SARS: lessons from a new disease

New diseases have been emerging at the unprecedented rate of one a year for the last two decades, and this trend is certain to continue. The sudden and deadly arrival of SARS on the global health stage early in 2003 was in some ways perhaps the most dramatic of all. Its rapid containment is one of the biggest success stories in public health in recent years. But how much of that success was a result of good fortune as well as good science? How narrow was the escape from an international health disaster? What tipped the scales? The international response to SARS will shape future strategies against infectious epidemics.
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The day-by-day struggle to control the outbreak of severe acute respiratory syndrome (SARS) represents a major victory for public health collaboration. Key lessons emerge that will be invaluable in shaping the future of infectious disease control – and being ready for the day when the next new disease arrives without warning. First and most important is the need to report, promptly and openly, cases of any disease with the potential for international spread in a closely interconnected and highly mobile world. Second, timely global alerts can prevent imported cases from igniting big outbreaks in new areas. Third, travel recommendations, including screening measures at airports, help to contain the international spread of an emerging infection. Fourth, the world’s best scientists, clinicians and public health experts, aided by electronic communications, can collaborate to generate rapidly the scientific basis for control measures. Fifth, weaknesses in health systems play a key role in permitting emerging infections to spread. Sixth, an outbreak can be contained even without a curative drug or a vaccine if existing interventions are tailored to the circumstances and backed by political commitment. Finally, risk communication about new and emerging infections is a great challenge, and it is vital to ensure that the most accurate information is successfully and unambiguously communicated to the public. WHO is applying these lessons across the Organization as it scales up its response to the HIV/AIDS emergency.

The first cases

On 12 March 2003, WHO alerted the world to the appearance of a severe respiratory illness of undetermined cause that was rapidly spreading among hospital staff in Hong Kong Special Administrative Region (China) and Viet Nam. Within two days, it was clear that the illness was also spreading internationally along major airline routes when hospitals in Singapore and Toronto, Canada, reported seeing patients with similar signs and symptoms. The potential for further international spread by air travel was vividly illustrated on 15 March. In the early hours of the morning, the head of WHO’s outbreak alert and response operations was woken by a call from health authorities in Singapore. A doctor who had treated the first cases of atypical pneumonia there had reported having similar symptoms shortly before boarding an international flight returning to Singapore from New York. Asked to intervene, WHO alerted the airline and health authorities in Germany, where the flight was scheduled for a stopover. The doctor and his wife disembarked in Frankfurt and were immediately hospitalized in isolation, becoming the first two cases in Europe. Because of these events, WHO issued a second, stronger alert later in the day. It set out a case definition, provided advice to
international travellers should they develop similar symptoms, and gave the new disease its name: severe acute respiratory syndrome (SARS). The global outbreak of SARS became the focus of intense international concern, and it remained so for almost four months.

Origins and international spread

SARS is a newly identified human infection caused by a coronavirus unlike any other known human or animal virus in its family. Analysis of epidemiological information from the various outbreak sites is still under way, but the overall case fatality ratio, with the fate of most cases now known, approaches 11%, but with much higher rates among elderly people. Transmission occurs mainly from person to person during face-to-face exposure to infected respiratory droplets expelled during coughing or sneezing, or following contact with body fluids during certain medical interventions. Contamination of the environment, arising from faecal shedding of the virus, is thought to play a small role in disease transmission, illustrated by the almost simultaneous infection in late March of more than 300 residents of a housing estate in Hong Kong where faulty sewage disposal was identified. At present, the disease has no vaccine, no curative treatment, and no reliable point-of-care diagnostic test, though antibody tests have been developed that can reliably confirm previous infection using acute and convalescent sera. Management of SARS is supportive, and control strategies rely on standard epidemiological interventions: identification of those fitting the case definition, isolation, infection control, contact tracing, active surveillance of contacts, and evidence-based recommendations for international travellers. Though demanding and socially disruptive, particularly when large numbers of people were placed in quarantine, these standard interventions, supported by high-level political commitment, proved sufficiently powerful to contain the global outbreak less than four months after the initial alert.

