and known SARS-CoV disease.

Material and Method
This study is carried out by literature search and critical review of the obtained facts. The various medical research databases like PubMed, Google scholar, and another national research databases. The terms entered for search are "Severe Acute Respiratory Syndrome (SARS), also known as SARS-CoV disease". Manual search was made by going through the reference list of retrieved articles to identify relevant additional study.

Observation and Discussion
Severe acute respiratory syndrome (SARS) is a viral respiratory disease of zoonotic origin caused by the SARS coronavirus (SARS-CoV). Between November 2002 and July

2003, an outbreak of SARS in southern China caused an eventual 8,098 cases, resulting in 774 deaths reported in 37 countries [3], with the majority of cases in Hong Kong (9.6% fatality rate) according to the World Health Organization (WHO) [4].

Epidemiology

The early cases of SARS appeared to have originated in southern China. In November 2002, there was an unusual epidemic of severe pneumonia of unknown aetiology in Foshan, Guangdong Province in southern China, with a high rate of transmission to healthcare workers [5]. A retrospective analysis of 55 patients admitted to a chest hospital with atypical pneumonia in Guangzhou between 24 January and 18 February 2003 showed positive SARS CoV in the nasopharyngeal aspirates, whereas 48 (87%) patients had positive antibodies to SARS CoV in their convalescent sera. Genetic analysis showed that the SARS CoV isolates from Guangzhou shared the same origin with those in other countries, with a phylogenetic pathway that matched the spread of SARS to other parts of the world [6]. By April 2003, the epidemic reached its peak in Beijing and several major cities. By the end of the SARS epidemic, there were 5327 probable cases within mainland China with a mortality rate of 7%.

Mode of Transmission

SARS-CoV has been isolated in sputum samples, nasal secretions, serum specimens, faces samples, and bronchial washings [7]. Evidence suggests that SARS-CoV is transmitted by contact and/or droplets [8] and that the use of any mask (surgical or N95) significantly decreases the risk of infection [9]. However, there are cases that defy explanation based on these modes of transmission, suggesting that alternative modes of transmission may also exist [10]. SARS-CoV remains viable in faces for days [11], and the outbreak at the Amoy Gardens apartments highlights the possibility of a faecal-oral or faecal-droplet mode of transmission [12]. A number of cases occurred in health care workers wearing protective equipment following exposure to high-risk aerosol- and droplet-generating procedures, such as airway manipulation, administration of aerosolized medications, non-invasive positive pressure ventilation, and bronchoscopy or intubation [13].

Symptoms

SARS symptoms are similar to those of the flu, including are:

- Fever over 100.4°F (>38° C)
- Dry cough
- Sore throat
- Problems breathing, including shortness of breath
- Headache
- Body aches
- Loss of appetite
- Malaise
- Night sweats and chills
- Confusion
- Rashes
- Diarrhoea

Breathing issues will appear within two to 10 days after a person is exposed to the virus. Health officials will quarantine a person who presents the above symptoms and family members if they have a history of foreign travel. The person will be quarantined for 10 days to prevent the virus from spreading.

Factors that increase your risk of contracting the disease include close contact with someone diagnosed with SARS and a history of travel to any other country with a reported SARS outbreak [14].

Most cases of SARS begin with a high fever. Other early symptoms include those common to flu, such as aches, chills, diarrhoea, dry coughing, and shortness of breath. These will develop over the course of a week.

Patients may go on to develop pneumonia, an infection of the lungs.

Serious complications, such as respiratory failure, heart failure, and liver failure may occur.

These complications are more likely in people aged over 60 years, and those with pre-existing co-morbidities, such as diabetes or hepatitis [15].

Diagnosis

Severe Acute Respiratory Syndrome (SARS): Laboratory diagnostic tests

Researchers in several countries are working towards developing fast and accurate laboratory diagnostic tests for the SARS coronavirus (SARS-CoV). However, until standardized reagents for virus and antibodies detection are available and methods have been adequately field tested, SARS diagnosis remains based on the clinical and epidemiological findings: acute febrile illness with respiratory symptoms not attributed to another cause and a history of exposure to a suspect or probable case of SARS or their respiratory secretions and other bodily fluids.

Those requirements are reflected in the current WHO case definitions for suspect or probable SARS. However in several countries (Canada, France, Germany, Hong Kong SAR, Italy, Japan, the Netherlands, Singapore, United Kingdom and the United States of America) samples from suspected and probable SARS cases are being tested for SARS-CoV.

Laboratory test criteria for confirming or rejecting the diagnosis of SARS remain to be defined-

- **Molecular tests (PCR)**

Polymerase chain reaction (PCR) can detect genetic material of the SARS-CoV in various specimens (blood, stool, respiratory secretions or body tissues sampling for Severe Acute Respiratory Syndrome (SARS) diagnostic tests). Primers, which are the key pieces for a PCR test, have been made publicly available by WHO network laboratories on the WHO web site. A ready-to-use PCR test kit containing primers and positive and negative control has been developed. Testing of the kit by network members is expected to quickly yield the data needed to assess the test's performance, in comparison with primers developed by other WHO network laboratories and in correlation with clinical and epidemiological data.

