

BRIEF NOTE

What You Need to Know About SARS¹

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INTRODUCTION

The World Health Organization (WHO) was informed by the Chinese Ministry of Health on 11 February 2003 that there were 305 cases of an acute respiratory syndrome of unknown etiology (WHO 2003a). These cases occurred in six municipalities in Guangdong Province of southern China during 16 November 2002 – 9 February 2003 (WHO 2003a).

As determined by a consensus of worldwide public health officials in March 2003, surveillance case definitions for Severe Acute Respiratory Syndrome (SARS) includes both “suspect” and “probable” cases (MMWR 2003a; CDC 2003a) (See below).

As of late February 2003, the Centers for Disease Control and Prevention (CDC) and WHO referred to the new outbreak as Severe Acute Respiratory Syndrome (SARS) (MMWR 2003a). By 17 April 2003, there were 3,389 suspected/probable cases of SARS in 25 countries with 165 deaths or a case-fatality proportion of 5% (WHO 2003b). By 1 May 2003, at least 5,865 suspected/probable cases of this disease had been reported to WHO from 27 different countries. At that time there were 391 deaths (case-fatality proportion of 6.7%) (WHO 2003c). As of 30 April 2003, there had been 289 cases of suspect or probable (only 56 were probable) SARS reported in the US with no known deaths (MMWR 2003f). On 8 May 2003, WHO assigned a case-fatality rate of 15% (Foxnews 2003), greater than the 3% initially assigned by WHO (MMWR 2003b), and far greater than the 2.8% fatality rate of the 1918 Influenza pandemic. This appears rather surprising considering that the latest WHO data (7 May 2003) indicates 495 deaths world-wide with 6,903 suspect/probable cases resulting in a 7% case-fatality rate (WHO 2003d).

CASE DEFINITIONS

A “suspect” case of SARS is defined as a respiratory illness of unknown etiology with onset since 1 February 2003, and with the following criteria (MMWR 2003a): 1) measured temperature >100.4° F (>38° C); 2) one or more clinical findings of respiratory illness (for example, cough, shortness of breath, difficulty breathing, hypoxic, or radiographic findings of either pneumonia or acute respiratory distress syndrome); and 3) travel within ten days of onset of symptoms to an area with suspected or documented community transmission of SARS. This

would exclude areas with secondary cases limited to health care workers, direct household contacts, or close contact within ten days of onset of symptoms with either a person with a respiratory illness and travel to a SARS area, or a person under investigation or suspected of having SARS.

A “probable” case is defined as a suspect case with either radiographic evidence of pneumonia or respiratory distress syndrome or autopsy findings consistent with respiratory distress syndrome without an identifiable cause (CDC 2003a). On 29 April 2003, CDC’s interim surveillance case definition for SARS had been updated to include laboratory criteria for evidence of infection with the SARS-associated coronavirus (MMWR 2003f). The basis of the revised definition is that the virus can now be detected by polymerase chain reaction (PCR), serological methods, or viral isolation methods. Although, at this time, no instances of SARS-associated coronavirus had been detected in persons who were asymptomatic, there remains the possibility of “sub-clinical” infection. In such cases laboratory detection may be able to identify patients with mild respiratory illness or those who are asymptomatic.

CLINICAL DESCRIPTION

What is the clinical description of SARS? Most patients with SARS have traveled to Mainland China, Hong Kong, Singapore, or Hanoi. More recently there has been an alarming increase in SARS cases in and around Toronto, Ontario (MMWR 2003e). Close contact with a SARS patient can also be a risk factor. SARS generally begins with a fever above 100.4° F and may include headache, malaise, and myalgia. The fever may be accompanied with chills and rigors. Rash, neurologic, and gastrointestinal findings are usually absent but several patients have had diarrhea. The incubation period appears to be 2-7 days although several cases may have had a 10-day incubation period. Three to seven days after initial symptoms appear, a lower respiratory phase begins with onset of dry, nonproductive cough and dyspnea possibly progressing to hypoxemia (CDC 2003b and MMWR 2003c). As many as 20% of such patients will require intubation and placement on a ventilator (MMWR 2003c).

Laboratory results early in the course of SARS usually show a decrease in lymphocytes with total white blood cell counts either normal or decreased. Later, during the respiratory phase of disease, about half of the patients show leukopenia and thrombocytopenia (MMWR 2003a). Creatine phosphokinase and hepatic transaminase are elevated. Chest x-rays may be normal

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throughout the illness (MMWR 2003d). Many patients, however, will present with patchy interstitial infiltrates during the lower respiratory phase of disease when viewed in lung radiograms. Severity of the illness is highly variable, ranging from mild illness to death.

