

EDITORIAL

Severe acute respiratory syndrome (SARS)

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In the second week of March of this year, the World Health Organization (WHO) received reports of >150 cases of acute respiratory illness associated with pneumonia [1]. The majority of these cases were from the South-East Asian countries of China (including Hong Kong), Vietnam, Indonesia, the Philippines and Singapore. The appearance of many cases over a short time period, the absence of a clear causative pathogen, the apparent spread between countries and the death of some cases led to the issue of a global alert. The subsequent increase in the number of cases in this region and the identification of possible cases in distant countries, such as Germany, Canada and the UK (table 1), increased alarm that

a transmissible agent was causing an epidemic that was being further spread by easy access to air travel. Alarm was fed by the prior report of the deaths of two members of a family from Hong Kong with H5 N1 influenza virus infection presumed to have been acquired from birds on the Chinese mainland and the reporting of an earlier outbreak of respiratory infection of unknown cause in the Guangdong Province in China that had affected >300 individuals of whom three died.

The WHO took a pivotal role in the investigation of the outbreak, with the development of a case definition for severe acute respiratory syndrome (SARS) (fig. 1) [1]. Global Outbreak Alert and Response teams assisted in outbreak management and the collection of epidemiological and clinical data to improve the understanding of the condition. A global network of 11 leading laboratories in 10 countries was established to collaborate in the search for the causative organism and daily updates were provided on the WHO website. Electronic grand rounds were commenced to enable sharing of information and experience of the condition.

Table 1.—Cumulative number of reported cases of severe acute respiratory syndrome (SARS) to March 29 2003

Country	Cumulative case(s) n	Deaths n	Local chain(s) of transmission [#]
Canada	37	3	Yes
China [†]	806	34	Yes
China, Hong Kong Special Administrative Region	470	10 [§]	Yes
China, Taiwan	10	0	Yes
France	1	0	None
Germany	4	0	None
Italy	2	0	None
Republic of Ireland	2	0	None
Romania	3	0	None
Singapore	89	2	Yes
Switzerland	3	0	None
Thailand	3	1	None
UK	3	0	None
USA	59 ⁺	0	To be determined
Vietnam	58	4	Yes
Total	1550	54	

[#]: national public health authorities report to the World Health Organization on the areas in which local chain/chains of transmission is/are occurring, provided on the list of affected areas [1]; [†]: the reporting period from the Guangdong Province is from November 16 2002 to February 28 2003; ⁺: due to differences in the case definitions being used at a national level, probable cases are reported by all countries except the USA, which is reporting suspect cases under investigation; [§]: one death attributed to Hong Kong Special Administrative Region of China occurred in a case medically transferred from Vietnam. Reproduced with permission from WHO from [1].

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Epidemiology

The current (March 29 2003) case total reported from 13 countries is 1,550, with 54 deaths. The total is rising by 50–200 cases per day. Most cases have been reported from China with 470 possible cases in Hong Kong alone [2]. Preliminary information from Hong Kong has tracked the epidemic to a single visitor from mainland China. The socioeconomic impact in South-East Asia has been significant. School classes have been suspended in Singapore and Hong Kong (where the central library was closed at one point). Screening for air travellers has been introduced in Hong Kong and there are already reports of a fall in the demand for air travel and holiday bookings in the region.

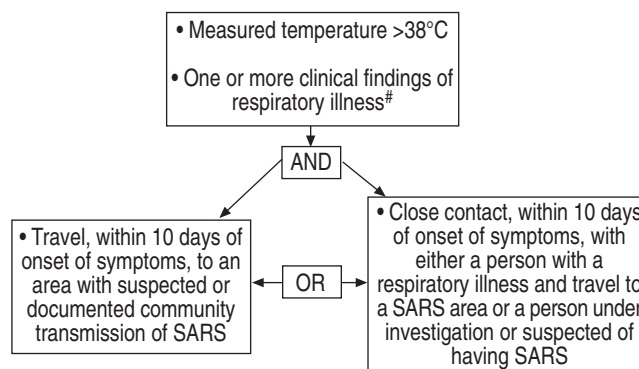


Fig. 1.—A case definition of severe acute respiratory syndrome (SARS) from the Center for Disease Control. Information taken from [2]. [#]: e.g. cough, shortness of breath, difficulty breathing, hypoxia, or radiographic findings of either pneumonia or acute respiratory distress syndrome.

