Update on virological, epidemiological and diagnostic aspects of Sars-Corona Virus (SARS-CoV): A newly emerging virus

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Introduction

Infectious diseases have shaped human history. Even today, they remain significant causes of morbidity and mortality worldwide. New infectious diseases emerge or cross natural barriers and some of these, like the severe acute respiratory syndrome (SARS) or West Nile fever, spread rapidly across continents. An infectious disease crisis in one country is likely to become every country's problem. Therefore, the need for dissemination of updates on emerging infectious disease/s is mandatory.

Virological Characteristics of SARS-CoV

In March 2003, a novel coronavirus (SARS-CoV) was discovered in association with severe acute respiratory syndrome (SARS) (1). SARS Coronavirus (SARS-CoV) belongs to the family of coronaviruses responsible for the common cold (2). The coronavirus responsible for SARS has probably never been seen before in humans according to the update of WHO; it is a new coronavirus (3). The coronaviruses (order *Nidovirales*, family *Coronaviridiae*, genus *Coronavirus*) are a diverse group of large, enveloped, positive-stranded RNA viruses that cause respiratory and enteric diseases in humans and other animals (1-2). Their genome (29, 727 nucleotide in length) is the largest found in any of the RNA viruses and has 11 open reading frames. There are three groups of coronaviruses; groups 1 and 2 contain mammalian viruses, whereas groups 3 contain only avian viruses (Figure 1). Within each group, coronaviruses are classified into distinct species by host range, antigenic relationships and genomic organization. Coronaviruses typically have narrow host ranges and are fastidious in cell cultures. The viruses can cause severe diseases in many animals; and several viruses, including infectious bronchitis virus, feline infectious peritonitis virus, and transmissible gastroenteritis virus, are important veterinary pathogens. Human coronaviruses (HCoVs) are found in both group 1 (HCoV-229E) and group 2 (HCoV-OC43) and they are responsible for 30% of mild upper respiratory tract illnesses (1). Phylogenetic analyses and sequence comparison showed that SARS-CoV is not closely related to any of the previously characterized coronaviruses (1). Human coronaviruses are usually difficult to culture in vitro; whereas most animal coronaviruses and SARS-CoV can be easily cultured in Vero cells (4).

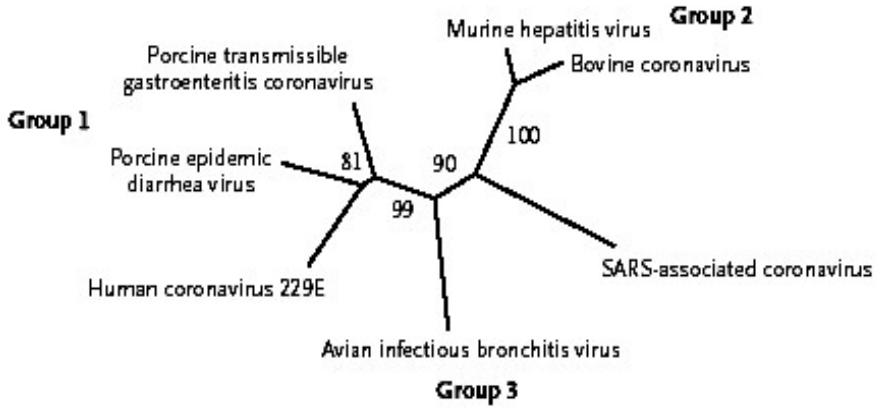

Figure 1: **Phylogenetic analysis of Coronaviruses. Adapted from Drosten *et al*. (4)**

Epidemiology

Source of Infection: SARS-CoV can replicate outside the virus. Epidemiological investigation showed that the virus could survive in stools for at least two days and in respiratory tract (4), indicating the multi-tropism nature of diarrhoeal stools, which have higher pH, for up to four

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days. It can also survive on plastic surfaces for up to 48 hrs, but it is not yet known how big a dose of the virus is required to cause infection (5). Information about the vitality of the virus strengthens the need for frequent hand washing, proper cleaning and disinfection control in hospitals managing cases of SARS. The incubation period for the disease is usually from 2-7 days.

Modes of transmission: The spread of SARS-CoV seems to be connected to a close contact with patients affected by the disease or with their respiratory secretions. It remains possible that the spread could come through other presently undefined ways (3).

Global distribution: Several hundred cases of severe atypical pneumonia of unknown etiology were reported in Guangdong Province of the People's Republic of China in November 2002. After similar cases were detected in patients in Hong Kong, Vietnam, and Canada during February and March 2003, the World Health Organization (WHO) issued a global alert for the illness, designated "severe acute respiratory syndrome" (SARS) (6-7). By July 2003, around 8437 SARS cases were reported to WHO from 32 countries with 813 deaths (8). Because of its ongoing epidemic and high death rate, SARS has shined an intense spotlight all over the world.