CAUSE OF DISEASE

What is the cause of the infection? On 24 March 2003, CDC announced that the causative agent of SARS was identified as a previously unrecognized coronavirus (MMWR 2003b). Initial identification was made by electron microscopy and confirmed by direct immunostaining, indirect immunofluorescent antibody assay, and reverse transcriptase-polymerase chain reaction with sequencing of a portion of the polymerase gene (MMWR 2003f). The family of Coronaviruses has been poorly studied because they are difficult to culture. Until now, coronaviruses have been associated with the "common cold" (Wilson and others 2001) and diarrhea (Brooks and others 2001) in humans and infections in animals, worldwide. The case for coronaviruses causing more severe disease in humans, such as bronchitis, was very tenuous (Tan 2002).

The Coronaviruses (Brooks and others 2001; Murry and others 1998) have a lipoprotein envelope and are shaped as long helical structures that measure 80 to 220 nm. These viruses get their name from the solar corona-like appearance surrounding the virion that is produced by the 20 nm long glycoprotein, petal-shaped projections that appear on the surface of the envelope. The virus contains a single-stranded positive sense RNA (like messenger RNA) that is the longest genome known among RNA viruses (approximately 30,000 bases). If the agent of SARS replicates like other human coronaviruses, it will do so in the cytoplasm of the infected cell. The virus would attach itself to cell receptors by means of the glycoprotein spikes on the viral envelope. The virus is then internalized by endocytosis. After uncoating, the viral genomic RNA is translated to produce an RNA dependent RNA polymerase in the cytoplasm. The new viral polymerase transcribes about seven messenger RNAs, specific for viral proteins. The newly synthesized genomic RNA interacts with newly synthesized nucleocapsid protein and associates with the viral glycoprotein modified membranes of the Golgi apparatus, thus forming virions. Mature virions migrate to the host cell membrane where they may exit or wait until cell death. Whether this process occurs with the agent of SARS is currently unknown.

Also of interest, coronaviruses readily change their genetic makeup with a high frequency of mutations and recombination between new strains. These activities are even higher than for most RNA viruses and may be the reason for the appearance of the new SARS coronavirus (Ksiazek and others 2003). It is likely that SARS is a recombinant of animal viruses. Several animal coronaviruses have been known to cause serious disease including avian infectious bronchitis virus of chickens and coronavirus infections of rats (Brooks and others 2001). Porcine respiratory coronavirus caused widespread epidemics in pigs in Europe during the 1980s. Antibodies

to coronaviruses of one genus are cross-reactive with those of other genera.

PUBLIC HEALTH MEASURES

In order to protect the general population from SARS exposure, a number of recommendations have been made by WHO, CDC, and health care professionals (CDC 2003b). Currently there is no treatment, other than supportive, and no vaccine is available (CDC 2003c). Although the mechanism of SARS transmission is somewhat unclear, it does appear that droplet and contact transmission predominates (CDC 2003d). As with most agents of disease, avoidance is still the best protection. As such, the WHO has issued a travel advisory to avoid going to endemic areas such as China, Singapore, Hong Kong, and Vietnam. Although Toronto was included in the advisory, as of 1 May 2003, it has been removed. People should avoid anyone who may have SARS or contact with SARS patients. Persons working with suspected cases of SARS should use appropriate hand washing and respiratory and contact precautions (CDC 2003d). It may be that once transmission is better defined, eye protection may also be worthwhile. Coronaviruses are very stable in the environment. They can survive on surfaces for up to 3 hours and can be transmitted by droplets, hand contamination, fomites, and small particles (MMWR 2003b). Coronavirus-like particles have been isolated from diarrhea and stool specimens (Brooks and others 2001). This has led to some speculation that SARS may be spread through sewage or poor toilet hygiene. Again, appropriate hand washing is important (CDC 2003d).

POSTWORD

During the 1970s there was a general attitude that we had learned all we need to know about infectious diseases. After all, we could treat or prevent most bacterial diseases and were able to prevent many viral infections. We could not have been more wrong. Soon there was Legionnaires' Disease, AIDS, multiple antibiotic resistant agents, and a whole new host of viral diseases. SARS is only the latest of what will be many infectious diseases on the horizon.

If there is a lesson to learn with SARS and its rapid spread, it is that physicians, health care workers, public health officials, and indeed, governments cannot hide from new infectious agents. They do not go away. It is possible that if isolation and quarantine methods were used early, the impact of SARS would have been lessened. Unfortunately, this was not done and SARS is the latest worldwide concern of health professionals.

As you are aware, our knowledge of SARS and the viral causative agent is evolving daily. It is difficult for the authors to decide when it is time to end the research and writing process. As such, it is our suggestion that, if you are interested in the topic, you should access several websites for the most recent information. Such websites might be: www.cdc.gov/ncidod/sars/; www.who.int/csr/sars/en/; and www.medscape.com.

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