Principally, existing PCR tests are very specific but lack sensitivity. This means that negative tests cannot rule out the presence of the SARS virus in patients. Furthermore,

contamination of samples in laboratories in the absence of laboratory quality control can lead to false positive results.
Positive PCR results, with the necessary quality control procedures in place. Recommendations for laboratories testing for SARS-corona virus are very specific and mean that there is genetic material (RNA) of the SARS-CoV in the sample. This does not mean that there is live virus present, or that it is present in a quantity large enough to infect another person.
Negative PCR results do not exclude SARS. SARS-CoV PCR can be negative for the following reasons: - The patient is not infected with the SARS coronavirus; the illness is due to another infectious agent (virus, bacterium, fungus) or a non-infectious cause. - The test results are incorrect ("false-negative"). Current tests need to be further developed to improve sensitivity. - Specimens were not collected at a time when the virus or its genetic material was present. The virus and its genetic material may be present for a brief period only, depending on the type of specimen tested.

- **Antibody tests**

These tests detect antibodies produced in response to the SARS coronavirus infection. Different types of antibodies (IgM and IgG) appear and change in level during the course of infection. They can be undetectable at the early stage of infection. IgG usually remains detectable after resolution of the illness.
The following test formats are being developed, but are not commercially available yet: - ELISA (Enzyme Linked Immuno Sorbant Assay): a test detecting a mixture of IgM and IgG antibodies in the serum of SARS patients yields positive results reliably at around day 21 after the onset of illness. – IFA (Immunofluorescence Assay): a test detecting IgM antibodies in serum of SARS patients yields positive results after about day 10 of illness. This test format is also used to test for IgG. This is a reliable test requiring the use of fixed SARS virus on an immunofluorescence microscope.
Positive antibody test results indicate a previous infection with SARS-CoV. Seroconversion from negative to positive or a four-fold rise in antibody titre from acute to convalescent serum indicates recent infection.

Negative antibody test results: No detection of antibody after 21 days from onset of illness seems to indicate that no infection with SARS-CoV took place.

- **Cell culture**

Virus in specimens (such as respiratory secretions, blood or stool) from SARS patients can also be detected by inoculating cell cultures and growing the virus. Once isolated, the virus must be identified as the SARS virus with further tests. Cell culture is a very demanding test, but currently (with the exception of animal trials) 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 (see negative PCR test result) [16].

- **SARS may be suspected in a patient who has-**
- Any of the symptoms, including a fever of 38 °C (100 °F) or higher
- Either a history of-

1. Contact (sexual or casual) with someone with a diagnosis of SARS within the last 10 days.
2. Travel to any of the regions identified by the World Health Organization (WHO) as areas with recent local transmission of SARS (affected regions as of 10 May 2003 were parts of China, Hong Kong, Singapore and the town of Gerald ton, Ontario, Canada).

For a case to be considered probable, a chest X-ray must be positive for atypical pneumonia or respiratory distress syndrome.
The World Health Organization (WHO) has added the category of "laboratory confirmed SARS" for patients who would otherwise be considered "probable" but who have not yet had a positive chest X-ray changes, but have tested positive for SARS based on one of the approved tests (ELISA, immunofluorescence or PCR) [17].

Prevention and control

There is no vaccine for SARS till date. Isolation and quarantine remain the most effective means to prevent the spread of SARS. Other preventive measures include are:

- Hand washing thoroughly using an alcohol-based hand detergent
- cover your mouth and nose when you sneeze or cough [18]
- Disinfection of surfaces for fomites
- Wearing a surgical mask
- Avoiding contact with bodily fluids
- Washing the personal items of someone with SARS in hot, soapy water (eating utensils, dishes, bedding, etc.) [19].
- Keep children home from school if they develop a fever or any breathing problems after coming in contact with someone with SARS.

Hospital infection was the main epidemic form of SARS in the early stage. Many measures such as control and isolation of the source of transmission-

- Setup of the fever clinic and medical observation area,
- Isolation and medical observation of suspected cases,
- Enforcing ventilation and disinfection of the ward area,
- Stopping fresh-air system,
- Forbidding outside visiting,
- Strengthen prevention of medical staffs were carried out and the SARS hospital infection could be prevented and controlled [20].

Treatment

The best treatment strategy for severe acute respiratory syndrome (SARS) is still unknown. Ribavirin and corticosteroids were used extensively during the SARS outbreak. Ribavirin has been criticized for its lack of efficacy. Corticosteroids are effective in lowering the fever and reversing changes in the chest radiograph but have the caveat of encouraging viral replication. The effectiveness of corticosteroids has only been suggested by uncontrolled observations, and the role of these agents in therapy remains to be established by randomized controlled studies. Both ribavirin and corticosteroids have very significant side effects.

The lopinavir / ritonavir combination has been shown to reduce the intubation rate and the incidence of adverse clinical outcomes when used with ribavirin. When patients deteriorate clinically despite treatment with ribavirin and corticosteroids, rescue treatment with convalescent plasma and immune-oglobulin may be beneficial. Non-invasive positive pressure ventilation is a sound treatment for SARS patients with respiratory failure if administered with due precaution in the correct environment. Interferons and other novel agents may hold promise as useful anti-SARS therapies in the future. The experience with traditional medicine is encouraging, and its use as an adjuvant should be further investigated [21].

Conclusion

The virus is predominantly spread by droplets or by direct and indirect contact. Shedding in faces and urine also occurs. Medical personnel, physicians, nurses, and hospital workers are among those commonly infected.

At present, the most efficacious treatment regimen for SARS is still subject to debate. For patients with progressive deterioration, intensive and supportive care is of primary importance and Immunomodulation by steroid treatment, Cleaning and disinfection of environmental surfaces, routine infection control in healthcare facilities are may be important.

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