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NOVEL EMERGING INFECTIONS: SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS (SARS-COV)

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ABSTRACT

Several new viral respiratory tract infectious diseases with epidemic potential that threaten global health security have emerged in the past 15 years. A severe viral illness caused by a newly discovered coronavirus was first reported in the 2003. In 2003, WHO issued a worldwide alert for an unknown emerging illness, later named severe acute respiratory syndrome (SARS). The disease caused by a novel coronavirus (SARS-CoV) rapidly spread worldwide, Coronaviruses are enveloped viruses with plus-stranded RNA genomes of 26-32 kb, the largest contiguous RNA genomes in nature. Symptoms of SARS include: high fever, cough pneumonia, breathing difficulties headache, chills, muscle aches and sore throat. According to the World Health Organization (WHO), From November 2002 to July 2003 a total of 8098 patients, in 25 countries, were affected by the atypical pneumonia which resulted in 774 deaths globally. The severe acute respiratory syndrome (SARS) is a febrile respiratory illness primarily transmitted by respiratory droplets or close personal contact. There are several laboratory tests used to detect SARS-CoV and other causes of respiratory illness. Many methods used in the treatment of viral infections have been only partially effective. For example, the standard treatment in HCV (with ribavirin and interferon-alpha) is effective in 50% of cases.

KEYWORDS: Severe acute respiratory syndrome; Coronaviruses; Transmission; Treatment.

INTRODUCTION

Severe acute respiratory syndrome (SARS) is an emerging, sometimes fatal, respiratory illness. The first identified cases occurred in China in late 2002, and the disease has now

spread throughout the world. On 11 February 2003 China reported to the WHO that 305 cases of a typical pneumonia of unknown etiology had been identified in Guangdong Province since 16 November 2002, and that five people had died.[1] The emergence of newly human viral diseases affecting the respiratory tract continues to threaten global public health security[2] By the 15th of March the disease was named Severe Acute Respiratory Syndrome (SARS)[3-5] and by the 27th of March the causative agent was identified as a completely novel coronavirus, termed SARS-CoV[6-8] SARS-CoV and MERS-CoV have clear zoonotic origins, although their exact paths from animal reservoir to human infection are not yet clear. Viruses with high nucleotide identity to SARS-CoV were found in key amplifying hosts such as palm civets and raccoon dogs in Guangdong Province China during the 2002–2003 SARS epidemics [9] Identified highly conserved viruses circulating in horseshoe bats, including some strains that are able to bind to, and infect, human cells. The existence of novel bat SARS-like coronaviruses that also use bat, civet and human angiotensin 1 converting enzyme 2 (ACE2) receptors for entry, such as SARS-CoV, strongly suggests an opportunity for further zoonotic disease outbreaks in human and animal populations [10-13] SARS causes an atypical pneumonia characterized by cough, fever and infiltrates with a ground-glass appearance on X-ray [14-15] Early-stage disease was characterized by acute DAD, with oedema, fibrin and hyaline membranes in the alveolar spaces, typical of ALI [16] Other patients predominantly showed an acute fibrinous and organizing pneumonia pattern or a mixture of the two patterns [17-18] Longer-term disease courses typically progressed to organizing phase DAD and eventual deposition of fibrous tissue. Autopsy of fatal SARS-CoV cases also revealed denuded airways, haemorrhage and increased macrophage populations in the lung [19-20] During the SARS epidemic, researchers noted that late-term disease progression was unrelated to viraemia but was more likely to be associated with immunopathological damage.[21]

EPIDEMIOLOGY

Severe acute respiratory syndrome (SARS) is a viral respiratory illness that was first reported in Asia in February 2003. Over the next few months, the illness spread to more than two dozen countries in North America, South America, Europe and Asia. According to the World Health Organization (WHO), From November 2002 to July 2003 a total of 8098 patients, in 25 countries, were affected by the atypical pneumonia which resulted in 774 deaths globally. The mortality rates were drastically increased in certain population [22] and age [23] groups to as high as 40%–55%. Further local outbreaks were reported in Singapore, Taiwan and

