1

A Global Outbreak

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SARS is the first severe and readily transmissible disease that emerged in the 21st century. SARS has a unique capacity of spreading quickly in hospitals and clinics, affecting thousands of healthcare workers in a very short time. The booming international air travel in recent decades has also enabled the infection to be quickly spread across the continents and becoming an international threat. One infected tourist from China checked into a hotel in Hong Kong and spread the infection to three countries. As at 3 July 2003, 32 countries have been affected and 8439 patients infected around the world.[1] On 12 March, the World Health Organization (WHO) issued the First Global Alert against an atypical pneumonia of unknown cause not responding to antibiotics. Three days later on 15 March, WHO issued the Second Global Alert in which, for the first time this new disease was named Severe Acute Respiratory Syndrome with its case definition laid down. Because of the seriousness of the infection and the high infectivity, "WHO regards every country with an international airport, or bordering an area having a recent local transmission, as at potential risk of an outbreak."[2] Travel advisory was issued based on (1) the magnitude of the outbreak in those countries;

(2) the pattern of local transmission; and (3) exportation of probable cases to other countries. Guidance was provided to the general public to postpone non-essential travel to areas with local transmissions and that met the above criteria. These travel advisories have generated huge and unprecedented economic and social impacts in countries like China (including Hong Kong SAR), Canada, Singapore and Taiwan.

The following is an account of events that happened within three weeks from late February to mid-March.

WHERE DID IT FIRST START?

The first cases of SARS are now known to have emerged in mid-November 2002 in Guangdong province of southern China. On November 27, the Global Public Health Intelligence Network (GPHIN), a computer application developed by the Heath Canada and used by WHO, picked up emails reporting atypical pneumonia in Foshan city of Guangdong. GPHIN is a customized search engine that continuously scans world Internet communications for rumors and reports of suspicious disease events in over 950 news feeds and electronic discussion groups around the world. Two months later, WHO received emails regarding atypical pneumonia outbreaks in Guangdong province. This was subsequently confirmed officially by the Ministry of Health of China as an outbreak of acute respiratory syndrome that involved 305 patients and five deaths in Guangdong. Around 30% of the cases affected were healthcare workers in the hospitals. WHO was further informed that the outbreak which involved six municipalities was not influenza. Further investigation from laboratories in China ruled out anthrax, pulmonary plague, leptospirosis and hemorrhagic fever. In the meantime, the disease was carried outside the country by travelers.

HOTEL M

Evidence has shown that during the period from late February to early March, there was a cluster of infected patients from southern China who traveled to Hong Kong. The most prominent case was a Professor of Nephrology, who had treated patients in his home town, and who came to Hong Kong on 21 February 2003 to attend a wedding banquet of his relative.[3] He brought the virus to the ninth floor of a four-star hotel

Fig. 1 Chain of transmission among guests at Hotel M of Hong Kong, February–March 2003 (adopted from *MMWR* of CDC with permission).

(Hotel M) in Hong Kong (Fig. 1). This medical doctor infected at least 12 other guests and visitors on the 9th floor of the hotel. Days later, guests and visitors to the hotel seeded outbreaks in eight countries including Ireland, Vietnam, Singapore, Hong Kong and Toronto.

HANOI

On 28 February, a 48-year-old Chinese-American businessman was admitted to the French Hospital in Hanoi with a 3-day history of respiratory symptoms of pneumonia. He had previously been in Hong Kong, where he visited an acquaintance staying on the 9th floor of Hotel M. Dr. Carlo Urbani, an epidemiologist from the WHO office in Hanoi, examined this gentleman who had features of atypical pneumonia. On 5 March, the businessman was air transferred to the Princess Margaret

Hospital in Hong Kong. Seven healthcare workers in Hanoi who had cared for him became ill. WHO staff were sent to Vietnam to help manage the epidemic. By 11 March, at least 20 hospital workers in Hanoi's French Hospital came down with the same symptoms. Dr. Urbani notified the WHO Regional Office for the Western Pacific. The WHO headquarters move into a heightened state of alert. Dr. Urbani continued to treat cases at the Hanoi French Hospital. On 11 March, Dr. Urbani was invited to give a presentation on tropical diseases in Bangkok. He was ill upon arrival and was immediately hospitalized. Dr. Urbani died of respiratory failure on 29 March in a Bangkok hospital.