The earliest cases of SARS are now thought to have emerged in mid-November 2002 in the southern Chinese province of Guangdong. Retrospective analysis of patient records, to date incomplete, has identified small clusters of cases, each traced to a different initial case, that occurred independently in at least seven municipalities, with the first case recorded on 16 November 2002 in Foshan City and the largest number of cases concentrated in Guangzhou City. Analysis has uncovered no links among the various initial cases in the clusters. Some cases with no previous known history of exposure also occurred (1, 2). Early collaborative studies conducted in Guangdong have detected a virus almost identical to the SARS coronavirus in domesticated game animals – the masked palm civet cat and the raccoon dog – sold in Guangdong live markets, suggesting that these animals might play a role in transmission of the virus to humans.

The initial phase of the Guangdong outbreak, characterized by small, independent clusters and sporadic cases, was subsequently followed by a sharp rise in cases during the first week of February 2003, thought to result from amplification during care in hospitals. Cases gradually declined thereafter. Altogether, some 1512 clinically confirmed cases occurred in the Guangdong outbreak, with health care workers in urban hospitals accounting for up to 27% of cases (1–3). This pattern – occurrence in urban areas, with most cases concentrated in hospitals, and amplification during care – was repeated as the disease began to spread outside Guangdong Province to other areas in China and then internationally.

The first recorded case of SARS outside China occurred on 21 February 2003, when a medical doctor who had treated patients in Guangzhou City and was himself suffering from respiratory symptoms spent a single night in a hotel in Hong Kong. Through presumed contact, the mechanism of which is not fully understood, he transmitted SARS to at least 16 other guests
and visitors, all linked to the same hotel floor. They carried the virus with them as they entered local hospitals or travelled on to Singapore, Toronto and Viet Nam. An international outbreak that eventually spread to 30 countries had thus been seeded. Figure 5.1 maps the distribution of 8422 cases and 916 deaths that had occurred by 7 August 2003.

Detection and response

On 15 March 2003, when the second alert was made, the cause of SARS had not yet been identified. Cases were concentrated in hospital workers and did not respond to medicines known to be effective against a number of different lung infections. Many patients were rapidly progressing to severe pneumonia. The situation was alarming: no patients, including young and previously healthy health workers, had recovered. Many of the patients were in a critical condition, several required mechanical ventilatory support, and two had died. The spread to major cities around the world meant that any city with an international airport was at potential risk of imported cases. From the outset, WHO’s objective was clear: to halt further international spread and interrupt human-to-human transmission through a global containment effort, and by so doing to minimize opportunities for the disease to establish endemicity (see Box 5.1).

The global response to SARS was in reality the roll out of a way of detecting and responding to outbreaks that had been developed over the preceding seven years by WHO and its partners, partly as a result of major weaknesses that came to light during the 1995 Ebola outbreak in the Democratic Republic of the Congo and during previous outbreaks of plague in India and cholera in Latin America. The SARS response depended on collaboration of the world’s top public health and laboratory experts, and took advantage of up-to-date communication technologies, including the Internet and video and telephone conferencing.

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**Figure 5.1 Probable cases of SARS worldwide, 7 August 2003**
Two principal partners of the WHO Global Outbreak Alert and Response Network (GOARN), an electronically interconnected network of experts and institutes formally set up in early 2000, contributed to the detection of the SARS outbreak. One was the Canadian Global Public Health Intelligence Network (GPHIN), a worldwide web-crawling computer application, used by WHO since 1997, that systematically searches for keywords in seven different languages to identify reports of what could be disease outbreaks. Throughout the outbreak, GPHIN provided the raw intelligence that helped WHO maintain up-to-date and high-quality information on indications that the disease might be spreading to new areas. The second partner was the WHO Influenza Laboratory Network of 110 laboratories in 84 countries that constantly keeps the world in general and vaccine manufacturers in particular informed of which strains of influenza are circulating, so that an effective influenza vaccine can be produced each year.