Beijing from accidental laboratory exposure and animal to human transmission in Guangzhou in late 2003 and early 2004.[24] This was directly related to the lifting of a ban on serving palm civets in wet markets and restaurants, which was implemented during the SARS outbreak.[25] As of 4 December 2012, nine laboratory-confirmed cases of severe pneumonia caused by the novel coronavirus have been reported to WHO. Five of the nine cases were fatal. Onset of disease was from April to October 2012; all cases were resident in Saudi Arabia, Qatar or Jordan during the presumed 10 days incubation period.[26] 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.[27] The most significant recent epidemiological development is the retrospective identification of novel coronavirus in preserved biological samples from two fatal cases of severe pneumonia in Jordan in April 2012. The two cases were part of a cluster of eleven cases with respiratory symptoms linked in time and space to a hospital near Amman, Jordan. Eight of the cases in the cluster were healthcare workers. The two confirmed cases were reported on 30 November 2012 through the Event Information Site for International Health Regulation Focal Points and in a WHO press statement.[26]

VIROLOGY

Coronaviruses (CoVs) infect and cause disease in a wide variety of species, including bats, birds, cats, dogs, pigs, mice, horses, whales, and humans.[28] Recent studies suggest that bats act as a natural reservoir for coronaviruses.[29] Coronaviruses (CoV) are found in a wide variety of animals in which they can cause respiratory, enteric, hepatic, and neurological diseases of varying severity. As a result of the unique mechanism of viral replication, CoV have a high frequency of recombination.[10] Until 2003, only two Coronaviruses were known to infect humans. Human Coronaviruses (HCoVs) HCoV-229E and HCoV-OC43 were identified in the 1960s as the causative agents' of-generally mild-respiratory illnesses.[30-31] In 2002 to 2003, a previously unknown coronavirus-severe acute respiratory syndrome coronavirus (SARS-CoV) caused a widespread outbreak of respiratory disease in humans, resulting in approximately 800 deaths and affecting around 30 countries.[32-33] Coronaviruses are enveloped viruses with plus-stranded RNA genomes of 26-32 kb, the largest contiguous RNA genomes in nature.[34-35] They are classified in 3 groups: groups I and II (pathogenic

viruses for mammals) and group III (poultry). Group I contains 2 prototypic human pathogenic coronaviruses: human coronavirus (hCoV)-NL63 and hCoV-229E.[31, 36] Human pathogenic group II viruses include hCoV-HKU1 and hCoV-OC43.[37-38] Another human pathogenic coronavirus within a subgroup of group II (termed group IIb) is the severe acute respiratory syndrome (SARS) coronavirus.[39-40]

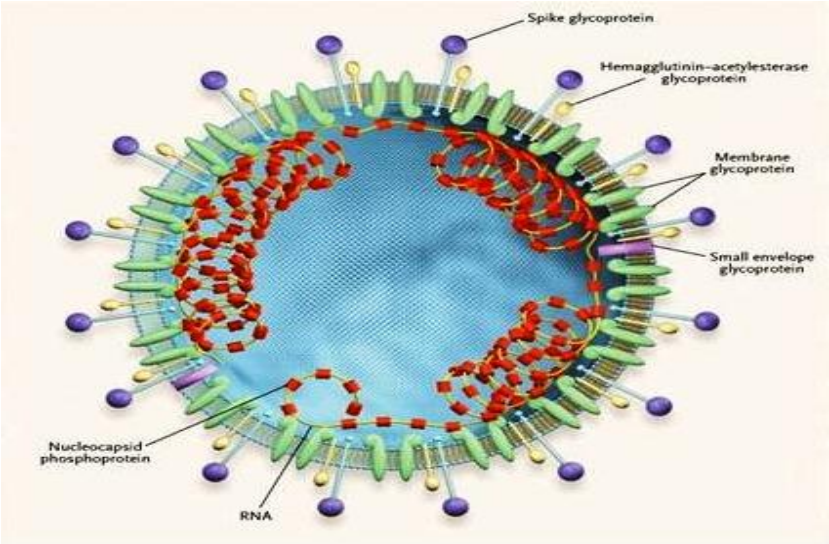

Figure: 1. Novel SARS-CoV [41]

