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What we have learnt from the SARS epidemics in mainland China?

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ABSTRACT

This article provides an overview of the severe acute respiratory syndrome (SARS) epidemics in mainland China and of what we have learned since the outbreak. The epidemics spanned a large geographical extent but clustered in two regions: first in Guangdong Province, and about 3 months later in Beijing and its surrounding areas. The resulting case fatality ratio of 6.4% was less than half of that in other SARS-affected countries and regions, partly due to younger-aged patients and a higher proportion of community-acquired infections. Strong political commitment and a centrally coordinated response were most important for controlling SARS. The long-term economic consequence of the epidemic was limited. Many recovered patients suffered from avascular osteonecrosis, as a consequence of corticosteroid usage during their infection. The SARS epidemic provided valuable experience and lessons relevant in controlling outbreaks of emerging infectious diseases, and has led to fundamental reforms of the Chinese health system. Additionally, the epidemic has substantially improved infrastructures, surveillance systems, and capacity to response to health emergencies. In particular, a comprehensive nationwide internet-based disease reporting system was established.

Keywords:
Severe acute respiratory syndrome
Epidemic
Internet-based disease reporting system
Surveillance systems

1. Introduction

In 2003, the world was confronted with the emergence of a new and in many cases fatal infectious disease: severe acute respiratory syndrome (SARS). The first case with typical symptoms of SARS emerged in Foshan municipality, Guangdong Province, China, with the onset date of November 16, 2002. Five index cases were reported in Foshan, Zhongshan, Jiangmen, Guangzhou, and Shenzhen municipalities of Guangdong Province before January 2003. The early-stage outbreak of SARS in Guangdong Province was sporadic and apparently not associated with the index cases. By January 2003, SARS had developed into a large-scale outbreak in Guangdong Province, and after February 2003, it had appeared in Hong Kong and seven other provinces, including Guangxi, Jiangxi, Fujian, Hunan, Zhejiang, Sichuan and Shanxi. Some cases from Shanxi Province and Hong Kong were imported to Beijing, and transmission from index cases was amplified within several health care facilities by March 2003. Soon Beijing became the epicenter of SARS and endangered various other provinces or cities in mainland China. At the same time, Singapore, Canada, the United States, and Vietnam were involved in the worldwide spread through imported cases from Hong Kong. The World Health Organization (WHO) issued the first global alert on March 12, 2003, regarding a cluster of cases of severe atypical pneumonia in hospitals in Hong Kong, Hanoi, and Guangdong. Three days later, the WHO issued an emergency travel advisory. On March 24, 2003, the WHO described the clinical features of SARS, which were revised on May 1, 2003. In April 2003, a novel coronavirus, named SARS-associated coronavirus, was identified as the infectious agent responsible for SARS. Soon thereafter, cases were reported from 32 countries and regions (later corrected to 29). In total, 8,437 probable SARS cases, of whom 813 had died, were reported during

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the SARS epidemic of 2002–2003. Mainland China was the most seriously affected area, reporting 5,327 probable SARS cases, of whom 343 died, between November 16, 2002 and June 11, 2003.

As a result of initial lack of awareness of SARS by health care workers (HCWs), the disease spread unnoticed in the early stages of the epidemic. This spreading of the disease was unduly prolonged by limited information sharing. At that time, a functional infectious diseases surveillance system was not yet available, and the reporting system was outdated, hampering data collection and delaying interventions. The SARS outbreak brought China virtually to a standstill, forcing the country to thoroughly review its infectious disease control policies. Since then, the Chinese government has implemented new and innovative strategies, strengthened the related aspects of the legal system and the disease prevention and control system, and made substantial investments to improve infrastructures, surveillance systems, and emergency preparedness and response capacity, such as the development of a real-time monitoring system that is now serving as a model for worldwide surveillance and response to infectious disease threats.12 The world has moved on since the SARS epidemic, but the insights gained in mainland China remain valuable, with comparable infectious disease threats presenting continuously.