On 10 February 2003, GPHIN and other partners of GOARN identified reports of an outbreak associated with health worker mortality and the closing of hospitals in Guangdong. One day later the Chinese government officially reported to WHO an outbreak of respiratory illness, beginning in mid-November, involving 300 cases and five deaths in Guangdong Province. Just over a week later, on 19 February, an outbreak of avian influenza was reported to the WHO Influenza Laboratory Network by the collaborating laboratory in Hong Kong. This outbreak first came to light when a 33-year-old man died of an unknown cause after returning from a family trip to Fujian Province, China. His 8-year-old daughter had died of a similar disease while in Fujian Province and his 9-year-old son was hospitalized in Hong Kong with the same symptoms. It was from this son that avian influenza virus was isolated and reported to the Influenza Laboratory Network. The same influenza virus had been identified in Hong Kong in 1997. Control efforts at that time required the slaughter and incineration of all chickens in the many live markets there; human-to-human transmission was never established.

Box 5.1 The response to SARS in the Western Pacific Region

More than 95% of SARS cases occurred in the Western Pacific Region. As an immediate response, a SARS outbreak response and preparedness team – including international experts – was established in the Regional Office. The main objectives were to:

- contain and control the outbreaks;
- support the health care infrastructure in affected countries;
- provide guidance and assistance to enable vulnerable countries to prepare for the possible arrival of the virus;
- provide the most up-to-date information to health officials and respond to public concerns.

Teams of epidemiologists and infection control experts were immediately sent to China, including Hong Kong Special Administrative Region, as well as to the Philippines, Singapore and Viet Nam and across the southern Pacific, training health care workers in infection control procedures and preparing them for the possible arrival of the disease. Practical infection control and preparedness guidelines and training tools were developed, and the first version of preparedness guidelines was issued at the beginning of April. Logistic support and supplies (personal protective equipment, including masks, collection materials for blood and respiratory samples, and internationally approved containers for shipment of samples) were sent to both affected and unaffected countries, supported by a US$ 3 million grant from the Government of Japan.

Countries were classified according to three levels of risk and three levels of capability to respond to SARS cases, in order for WHO to prioritize its support to countries. WHO worked closely with countries to ensure that enhanced surveillance was put in place to enable early detection of cases and contact tracing. Guidelines were drawn up on enhanced surveillance, hospital and community infection control, international travel, laboratory procedures and public awareness. To improve public awareness, close contact was established with national media focal points, and the web site of the Western Pacific Regional Office was regularly updated.

A regional laboratory network was established to ensure that necessary testing for SARS could be done for countries with limited laboratory capacities. National and regional reference laboratories were identified and shipping of specimens was arranged between the laboratories. WHO’s efforts were paralleled by the contribution of Member States. Viet Nam was the first to interrupt local transmission of the virus. Other countries introduced a wide range of measures, including isolation, home quarantine and comprehensive contact tracing. The willingness of governments in the Western Pacific Region to put public health considerations ahead of economic concerns about the impact of SARS was crucial to the success of the collaborative effort.
This heightened level of alert led to the identification of an early SARS case in Viet Nam on 28 February 2003. At the same time as GOARN collected information about this outbreak in real time, it sent an international team of partners to work with the Viet Nam authorities to better understand the disease, and by 12 March GOARN had accumulated the initial information necessary to issue the first global alert. It was through the continued instant sharing of information by governments, public health experts, clinicians and laboratory scientists that evidence-based decisions could progressively be made, culminating in the successful containment of SARS.

Under GOARN, a virtual collaborative network of 11 leading laboratories, linked by a secure web site and daily teleconferences, identified the SARS causative agent and developed early diagnostic tests. The network, in turn, served as a model for similar electronically linked groups of clinical and epidemiological experts who pooled clinical knowledge and compiled the epidemiological data needed to chart the outbreak’s evolution and assess the effectiveness of control interventions.