SINGAPORE

On 1 March, a 26-year-old former flight attendant was admitted to a hospital in Singapore with respiratory symptoms. This patient was also a guest on the 9th floor of Hotel M in Hong Kong. The government of Singapore notified WHO on 15 March by urgent communication that a similar illness had been found in a 32-year-old physician who had treated cases with a severe respiratory symptom in Singapore, all subsequently linked to Hotel M. The Singapore physician traveled to the United States for a medical conference and at the end of the conference boarded a return flight from New York. The physician and his two accompanying family members were removed from the flight at a stopover in Frankfurt where the three were immediately isolated and placed under hospital care.

HONG KONG

On 28 February, a 26-year-old man presented to the Prince of Wales Hospital with a 3-day history of fever, chills and rigor. He was diagnosed to have upper respiratory tract infection and discharged at the hospital's emergency room. His fever did not respond to the medication and the patient returned on 4 March with productive cough. During that visit, he also had diarrhea with brownish loose stool and vomited undigested food. He denied any history of travel (until after the story of Hotel M was disclosed in Hong Kong). Chest examination showed a bronchial breath sound at the right upper zone. Chest X-ray showed a right upper lobe consolidation. A diagnosis of community-acquired pneumonia was made and he was admitted to ward 8A. From March 6 to March 14, because of

his shortness of breath, this patient was treated with bronchodilator via a jet nebulizer delivered by oxygen for a total of seven days. Within two weeks, a total of 156 patients were hospitalized, of whom 138 were identified as either secondary cases or tertiary cases of this index case. This included 69 healthcare workers (20 doctors, 34 nurses, 15 allied health workers); 16 medical students who had worked in the index ward; and 54 patients who were either nursed in the same medical ward or had visited their relatives.

TORONTO

A 78-year-old Toronto woman who had been a guest on the 9th floor of Hotel M developed fever, myalgia, sore throat and progressive dyspnea two days after she returned home. She died at home on March 5. Several family members of the index patient subsequently developed symptoms of pneumonia and was admitted to Scarborough Grace Hospital, which became the epicenter of the infection. SARS spread to healthcare workers and other patients in the hospital prior to a significant awareness of the disease in the local medical community. Other Toronto hospitals were involved when patients were transferred between institutions. This led to additional patients, healthcare workers and visitors contracting the disease in hospitals in the Toronto area. On March 14, WHO was alerted by Health Canada that steps had been taken to alert hospital workers, ambulance services and public health units across the provinces of the country.

BEIJING

On March 15, a 72-year-old man boarded a flight from Hong Kong to Beijing. He visited ward 8A at the Prince of Wales Hospital from 4 to 9 March and developed a fever on 11 March. On this flight, there were at least 22 passengers who were subsequently confirmed to have SARS, including travelers from Taiwan, Singapore, Bangkok, Hong Kong and Inner Mongolia. This patient died of the disease in Beijing. In late March, the Chinese authorities issued updated data on cases and deaths relating to outbreak of atypical pneumonia in Guangdong province reported earlier, raising the cumulative total number of cases from 305 to 792, and of death from 5 to 31. On 4 April, a retired medical doctor in Beijing wrote to

television channels in China exposing an epidemic of SARS in the city. He was then interviewed by *TIME* magazine and disclosed a cover-up of the epidemic. On 20 April, the health authority reported the number of SARS cases in Beijing which jumped from dozens to 346.

GLOBAL EPIDEMIC AND INTERNATIONAL RESPONSE

From November 2002 to 3 July 2003, the day when the last SARS cases were reported to the WHO, there was a total of 8439 cases reported from 32 countries involving six continents. The last case in this epidemic was reported from Toronto, Canada on 27 June 2003. Eight hundred and twelve people died, making an overall mortality of 9.6%. There is a wide variation in mortality among the heavily hit countries, ranging from 6.5% to 16.9%.

In combating of the serious infection, the international scientific community has come to put their efforts together.