2. Description of the epidemic

During the 2002–2003 SARS outbreak, mainland China reported 5,327 probable cases, of whom 343 died, amounting to a case fatality ratio (CFR) of 6.4%. The epidemic spanned a large geographical extent (170 counties of 22 provinces) but clustered in two areas: first in Guangdong Province, and about 3 months later in Beijing and its surrounding areas Shanxi, Inner Mongolia, Hebei, and Tianjin. Fig. 1 shows the temporal distribution of SARS in the six most seriously affected geographic areas of mainland China. Spatiotemporal analyses indicated that the spread of SARS occurred in two different patterns.13 In the early stage of the epidemic, especially before strict control measures were taken, SARS spread to new areas randomly through certain index cases. Thereafter, human travel along transportation routes influenced the transmission of SARS, as illustrated by the spread of SARS in middle North China and South China. The epidemic period in middle North China was shorter than in South China, but the geographic spread was wider. SARS not only spread locally, but also diffused quickly and resulted in several outbreaks in areas of middle North China close to Beijing. In contrast, the SARS epidemic in South China was mainly limited to Guangdong Province.

Transportation routes accelerated the spread of SARS in mainland China. National highways and inter-provincial freeways appeared to play a critical role, whereas railways seemed to be less important.15

For the definition of SARS cases, a distinction was made between probable and suspected cases on the basis of contact history and the number and severity of symptoms. In China, it was only possible late in the epidemic to confirm SARS through serological tests. In a study comparing clinical characteristics of probable and suspected cases, it was found that although symptoms hardly differed, there were clearly different hematological profiles, justifying the distinction between probable and suspected cases and confirming that the suspected cases most likely did not have SARS.14

The average duration (3.8 days) and pattern (including time of epidemic) of onset of symptoms to hospital admission among SARS patients in mainland China were comparable to those of other affected areas.15 The duration of hospital admission to discharge for those who survived (29.7 days) was shorter than elsewhere in the world, possibly because of different hospitalization policies. The duration of hospital admission to death in mainland China was 17.4 days, which was also shorter than in other areas.

Over the course of time, hospital epidemics were rapidly brought under control, with increasing efficiency.16 This was due to increasing understanding of the disease and more effective preventive measures, such as establishing isolation wards, training and monitoring hospital staff in infection control, screening HCWs, and compliance with the use of personal protection equipment.17

3. Case fatality

Because of their deteriorated health status and apparent complications, the mortality rate increased significantly among patients aged 50 and above. The Tianjin SARS outbreak happened mainly within hospitals, leading to a high impact of comorbidity, which explains the relatively high CFR. Guangdong Province showed a considerably lower CFR than Beijing, the reason for which is still unclear (Fig. 2). In China, the overall CFR in mainland China was 6.4%, which was much lower than 17.2% in Hong Kong. And it was also lower than that reported in other areas and countries, e.g., CFR in Vietnam (9.7%). The much lower CFR in mainland China was also in contrast with the shorter duration of hospital admission to death compared with other countries or regions. The obvious reasons for the lower CFR are the young ages of the patients and a relatively higher number of community-acquired infections as opposed to hospital acquired infections. However, the relatively young ages of the cases (median age 33 years) only partly (approximately 25%) explains the low CFR in mainland China compared with other affected areas and countries, where patient median age varied from 37 years in Singapore to 49 years in Canada (Table 1).18 The relatively lower proportion of hospital-acquired infections in mainland China (reflected in the lower proportion of infections among HCWs compared with other areas [19% vs. 23%–56%; see Table 1]) is

Fig. 1. The temporal distribution of SARS outbreaks in the six most seriously affected geographic areas of mainland China. Number of new cases per day of onset since the first SARS case on November 16, 2002, in Guangdong Province. SARS: severe acute respiratory syndrome.

Table 1. Comparison of characteristics of SARS cases and deaths in the six regions of China