WHO issued daily updates about the outbreaks on its web site to keep the general public – especially travellers – informed and, as far as possible, to counter rumours with reliable information. Equally important, the web site was used to issue a range of evidence-based technical and practical guidelines for control as knowledge and information about the disease progressed and became available through the virtual groups of experts.

As more and more evidence accumulated through real time collaboration of public health experts, a range of additional evidence-based control measures became possible. It was soon evident, for example, that people with SARS continued to travel internationally by air after 15 March, and that some of them had infected passengers sitting nearby. At the same time it was also apparent that contacts of SARS patients likewise continued to travel, becoming ill once they arrived at their destination. Recommendations were therefore made that countries with major outbreaks should screen departing passengers to make sure that they did not have fever and other signs of SARS, or known contact with SARS patients.

As the outbreak continued in Hong Kong, contact tracing there further demonstrated that transmission of SARS was occurring outside the confined environment of the health care setting, and later suggested that it was also occurring following exposure to some factor in the environment, thus creating further opportunities for exposure in the general population. Additional evidence-based guidance was therefore made for sites where contact tracing could not link all cases to a chain of transmission, on the understanding that if the disease were spreading in the wider community it would greatly increase the risk to travellers and the likelihood that cases would be exported to other countries. This guidance was aimed at international travellers, and recommended that they postpone all but essential travel to designated areas in order to minimize their risk of becoming infected. Such guidance was also needed in view of the confusion created by several different national recommendations, many of which were based on criteria other than epidemiological data.

Authorities in areas where outbreaks were occurring responded to SARS with mass public education campaigns and encouraged populations to conduct daily fever checks. Hotlines and web sites answered questions. Screening measures were set up at international airports and border crossings, and procedures of infection control were reinforced in hospitals. Singapore drew on its military forces to conduct contact tracing, while Hong Kong adapted a tracing system that had been developed for use in criminal investigations and electronically mapped the location of all residences of cases. Chinese authorities opened hundreds of fever clinics throughout the country where suspected SARS cases were triaged. Heads of state and
ministers of health of countries of the Association of Southeast Asian Nations (ASEAN) and the Asia–Pacific Economic Cooperation (APEC) met and resolved to establish closer collaborative mechanisms for disease surveillance and response. Health staff everywhere worked with dedication, and many, including WHO staff member Dr Carlo Urbani, lost their lives.

On 5 July 2003, WHO announced that Taiwan, China, where the last known probable case of SARS had been isolated 20 days earlier, had broken the chains of human-to-human transmission. A recurrence of SARS cannot, however, be ruled out. Further research on many unresolved questions is needed. In the meantime, systems are now in place to detect a re-emergence should it occur (4).

The impact of SARS

The economic impact of the SARS outbreak has been considerable and illustrates the importance that a severe new disease can assume in a closely interdependent and highly mobile world. Apart from the direct costs of intensive medical care and control interventions, SARS caused widespread social disruption and economic losses. Schools, hospitals, and some borders were closed and thousands of people were placed in quarantine. International travel to affected areas fell sharply by 50–70%. Hotel occupancy dropped by more than 60%. Businesses, particularly in tourism-related areas, failed, while some large production facilities were forced to suspend operations when cases appeared among workers.

A second impact is more positive: SARS stimulated an emergency response – and a level of media attention – on a scale that has very likely changed public and political perceptions of the risks associated with emerging and epidemic-prone diseases. It also raised the profile of public health to new heights by demonstrating the severity of adverse effects that a health problem can also have on economies and social stability. The resulting high level of political commitment was decisive in the containment of SARS and has much to say about the ability of nations to achieve public health results even when drugs and vaccines are not available to cure or prevent the infection.

Lessons learnt

Although much about SARS – including its potential to reoccur – remains to be learnt through systematic analysis of existing data, and focused research activities in China, several important lessons are already apparent. WHO is applying these lessons across the entire Organization as it responds to the HIV/AIDS emergency.