SYMPTOMS & COMPLICATIONS

Symptoms of SARS include: high fever (temperature greater than 38°C), which is often the first symptom, cough pneumonia (lung infection or inflammation), breathing difficulties (about 20% require artificial ventilation in an intensive care unit), headache, chills, muscle aches, poor appetite, dizziness, diarrhoea (in 10 to 20% of patients) and sore throat.[3, 5, 42] SARS presents as an atypical pneumonia [43-44] with pneumocytes being the primary target of infection. Infection results in haemorrhagic inflammation in most pulmonary alveoli with alveolar thickening diffuse alveolar damage, desquamation of pneumocytes, formation of hyaline membranes and multinucleated pneumocytes with capillary engorgement and microthrombosis.[45] Approximately 60% of patients deteriorated in the second week of infection, presenting with persistent fever, dyspnoea and oxygen desaturation. Approximately 20%–30% of patients were subsequently admitted to intensive care, where mechanical ventilation was necessary.[46] A surprising finding with the SARS outbreak was that it was not as great a threat to infants and children.[47] Clinical presentation was less severe in infants and no children aged between 1 and 12 required intensive care or mechanical

ventilation.[48-49] This is in sharp contrast to the age related burden of other respiratory infections and the underlying biological mechanism remains unclear.[32]

TRANSMISSION

The severe acute respiratory syndrome (SARS) is a febrile respiratory illness primarily transmitted by respiratory droplets or close personal contact. The fact that the majority of new infections occurred in close contacts of patients, such as household members, healthcare workers, or other patients who were not protected with contact or respiratory precautions, indicates that the virus is predominantly spread by droplets or by direct and indirect contact.[50] The airborne spread of SARS does not seem to be a major route of transmission. However, the apparent ease of transmission in some instances is of concern.[51] Airborne transmission of infectious agents refers to the transmission of disease caused by dissemination of droplet nuclei that remain infectious when suspended in air over long distance and time. Airborne transmission can be further categorized into obligate or preferential airborne transmission.[52] The transmission of SARS in the Metropole Hotel and the Amoy Gardens has been attributed in part to environmental contamination, with a possible animal vector19 contributing to the spread of the virus in the Amoy Gardens outbreak. There has also been limited transmission associated with air travel.[53]

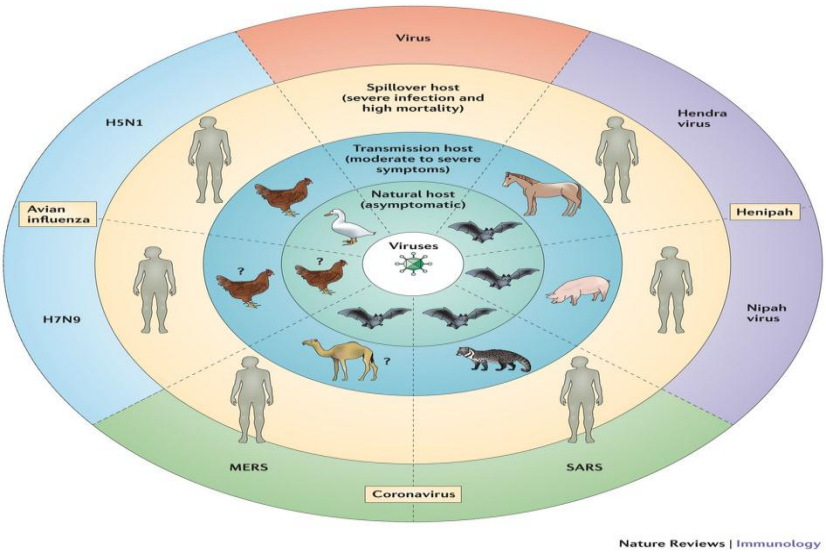

Figure 2: Emerging infectious diseases is influenced by the host-pathogen interaction

DIAGNOSIS

There are several laboratory tests used to detect SARS-CoV and other causes of respiratory illness. Laboratory test results should always be considered with clinical observations and

epidemiologic data in making a final diagnosis. Laboratory diagnostics are essential for detecting and documenting a reappearance of SARS-CoV, responding to and managing outbreaks, and managing concerns about SARS in patients with other respiratory illnesses.

