Review Article

Severe Acute Respiratory Syndrome (SARS): A Deadly Disease

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SARS or severe acute respiratory syndrome is a term used to describe a serious respiratory illness, which has recently been reported in parts of the world and has spread widely over the past 6 months. At this moment, public health authorities, physicians and scientists around the world are struggling to cope with this rapidly spreading multicountry outbreak of an unexplained new disease in humans[1]. This appears to be the first severe and easily transmissible disease to emerge in the 21st century[2]. Though much about the syndrome remains poorly understood, including the exact identity of the causative virus, the indications are that the outbreak is otherwise being contained[3].

No one exactly knows for sure where SARS began but it was first identified in the province of Guandong in Southern China in November of 2002[4]. In late February the disease was first brought to Hong Kong from Guandong by an infected medical doctor who spread the virus to at least 13 guests and visitors, all on the same floor of the hotel where he stayed. These people carried the disease with them when they returned home[5]. Cases of SARS have now been reported in 30 different countries. As of today, (June 6, 2003), SARS has sickened more than 8400 people globally and caused nearly 800 deaths[6,7]. The largest numbers so far have been reported in China (5322), Hong Kong (1728), Taiwan (596), Singapore (206) and Canada (148). The World Health Organization (WHO) has warned that the death rate may rise to 10% or more[8].

CDC's interim suspected SARS case definition continues to be based on clinical criteria and epidemiologic linkage to other SARS cases or areas with community transmission of SARS[9]. The WHO case definition of probable SARS include radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome on chest radiograph[10].

The clinical criteria includes :

- Asymptomatic or mild respiratory illness.
- Moderate respiratory illness
  1. Temperature of >100.4 °F (>38 °C) and
  2. One or more clinical findings of respiratory illness (e.g., Cough, shortness of breath, difficulty breathing, or hypoxia).
- Severe respiratory illness
  1. Temperature of >100.4 °F(>38 °C).
  2. One or more clinical findings of respiratory illness (e.g. cough, shortness of breath, difficulty breathing, or hypoxia).
- Radiographic evidence of pneumonia, or
- Respiratory distress syndrome, or
- Autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause[11].

The epidemiologic criteria is based on

- History of travel (including transit in an airport) within 10 days of onset of symptoms to an area with current or previously documented or suspected community transmission of SARS, or
- Close contact within 10 days of onset of symptoms with a person known or suspected to have SARS[12].

The Coronaviruses have been implicated in the pathogenesis of SARS. These (order Nidovirales, family Coronaviridae, genus Corona virus) are a diverse group of large, enveloped, positive-stranded RNA viruses that cause respiratory and enteric diseases in humans and other animals.

In March 2003, a novel corona virus (SARS - CoV) was discovered in association with cases of SARS[13]. Unlike other human corona viruses, it was possible to isolate SARS-CoV in Vero cells. Evidence of SARS–CoV infection has now been documented in SARS patients throughout the world. SARS-CoV RNA has frequently been detected in respiratory specimens, and convalescent phase serum specimens from SARS patients contain antibodies that react with SARS-CoV. There is strong evidence that this new virus is etiologically linked to the outbreak of SARS[14-21].

Human sera collected before the SARS outbreak do not contain antibodies directed against SARS – CoV[22,23], suggesting that this virus is new to humans. Additional studies on human sera from the region where the outbreak began are needed to confirm this finding. The unanswered question still is did SARS- CoV jump to humans by mutation of an animal corona virus or by recombination between several known human or animal corona viruses[24]. A small group of scientists believe that SARS may have came from animals[25]. In several cases of SARS, metapneumovirus has been isolated also, however the role in the pathogenesis in SARS remains unclear[26].

Confirmation of SARS is dependent on the laboratory criteria which includes

- Detection of antibody to SARS-corona virus (SARS–CoV) in specimens obtained during acute illness or >21 days after illness onset, or
- Detection of SARS–CoV RNA by RT-PCR confirmed by a second PCR assay, by using a second aliquot of the specimen and different set of primers, or
- Isolation of SARS – CoV.

- Negative cases show an absence of antibody to SARS – CoV in convalescent sera obtained >21 days after symptom onset.
- Undetermined cases are those in which laboratory testing has either not been performed or is incomplete[12].