The first and most compelling lesson concerns the need to report, promptly and openly, cases of any disease with the potential for international spread. Attempts to conceal cases of an infectious disease, for fear of social and economic consequences, must be recognized as a short-term stop-gap measure that carries a very high price: the potential for high levels of human suffering and death, loss of credibility in the eyes of the international community, escalating negative domestic economic impact, damage to the health and economies of neighbouring countries, and a very real risk that outbreaks within the country’s own territory will spiral out of control. Following the adoption during the World Health Assembly in May 2003 of a resolution on the International Health Regulations, WHO has been confirmed in its responsibility to take on a strong coordinating role in leading the fight against any infectious disease that threatens international public health (5). In a second resolution specific to SARS,
all countries are urged to report cases promptly and transparently, and to provide information requested by WHO that could help prevent international spread. It was explicitly acknowledged that across-the-board strengthening of systems for outbreak alert and response was the only rational way to defend public health security against not only SARS but also against all future infectious disease threats, including those that might be deliberately caused (6).

The second lesson is closely related: timely global alerts, especially when widely supported by a responsible press and amplified by electronic communications, worked well to raise awareness and vigilance to levels that can prevent imported cases of an emerging and transmissible infection from causing significant outbreaks. The global alerts issued by WHO on 12 and 15 March provide a clear line of demarcation between areas with severe SARS outbreaks and those with none or only a few secondary cases. Following the SARS alerts, all areas experiencing imported cases, with the exception of Taiwan, China, either prevented any further transmission or kept the number of locally transmitted cases very low. Figure 5.2 shows the weekly onset of 5910 cases. A climate of increased awareness also helps to explain the speed with which developing countries readied their health services with preparedness plans and launched SARS campaigns, often with WHO support, to guard against imported cases.

The third lesson is that travel recommendations, including screening measures at airports, appear to be effective in helping to contain the international spread of an emerging infection. Initial analysis of data on in-flight transmission of SARS has implicated four flights in the exposure of 27 probable cases, of which 22 occurred on a single flight from Hong Kong to Beijing, China, on 15 March. Some of these cases may also have been exposed elsewhere because of being in the same tour group. Following the recommendation of airport screening measures on 27 March, no cases associated with in-flight exposure were reported; and initial information reveals that two probable SARS cases were identified by airport screening procedures in Hong Kong and immediately hospitalized. Travel recommendations based on the

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**Figure 5.2 Probable cases of SARS worldwide, a 1 November 2002–11 July 2003**

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*a This graph does not include 2527 probable cases of SARS (2521 from Beijing, China), for whom no dates of onset are currently available.*
epidemiological evidence also gave areas where outbreaks were occurring a benchmark for quickly containing SARS, and then regaining world confidence that the area was safe from the risk of SARS transmission. In fact, passenger movement figures provided by Hong Kong International Airport show a rapid rebound from the lowest number of passengers, 14,670 (recorded just before 23 May when the travel recommendations were removed) to 54,195 on 12 July, a little over a month later.

The fourth lesson concerns international collaboration: the world’s scientists, clinicians and public health experts are willing to set aside academic competition and work together for the public health good when the situation so requires. International collaboration greatly advanced understanding of the science of SARS. One month after the laboratory network was established, participating scientists collectively announced conclusive identification of the SARS virus; complete sequencing of its RNA followed shortly afterwards. The network of clinical experts provided a platform for comparison of patient management strategies to indicate to the world which treatments and strategies were effective. In addition, the epidemiology network confirmed the modes of transmission of SARS and began the long-term collaboration needed to understand clearly the clinical spectrum of disease, including its case fatality ratio, while also providing the information needed to regularly reassess and adjust the case definition.