Polymerase chain reaction (PCR): It can detect genetic material of the SARS-CoV in various specimens like blood, stool, respiratory secretions or body tissues sampling for Severe Acute Respiratory Syndrome (SARS) diagnostic tests.[55-58]

ELISA (Enzyme Linked ImmunoSorbant 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.[55-56, 58]

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 fourfold rise in antibody titre from acute to convalescent serum indicates recent infection.[55, 57-58]

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. Patients with a negative antibody test result whose specimens were obtained 28 days before illness onset or before should have another serum specimen collected >28 days after onset of symptoms.[55, 57]

TREATMENT & PREVENTION

People who are thought to have SARS should be checked right away by a health care provider. If they are suspected of having SARS, they should be kept isolated in the hospital. Treatment may include [59]:

- Antiviral medications (although how well they work for SARS is unknown)
- Antibiotics to treat bacteria that cause pneumonia
- High doses of steroids to reduce swelling in the lungs
- Oxygen, breathing support (mechanical ventilation), or chest therapy.

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.

Ribavirin, a nucleoside analogue that has activity against a number of viruses in vitro, was widely used for treating SARS patients after observing the lack of clinical response to broad-spectrum antibiotics and Oseltamivir.[21, 60]

Antibiotic therapy: Antibacterial agents are routinely prescribed for SARS because its presenting features are nonspecific and rapid laboratory tests that can reliably diagnose the SARSCoV virus in the first few days of infection are not yet available.[61]

Protease inhibitor: Lopinavir-ritonavir co-formulation (Kaletra®, Abbott Laboratories, USA) is a protease inhibitor preparation used to treat human immunodeficiency virus (HIV) infection. Many methods used in the treatment of viral infections have been only partially effective. For example, the standard treatment in HCV (with ribavirin and interferon-alpha) is effective in 50% of cases.[62] Administration of convalescent plasma, serum, or hyperimmune immunoglobulin may be of clinical benefit for treatment of severe acute respiratory infections (SARIs) of viral etiology.[63]

Infection control measures in the home[64]

- Hand hygiene: All persons in the household should carefully follow recommendations for hand hygiene (i.e., hand washing with soap and water or use of an alcohol-based hand rub) after touching body fluids (e.g., respiratory secretions, stool, urine, vomitus) and potentially contaminated surfaces and materials.
- Source control: Patients should cover the nose/mouth when coughing and dispose of tissues in a lined waste container. If possible, the patient should wear a surgical mask when others are present.
- Gloves and other protective attire: Use of disposable gloves should be considered for any direct contact with the body fluids of a patient with possible or known SARS-CoV disease.
- Laundry (e.g., bedding, towels and clothing): Towels and bedding should not be shared.
- Dishes and other eating utensils: Objects used for eating should not be shared, but separation of eating utensils for use by the SARS patient is not necessary.

CONCLUSION

Severe acute respiratory syndrome (SARS) is a new infectious disease which was first recognized in late February 2003. Respiratory viruses can cause a wide spectrum of

pulmonary diseases, ranging from mild, upper respiratory tract infections to severe and life-threatening lower respiratory tract infections. Mortality, initially believed to be around 3 %, may well be as high as 15 %.The SARS coronavirus (SARS CoV) is predominantly spread in droplets that are shed from the respiratory secretions of infected persons. Fecal or airborne transmission seems to be less frequent. In the absence of effective drugs or a vaccine for SARS, control of this disease relies on the rapid identification of cases and their appropriate management, including the isolation of suspect and probable cases and the management of their close contacts. In the great majority of countries, these measures have prevented imported cases from spreading the disease to others. 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. Immunomodulation by steroid treatment may be important.

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