SARS spreads when other people breath in droplets from the sneezing or coughing of SARS infected patients. It may also spread when people touch objects (such as door handles and water taps) that have been contaminated by infected individuals. Scientists believe that there are "Super spreaders" who are capable of spreading the disease to many people and were responsible for the early out break, before health officials knew what kind of preventive measures to take. Since the implementation of preventive measures, no new super spreaders have emerged[27,28].

Preliminary studies in some research laboratories suggest that the virus may survive in the environment for several days. The length of survival time depends on a number of factors like the type of material or body fluid containing the virus, environmental temperature and humidity etc. Researchers at CDC and other institution are designing standardized experiments to measure how long SARS Co-V can survive in situations that simulate natural environmental conditions[27].

Several laboratory tests can be used to detect the SARS – associated corona virus (SARS - CoV). However, at this time, tests for SARS–CoV are being refined, and the sensitivity and specificity though uncertain is still being evaluated. Several types of newly developed tests are being used to test for SARS – CoV and these include:

1. Serum antibody tests, both enzyme immunoassay (EIA) and indirect fluorescent antibody (IFA) formats, have been developed. At this time CDC is interpreting positive test results to indicate previous infection.
2. Reverse transcription – polymerase chain reaction (RT - PCR); This test can detect SARS – CoV. RNA in clinical specimens, including serum, stool and nasal secretions.
3. Viral isolation for SARS – CoV from clinical specimens of SARS patients has also been done[29].

CDC currently recommends that patients with SARS receive the same treatment that would be used for any patient with serious community acquired atypical pneumonia of unknown cause. At present the most effective treatment regimen is still unknown[30].

Hence, preventive measures can play a major role in preventing the spread of disease from person to person and to the community at large. Infection control measures should primarily be aimed at preventing the entry of the disease into the country, especially where all the factors favouring spread are present. WHO has recommended pre-departure screening of airline passengers for symptoms of SARS. CDC's inspectors are distributing health alert cards to passengers returning in airplanes from regions for which CDC has issued travel alerts and advisories. The notices inform travelers about SARS and its symptoms and asks them to monitor their health for 10 days and to see a doctor if they get a fever with cough or have difficulty breathing[31].

Research is in progress in different laboratories of the world to develop an effective vaccine against SARS. Killed in-activated viral vaccine, gene based vaccines including DNA and replication defective adeno-viral vectors, live attenuated vaccines, and vaccines based on purified viral proteins or using recombinant DNA to create vaccine vectors are all under process[32].

Presently there are no known cases of SARS transmission via blood products. However, detection of the genes of the possible causative virus in blood has been reported in patients with SARS. FDA has issued guidelines in this regard and has recommended to temporarily defer potential donors who have recently been exposed to SARS[33].

Conclusion

The international spread of the disease underscores the need for strong global public health systems, robust health service infrastructures and expertise that can be mobilized quickly across national boundaries to mirror disease movements.

Although the last decades of the previous century witnessed the emergence of several new diseases, SARS, needs to be regarded as a particularly serious threat for several reasons. If the SARS virus maintains its present pathogenicity and transmissibility, SARS could become the first severe new disease of the 21st century with global epidemic potential. As such, its clinical and epidemiological features, though poorly understood, give cause for particular alarm. With the noticeable exception of AIDS, most new diseases that emerged during the last two decades of the previous century or established endemacity in new geographical areas have features that limit their capacity to pose a major threat to international public health. In contrast, SARS is emerging in ways that suggest great potential for rapid international spread under the favorable conditions created by a highly mobile, closely interconnected world. Data indicates that an incubation period of 2 to 10 days allows the infectious agent to be transported, unsuspected and undetected, in a symptomless air traveler in the world from one city to any other. Should SARS continue to spread, the global economic consequences could be great in a closely interconnected and interdependent world.