As the epidemic has progressed, knowledge of the condition has improved. While the true danger of the epidemic is currently not known, the condition, while passed from human to human, does not appear to be as transmissible as at first feared, with most secondary cases being reported in close contacts of the case or healthcare workers involved in the care of an SARS patient. Of the cases in Hong Kong, one third have been in healthcare workers [2]. Some healthcare workers have died, including the WHO Infectious Disease specialist who first identified the outbreak in Hanoi, Vietnam.

Causative agent

Researchers appear to be close to identifying the causative agent, which will probably have been established by the time this is printed. Despite initial claims that the Guangdong outbreak was caused by *Chlamydia pneumoniae* (and it is not certain that this case-cluster has the same causative agent), the illness appears to be viral in origin, with a paramyxovirus or coronavirus the most likely culprit. A virus has been consistently isolated in tissue culture from clinical samples from a number of patients and appears to be a new, or perhaps more likely, previously unrecognised species. Progress is being made in the development of polymerase chain reaction-based and immunofluorescent diagnostic tests, and a start is being made on sequencing the virus.

Clinical presentation

The clinical illness is characterised by a prodromal phase, typically with sudden onset of high fever accompanied by rigors, headache and myalgia, with, in a few cases, diarrhoea [1, 3]. Mild respiratory symptoms may be present, but typically these develop over the next few days with nonproductive cough and dyspnoea, which may be accompanied by hypoxaemia. In 80–90% of cases improvement then occurs after 6–7 days, but in ~10% progressive respiratory failure develops, which may require assisted ventilation. The case fatality rate to date is ~3% and although this figure at first sight is not very high, it is when seen in the context of a community respiratory infection. Laboratory features are again nonspecific, with leukopaenia, thrombocytopenia, abnormal liver function and raised creatine phosphokinase being reported. The chest radiograph may be normal throughout the illness, but typically shows patchy shadowing, which may become confluent and more generalised. No treatment has been found to influence disease progression, and management should therefore be directed to the support of fluid balance and gas exchange. However, because of the similarity to other pneumonias, appropriate broad spectrum antibiotic therapy tailored to the common local pathogens and local antibiotic resistance prevalence should be given until a precise diagnosis with a specific causative organism is identified. Health workers who identify a possible case (fig. 1) should follow their local national guidance on SARS, with further information available on the international websites [1, 2].

From the start, investigation has been hampered by the lack of unique clinical features of the illness and the sharing of features with illnesses due to other common respiratory pathogens, particularly other causes of pneumonia. Until the cause is found and a definitive diagnostic test(s) is developed it is likely that some reported cases and outbreaks of SARS will be found to have other, already known, causes. This occurred in the possible case seen in Manchester, UK, who was subsequently found to have influenza virus infection. Separation of such cases may lead to greater clarity about the syndrome and its management.

Lessons from the past

This is not, of course, the first SARS nor will it be the last. The outbreak of Legionnaires' disease, in August 1976, at the American Legion Convention in Philadelphia, USA, will be known to most people [4]. It wasn't until the following year that the causative bacterium was found. More recently, the outbreak of Hantavirus Pulmonary Syndrome in 1993 in South-Western USA caught the headlines [5]. The 1994 occurrence of Hendra virus infection causing acute respiratory failure and death [6] is another example, as is the six deaths in 18 cases of human H5 N1 influenza virus infection in Hong Kong in 1997 [7]. Nipah virus encephalitis appeared in 1999, with two of 11 cases presenting with atypical pneumonia in one series [8] and 6% of 94 cases having pulmonary shadowing in another [9]. With the exception of Legionnaires' disease, these infections have one thing in common: the origin of the infective agent in animals, either domestic or wild. *C. pneumoniae* and human metapneumovirus are examples of recently identified pathogens causing severe acute respiratory illnesses in which humans have always been the likely host. The source of the SARS infective agent remains to be determined.

Infective illness in the 21st century

While the appearance of severe acute respiratory syndrome is not without precedent, what is remarkable is the speed with which the health community has been able to act in a coordinated way, to identify, map, track and investigate the condition. This has led, within the space of <1 month, to the identification of a likely microbial cause and progress in the development of specific diagnostic tests. This episode serves to confirm the continuing threat of infectious disease, the ability of "new" infections to appear and, above all, the global nature of infective illness in the 21st century. Hopefully, the lessons learnt from this will provide a useful template with which to approach the next such outbreak of acute respiratory infection when it comes along, as it surely will.

References

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