| Region | Total Cases | Total Deaths | Median Age (years) | CFR (%) |
|--------|-------------|--------------|-------------------|--------|
| Guangdong | 1,429 | 26 | 33 | 1.8 |
| Shanxi | 950 | 19 | 32 | 2.0 |
| Beijing | 590 | 13 | 35 | 2.2 |
| Inner Mongolia | 260 | 4 | 34 | 1.5 |
| Hebei | 171 | 2 | 33 | 1.2 |
| Tianjin | 144 | 1 | 32 | 0.7 |
cases used in the calculations and the relatively more important impact of so-called “super-spreading events.” In Guangdong Province, where the epidemic started, standard control measures, such as isolation and contact tracing (arrow 2), seem to already have helped to largely interrupt transmission in this province. However, during the period from day 80 to day 140, the number of new SARS cases steadily increased, due to the spread to and within other parts of China (i.e., mainly Beijing and its surrounding provinces). The first official report of an outbreak in Guangdong Province (arrow 3) and the WHO global alerts (arrow 4) were by no means reflected in a consistent reduction of $R_t$. Additionally, the first interventions in Beijing were not effective enough to cause any downward trend in the transmission (arrow 5). It was only around April 11 to April 14, 2003, that the Chinese authorities gained full control of all activities to combat SARS, with national, unambiguous, rational, widely followed guidelines and control measures, under central guidance (arrow 6). Immediately, the reproduction number decreased dramatically and consistently. Within 1 week, $R_t$ was below 1. Strikingly, this marked decrease after the period from April 11 to April 14, 2003, was consistently present in the patterns of $R_t$ for all heavily affected areas in mainland China. The stringent control measures to prevent human contacts (arrow 7), including the decision to cancel the public holiday of May 1 (arrow 8), were all initiated after $R_t$ was below 1 (i.e., when the epidemic was already dying off), again consistently for all areas in mainland China. Given the information available at the time, the most stringent interventions were rational because it was not clear to which extent the epidemic was under control. However, looking retrospectively, we can now conclude that these measures, which severely affected public life, contributed little to the factual containment of the SARS epidemic; the essential moment had occurred earlier. That being said, the late interventions may still have played a role in speeding up the elimination of SARS. Additionally, cancelling the public holiday—when millions of people travel long distances to visit their family—may have prevented (smaller) outbreaks in yet unaffected locations.

We conclude that strong political commitment and a centrally coordinated response were the most important factors in the control of SARS in mainland China. With respect to future outbreaks of emerging infectious diseases, we emphasize that it is of first and foremost importance that effective control is based on clear national and international guidelines and well-built communication and reporting networks, along with firm determination and responsibilities at all levels.

5. Consequences of the epidemic

There were many obvious immediate consequences of the epidemic, such as substantial morbidity and mortality, fear over the possibility of becoming infected, panic in the public domain, stringent quarantine measures, travel restrictions, etc. In addition, two important mid- and long-term consequences of the epidemic were identified. First, there was the economic impact. This was studied for Beijing by Beutels et al. through associating time series of daily and monthly SARS cases and deaths and volume of public train, airplane and cargo transport, tourism, household consumption patterns and gross domestic product growth in Beijing. The authors concluded that leisure activities, local and international transport, and tourism were severely affected by SARS, particularly in May 2003. Much of this consumption was merely postponed; however, irrecoverable losses to the tourism alone were estimated at about USD 1.4 billion, or 300 times the cost of treatment for SARS cases in Beijing.

Table 1 The characteristics of SARS outbreak in some countries or regions with high prevalences.

| Country or area       | Total case (person) | Death case (CFR) [person(%)] | Median age (year) | Infected HCWs (percentage) [person(%)] |
|-----------------------|---------------------|------------------------------|-------------------|----------------------------------------|
| Mainland China        | 5,327               | 343 (6.4)                    | 33                | 1,021 (19.2)                           |
| Hong Kong, China      | 1,755               | 302 (17.2)                   | 40                | 405 (23.1)                             |
| Taiwan, China         | 674                 | 87 (12.9)                    | 46                | 205 (30.3)                            |
| Singapore             | 238                 | 33 (13.9)                    | 37                | 97 (40.8)                              |
| Vietnam               | 62                  | 6 (9.7)                      | 43                | 35 (56.5)                              |
| Canada                | 251                 | 43 (17.1)                    | 49                | 101 (40.2)                             |

SARS: severe acute respiratory syndrome; CFR: case fatality ratio; HCWs: health care workers.
Second, there were long-term health consequences among the SARS patients who were treated with corticosteroids. Lv et al. investigated the relationship between avascular necrosis (AVN) and corticosteroid treatment given to SARS patients through a longitudinal study of 71 SARS patients (mainly HCWs) who had been treated with corticosteroids, with an observation time of 36 months. Magnetic resonance images and X-rays of the hips, knees, shoulders, ankles and wrists were taken as part of the post-SARS follow-up assessments. Thirty-nine percent developed AVN of the hips within 3-4 months after starting treatment. Two more cases of hip necrosis were seen after 1 year and another 11 cases of AVN were diagnosed after 3 years, 1 with hip necrosis and 10 with necrosis in other joints. In total, a staggering 58% of the cohort had developed AVN after 3 years of observation. The sole factor explaining AVN in the hip was the total dose of corticosteroids received. The use of corticosteroids has been debated, with conflicting opinions about steroids being the key component in the treatment of SARS. It has remained uncertain whether the aggressive use of corticosteroids during the SARS epidemic has tipped the balance. Has the use of high-dose corticosteroids saved more lives and been responsible for the lower case fatality in mainland China? Do immediate benefits, in terms of saving lives, outweigh the adverse effects, including AVN?