References

1. CDC. Outbreak of severe acute respiratory syndrome worldwide, 2003. MMWR 2003;52;226-8.
2. Severe Acute Respiratory Syndrome (SARS) – multi-country outbreak –Update 27. April 11, 2003. Available at http://www.who.int/csr/sarsarchive/2003 04 11/en/

3. Parry J. Data shows that SARS is gradually coming under control. BMJ 2003; 326(7400):1166-b.
4. Update : Outbreak of Severe Acute Respiratory Syndrome – Worldwide, JAMA 2003;289(15):1918-1920.
5. Update 74 – Global decline in cases and deaths continues. June 5, 2003. Available at http://www.who.int/csr/don/2003_06_05/en/
6. Warner J. SARS Outbreak continues to decline. WebMD Medical News, June 06, 2003. Available at http://my.webmd.co/content/article/66/7930.htm
7. Update : Severe Acute Respiratory Syndrome – United States, June 04, 2003. MMWR Weekly, June 06, 2003/52 (22);525-526. Available at http://www.cdc.gov/mmwr/PDF/wk/mm5224.pdf
8. Parry J. WHO warns that death rate from SARS could reach 10%. BMJ 2003;326:999.
9. CDC. Update: outbreak of severe acute respiratory syndrome - worldwide, 2003. MMWR ;52:241-8.
10. World Health Organization. Case definitions for surveillance of severe acute respiratory syndrome (SARS). Available at http://www.who.int/csr/sars/casedefinition/en.
11. Booth CM, Matukas LM, Tomlinson GA, et al. Clinical features and short term outcomes of 144 patients with SARS in the greater Toronto area. JAMA 2003;289:2801-2809.
12. CDC. Updated Interim U.S. Case Definition of Severe Acute Respiratory Syndrome (SARS), June 05, 2003. (11) Available at http://www.cdc.gov.ncidod/sars/case definition.htm
13. Rota PA, Oberste MS, Monroe SS, et al. Characterisation of a Novel Coronavirus associated with Severe Acute Respiratory Syndrome.Science 2003;300:5624, 1394-1399.
14. Ksiazek TG, et al,. N. Engl. J. Med. 2003;348,1947.
15. Peiris JS, et al,. Lancet 2003;361; 1319.
16. Drosten C, et al.. N. Engl. J. Med. 2003; Available at http://nejm.org/earlyrelease/sars.asp#4-2.
17. Lai MMC, Holmes KV, in Fields Virology, D.M. Knipe, P. M. Howley, Eds. (Lippincot Williams & Wilkins, New York, ed. 4, (2001), chap.35.
18. Enjuanes L, et al, in Virus Taxonomy, M. H. V. van Regenmortal et al., Eds. (Academic Press, New York, 2000), pp.835-849.
19. Holmes KV, in Fields Virology, D. M. Knipe, P. M. Howley, Eds. (Lippincot Williams & Wilkins; New York, ed. 4, (2001), chap. 36.
20. Holmes KV. Coronaviruses. In Fields Virology. D. Knipe, et al., editors.Lippincot Williams & Wilkins, Philadelphia, Pennysylvania, USA.2001; 1187-1203.
21. Dyer O. Two strains of the SARS virus sequenced. BMJ 2003;326:999.
22. Peiris JSM, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 2003;361:1319-1325(25)
23. Ksiazek TG, et al. A novel coronavirus associated with severe acute respiratory syndrome. N. Engl. J Med 2003. In press.(26)
24. Bhattacharya S, MacKenzie D. Exotic animals likely source SARS. Available at http://www.newscientist.com/hottopics/secindex.jsp/sub+newsupdate.
25. Severe Acute Respiratory Syndrome – SARS – Preliminary Implications on the Economy and Disease Overview, Briefing Paper by the Business Development Group Available at http://www.findarticles.com/cf-dls/mEIN/2003_april_11/99921266/pl/article.
26. Severe Acute Respiratory Syndrome. April, 26, 2003. Available at http://www.medfriendly.com/severeacuterespiratorysyndrome.html.
27. SARS web information. Available at ttp://www.nim.nih.govlmedlineplus/severeacuterespiratorysyndrome.html.
28 CDC. Fact sheet for clinicians: Interpreting SARS test results from CDC and other Public Health Laboratories. June 2, 2003. Available at http://www.cdc.gov.ncidod/sars/testresultsc.htm.
29. CDC. Severe Acute Respiratory Syndrome (SARS) – Diagnosis/Evaluation, April, 20, 2003. Available at http://www.cdc.gov.ncidod/sars/diagnosis.html.
30. CDC. Questions and Answers : Travel and Quarantine, may, 23, 2003. Available at http://www.cdc.gov.ncidod/sars/travelandquarantine.htm
31. FDA. Issue guidance on Severe Acute respiratory Syndrome to further safeguard the blood supply, April,17, 2003. Available at http://www.fda.gov/bbs/topics/answers/ 20033/ans01215.html