Lesson five is that weaknesses in health systems can permit emerging infections to amplify and spread, and can compromise patient care. The strengthening of health systems thus deserves high priority. The people at greatest risk for SARS were health workers who either became infected by close face-to-face contact with patients or by procedures that brought them into contact with respiratory secretions. Women predominate among the lower ranks of health personnel in many countries; available data reveal that infected health care workers were 2.7 times more likely to be women than men, while infection was roughly equal between the sexes in the general population. The surge of SARS patients placed an enormous burden on health services, requiring facilities for isolation, long periods of intensive and expensive care, and the use of demanding and socially disruptive measures such as mass screening, contact tracing, active surveillance of contacts and – at some outbreak sites – enforced quarantine. Even in areas with highly developed social services, the burden of coping with SARS, including the large number of hospitals with patients and the high number of health workers who became infected, often required closing some hospitals and sections of others. As a result of SARS outbreaks, many long-standing and seemingly intractable problems that have traditionally weakened health systems are being corrected in fundamental and often permanent ways. New surveillance and reporting systems, methods of data management, mechanisms for collaborative research, hospital policies, procedures for infection control, and channels for informing and educating the public are part of the initial positive legacy of SARS that will shape the capacity to respond to future outbreaks of new or re-emerging infections.

Lesson six is that in the absence of a curative drug and a preventive vaccine, existing interventions, tailored to the epidemiological data and supported by political commitment and public concern, can be effectively used to contain an outbreak. The virtual laboratory, and clinical and epidemiological collaborating networks regularly provided information that was used by WHO and its partners to update guidance for containment. Initial guidance was provided for containing outbreaks nationally – as additional evidence was obtained, guidance to limit international spread was also provided. Areas where outbreaks were occurring, and countries which considered themselves at risk of imported cases from these areas, adapted WHO guidance for their use. Some countries introduced active surveillance of suspected contacts using
surveillance cameras or military personnel. Others relied on self-surveillance by contacts who voluntarily isolated themselves in their homes and regularly checked for fever. Measures introduced at airports ranged from passive screening of passengers, involving optional completion of questionnaires, to the use of interviews conducted by health workers and sophisticated infrared equipment to screen all passengers for fever and indications of possible exposure. In addition to maximizing the impact of surveillance and screening, these measures were also considered by governments to be reassuring for national citizens as well as international travellers.

The seventh lesson highlights one of the major difficulties faced during the containment activities for SARS: risk communication about new and emerging infectious diseases is a great challenge. Work along these lines is currently under way in conjunction with the risk that a biological agent might be used in an act of terrorism.

SARS will not be the last new disease to take advantage of modern global conditions. In the last two decades of the 20th century, new diseases emerged at the rate of one per year, and this trend is certain to continue (7). Not all of these emerging infections will transmit easily from person to person as does SARS. Some will emerge, cause illness in humans and then disappear, perhaps to recur at some time in the future. Others will emerge, cause human illness and transmit for a few generations, become attenuated, and likewise disappear. And still others will emerge, become endemic, and remain important parts of our human infectious disease ecology.

The rapid containment of SARS is a success in public health, but also a warning. It is proof of the power of international collaboration supported at the highest political level. It is also proof of the effectiveness of GOARN in detecting and responding to emerging infections of international public health importance. At the same time, containment of SARS was aided by good fortune. The most severely affected areas in the SARS outbreak had well-developed health care systems. Had SARS established a foothold in countries where health systems are less well developed cases might still be occurring, with global containment much more difficult, if not impossible.

Although control measures were effective, they were extremely disruptive and consumed enormous resources – resources that might not have been sustainable over time. If SARS reoccurs during an influenza season, health systems worldwide will be put under extreme pressure as they seek to isolate all those who fit the clinical case definition until diagnosis can be ascertained. Continued vigilance is vital.

This chapter has illustrated how quickly a new disease can threaten global health. Thankfully, not all diseases move at such speed; but some are more stealthy and more lethal. Chapter 6 looks at three epidemics that are advancing at different rates in developing countries today: the spread of cardiovascular and other noncommunicable diseases; the tobacco epidemic; and the rising toll of deaths and injuries from road traffic hazards.

Note: The evolution of the global SARS outbreak has been chronicled in daily situation updates, archived on the SARS pages at the WHO web site: http://www.who.int/csr/sars/en/index.html.
References