6. Lessons learned and actions taken in China regarding epidemic preparedness

The SARS epidemic provided valuable experience and lessons with regard to controlling outbreaks of newly emerging infectious diseases, which are surely due to come. Human infection with avian influenza viruses, the novel A influenza (H1N1), and imported infectious diseases such as the Zika virus disease and yellow fever disease are already knocking at our doors! Important lessons learned in China included the need for more honesty and transparency, improvement of surveillance, better laboratory facilities, and optimized case management. Also, public health measures to control infectious diseases, reporting systems, and central guidance and coordination came under scrutiny. Another lesson was the need to inform the public about, and involve them in, control measures in an adequate and timely manner. There was a strong realization that the best defense against any threat of newly emerging infectious diseases is a robust public health system in its science, capacity, and practice, and through collaboration with clinical and veterinary medicine, academia, industry, and other public and private partners.

An important resolution of the Chinese government was to improve its disease surveillance system to rapidly identify newly emerging infectious diseases and to minimize their spread in China and to the rest of the world. The traditional surveillance network using reporting cards filled out by hand and sent by mail or fax has been replaced with an automatic information system called the China Information System for Disease Control and Prevention, which is the world’s largest internet-based disease reporting system. The government has also increased their investment in enhancing the capabilities of detecting, diagnosing, preventing, and controlling newly emerging infectious diseases at various levels. New and innovative strategies have been established for response to health emergencies, such as the establishment of the parallel laboratory confirmation mechanism for newly emerging infectious pathogens to reduce the risk of errors, rapid disclosure of information to the WHO and to the public, international information exchange and collaboration, and the provision of more information on public health and on infectious diseases to the public. Furthermore, the Chinese government has strengthened both the related aspects of the legal system and the disease prevention and control system. For example, the government issued the Law of the People’s Republic of China on Prevention and Treatment of Infectious Diseases (Revised Draft) in 2004 and Regulations on Preparedness for and Response to Emergent Public Health Hazards in 2003, created the Chinese Centre for Disease Control and Prevention, and improved surveillance systems of infectious diseases and preparedness and response capacity for emerging public health events.

7. Conclusion

The epidemic of a new infectious disease, SARS, took firstly China and subsequently many other areas in the world completely by surprise. Fortunately, the consequences of this epidemic, in terms of people afflicted and economic loss, were not entirely catastrophic. Also, it turned out that SARS could be controlled relatively easily through standard interventions. However, the epidemic revealed some important weaknesses in the Chinese public health system, which have been dealt with efficiently and
successfully by the Chinese government. At the moment, China is better prepared than ever for epidemics, which may be much worse than SARS in terms of speed of spread and fatality rate. In fact, SARS can be viewed as a wake-up call.

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Competing interests

The authors declare that there is no conflict of interest.

References

1. Zhong NS, Zeng GQ. Management and prevention of SARS in China. SARS: a case study in emerging infections. Hong Kong: Oxford University Press; 2005. p. 31-4.
2. He JF, Xu RH, Yu DW, et al. Severe acute respiratory syndrome in Guangdong Province of China: epidemiology and control measures. Zhonghua Yu Fang Yi Xue Za Zhi 2003;37(4):227-32 (in Chinese).
3. Zhao Z, Zhang F, Xu M, et al. Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China. J Med Microbiol 2003;52(Pt 8):715-20.
4. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348(20):1953-66.
5. Xu RH, He JF, Yu DW, et al. Severe acute respiratory syndrome, Beijing 2003. Emerg Infect Dis 2004;10(1):25-31.
6. Liang W, Zhu Z, Guo J, et al. Epidemiologic clues to SARS origin in China. Emerg Infect Dis 2004;10(6):1030-7.
7. Tsang KW, Ho PL, Ooi GC, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348(20):1967-76.
8. World Health Organization. WHO issues a global alert about cases of atypical pneumonia: cases of severe respiratory illness may spread to hospital staff. ,https://www.who.int/csr/sars/clinical/en/. Accessed January 5, 2018.
9. Drosten C, Gunther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 2003;348(20):1953-66.