Clinical diagnosis

WHO (9) defines a "suspected case of SARS" as a case of a person with:

- high fever (> 38ºC) and has one or more respiratory symptoms such as cough, breathing difficulties and has had close contact with a person who is affected by SARS; has traveled in the last ten days in areas with recent local transmission of SARS; is living in areas with recent local transmission of SARS;
- unexplained acute respiratory syndrome illness resulting in death after November 2002 on whom no autopsy was performed, with close contacts with a person suspected of SARS, with history of travel to an endemic area for SARS, residing in an area with recent local transmission of SARS.

WHO (9) defines a "probable" case of SARS as a case of a person with:

- radiographic evidence of infiltrates consistent with pneumonia or distress pneumonia;
- a suspect case that is positive for SARS-CoV by one or more laboratory methods for SARS diagnosis;
- a suspected case with autopsy findings consistent with the pathology of respiratory distress syndrome without a cause.

Laboratory diagnosis

At the moment the laboratory diagnosis of SARS is a diagnosis of exclusion. The World Health Organization (WHO) has promptly established a network of international laboratories consisting of 13 members around the 10 countries to facilitate the identification of the causative agent of SARS (2). Attempts to identify the etiology of the SARS outbreak were successful during the third week of March 2003, when laboratories in the United States, Canada, Germany, and Hong Kong isolated a novel coronavirus (SARS-CoV) from SARS patients (1). Currently, there are two methods available for the diagnosis of a SARS case, namely PCR and serological methods (3).

a) Polymerase chain reaction (PCR) PCR analysis should be performed on two clinical specimens; usually nasopharyngeal and stool specimens or the same specimen could be collected on two different days (3). PCR tests can detect genetic material of the virus in all different specimens. Primers for the PCR test have been available at WHO network laboratories; at the moment, the initial experience of the test seems to be inadequate sensitivity, rather than specificity. A positive PCR result means that there is a coronavirus gene (RNA) of the SARSCoV in the sample: the result, however, does not mean that there is a sufficient amount of virus to infect other patients. Negative PCR test result means that the patient is not infected or that the result may be a false negative result. Inappropriate sampling may also give false negative results. WHO recommends that PCR testing should be performed only in laboratories that have experience with this method. It is very important that all positive results should be repeated or the result be confirmed by another collaborating research laboratory. Confirmation is crucial in low prevalence areas, where the positive predictive value is lower. All problems connected with false positive tests should be referred to technical problems in the laboratory (contamination). A commercial PCR kit for SARS is now available.

b) Serological methods

Serological tests include the search for antibodies of class IgG and IgM in patient sera (3). The tests, selected by the WHO task force laboratories, are performed in ELISA or in IFA; data with both methods can demonstrate the first appearance of antibody response in sera, can discriminate between IgG and IgM and detect the degree of positivity of these two classes. Antibodies usually first appear 10 days after the onset of the disease; they remain positive after the patient recovers from pneumonia. Two sera should be taken in the acute and convalescent phases of the disease. A four-fold rise in the titer of antibodies in paired sera can easily demonstrate a seroconversion. Serological tests are negative in healthy populations: no positive specimens have been found in areas not exposed to the virus. At present, one should consider that a positive serological test couldn't be found before ten to fifteen days from the onset of the illness.

Prevention and control of SARS

- All suspected cases should be isolated in rooms with independent aeration;
- All air conditioning systems should be turned off if they are not independent;

- All patients who are suspected cases should be isolated until clear diagnosis is made;
- Health care professionals should wear disposable clothing. In case of reuse of equipment these should be sterilized and cleaned with proper disinfectant;
- In case of transport of a patient to other health care facilities, patients should wear protective masks.
- Hand washing is the most important procedure to prevent transmission. An alternative can be to wear gloves that are cleaned constantly.
- Successful control of the global SARS epidemic will further require the development of vaccines and antiviral compounds that effectively prevent or treat this disease as well as rapid and sensitive diagnostic tests to monitor its spread (1, 3, 10).

Conclusion

In conclusion, the SARS epidemic is a challenge in the strategy of treating and defeating infectious diseases. Many other scenarios are present at the moment in the world as far as infectious diseases are concerned. The SARS problem has been addressed and won thanks to the compact team and task force that have operated to face the epidemic under the aegis of WHO. A similar strategy should be followed for other important health issues (Tuberculosis, Malaria, HIV, etc). What could have happened if such an epidemic started from third world countries where surveillance system is very poor? Since globalization is becoming increasingly evident, there should be strong and effective global surveillance system to secure the world from easy transmission of infectious diseases. There should be established health care facility, essential diagnostic tests, and infection control strategies to tackle such an epidemic. Community based health facilities and networking the health facilities are vital.

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