On 15 March 2003, the day WHO issued an emergency travel advisory in response to SARS, it set up a network of scientists from 11 laboratories around the world to expedite the identification of the causative agent of SARS. They were asked to share among themselves scientific data and clinical specimens. The collaboration was continued through daily teleconferences and use of the WHO website to post electron microscopy pictures of candidate viruses, protocols for testing, phylogenetic trees, PCR primer sequences and results of various diagnostic tests. These arrangements allow simultaneous analyses of samples from the same patients in several laboratories with different approaches. With these efforts, in just about one month, a new species of coronavirus now called SARS-CoV was identified. The clinical management groups from different countries were also connected by teleconferences to share experiences in the clinical management of SARS patients. Information, including natural course of the disease, incubation period, clinical presentation and response to various modalities of treatment, was discussed. It is through these international collaborative efforts of unprecedented scale that our knowledge of the disease and hence its management scheme can be developed in such a short time.

With the exception of AIDS, most new diseases that emerged in the past two decades have features that limit their capacity to pose a major

Table 1 Cumulative Number of Reported Probable Cases of SARS from 1 Nov 2002 to 3 July 2003

Country	Cumulative No. of Cases	No. of Death	No. Recovered	Date Last Probable Case Reported
Australia	5	0	5	12 May 2003
Brazil	1	0	1	9 June 2003
Canada	251	38	193	27 June 2003
China	5327	348	4933	25 June 2003
Hong Kong SAR	1755	298	1429	11 June 2003
Macao SAR	1	0	1	21 May 2003
Taiwan	674	84	498	19 June 2003
Colombia	1	0	1	5 May 2003
Finland	1	0	1	7 May 2003
France	7	0	6	9 May 2003
Germany	10	0	9	4 June 2003
India	3	0	3	13 May 2003
Indonesia	2	0	2	23 April 2003
Italy	4	0	4	29 April 2003
Kuwait	1	0	1	9 April 2003
Malaysia	5	2	3	20 May 2003
Mongolia	9	0	9	6 May 2003
New Zealand	1	0	1	30 April 2003
Philippines	14	2	12	15 May 2003
Republic of Ireland	1	0	1	21 March 2003
Republic of Korea	3	0	3	14 May 2003
Romania	1	0	1	27 March 2003
Russian Federation	1	0	0	31 May 2003
Singapore	206	32	171	18 May 2003
South Africa	1	1	0	9 April 2003
Spain	1	0	1	2 April 2003
Sweden	3	0	3	18 April 2003
Switzerland	1	0	1	17 March 2003
Thailand	9	2	7	7 June 2003
United Kingdom	4	0	4	29 April 2003
United States	73	0	65	23 June 2003
Vietnam	63	5	58	14 April 2003
TOTAL	8439	812	7427	

threat to international public health. Avian influenza, Nipah virus, Ebola virus, and Hanta virus did not establish efficient human-to-human transmission. Others require a vector for the transmission. SARS is unusual in its high morbidity and mortality. Indeed, the endemic in early 2003 mimics the 1918 influenza panendmic. SARS-CoV shared several biological

features with influenza A virus. Both viruses are zoonoses. Both have dual tissue tropism for respiratory and gastrointestinal tissues. As RNA viruses, both possess mechanisms for mutations and generate genetic variability. At the turn of 20th century, it took three panendemics before influenza was brought under control. Considering the rapidity of spread of SARS and the high mortality of this disease in such a short time, this formidable disease has more serious effects compared to influenza.

The SARS endemics have exposed problems of the healthcare system of many countries. Weaknesses of the public health system, fragmentation of organization of national healthcare, slow communication and inadequate alert system are some of the lessons learned by the international community. The final success in the containment of the disease was the result of efforts from high-level governmental intervention. Legislation of prevention and control of infectious disease and promotion of public alertness and response turned out to be the crucial factors in controlling SARS. Although the recent endemic appeared to be contained, the world should not be complacent. There are still many unanswered questions about SARS-CoV and the disease it causes. Scientists and clinicians around the world should continue their joint efforts until we have a thorough understanding of the nature of the virus, its source, mode of transmission, pathological effects and therapeutic options. Until then, the world is still under the shadow of the come back of SARS.