COMMENTARY

ACTING ON THE LESSONS OF SARS: WHAT REMAINS TO BE DONE?

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“Those who do not learn from history are doomed to repeat it.” — George Santayana

On November 16, 2002, a man was admitted with a diagnosis of atypical pneumonia to People’s Hospital #1 in Foshan City, Guangdong Province, People’s Republic of China. Although it was not recognized at the time, he was the earliest known case of a new human infectious disease, Severe Acute Respiratory Syndrome, or SARS. Within 4 months SARS was global, eventually infecting 8,098 people in 29 countries on 6 continents and killing 774 of them.

Even more concerning than these numbers is the fact that in many locations most of the victims were infected in hospitals and 21% of the victims were healthcare workers. At the time, SARS caused great alarm in the public health and medical preparedness communities. National and international guidance was issued, many health departments and hospitals created SARS plans, personal protective equipment was purchased, and healthcare workers were trained in respiratory precautions.

In the months following the SARS pandemic, a number of conferences were held and reports issued on lessons learned from SARS. Now, from the vantage point of 8 years’ distance, what did we really learn? What are the remaining unanswered questions? What remains to be done?

DISEASES JUMP THE SPECIES BARRIER

The risk of infectious diseases jumping the species barrier remains a clear and present danger. People have been catching diseases from animals (zoonoses) as long as there have been people. In recent years, most emerging infectious disease events have been the result of mutations in wildlife pathogens that have allowed infection of human hosts. In the past, such events contributed to some of history’s great pandemics, including influenza, plague, smallpox, and HIV. SARS was caused by a coronavirus that was endemic among fruit bats in China; it adapted to a human host after establishing itself in the captive animals in the wild animal markets of Guangdong Province.

As humans encroach ever more deeply into previously wild areas, the incidence of zoonotic infections will likely increase. In recent years we have seen zoonotic outbreaks of ebola, Marburg, nipah, and hendra. As zoonotic infections continue, some microbes are likely to adapt to a human host and cause efficient and sustained human-to-human transmission. But this is not an entirely unpredictable event. Certain microorganisms, by virtue of their biology, are more likely than others to evolve into human pathogens. By understanding the characteristics that make some microorganisms a greater risk than others, for example, Donald Burke was able to predict the emergence of a novel human coronavirus years before SARS appeared.

MORE INTERCONNECTED AND URBANIZED

The risk of pandemics grows as the world becomes more interconnected and urbanized. Modern urban environments have conditions, such as high population density, poor sanitation, and many poor, malnourished people, that may accelerate the spread of emerging infections. For
instance, the large outbreak of SARS at the Amoy Gardens apartment complex in Hong Kong (529 patients) is at least partially related to its enormous size and density—19,000 residents in 0.04 km².6

Because of their great population density, the burgeoning megacities around the world may contribute to the spread of novel contagious diseases.7,8 The introduction of a highly contagious novel pathogen into such an environment may result in an explosive outbreak. This phenomenon has been seen with each influenza pandemic, but today our cities are bigger and more congested than ever. There are now 26 megacities with populations over 10 million,9 and population densities in some cities are approaching 30,000 people per km².10

Furthermore, many large, congested cities, like Hong Kong, are major transportation hubs. Once SARS was introduced by 1 individual into 1 floor of 1 tourist hotel in Hong Kong, it was spread globally within a few days by modern air travel.

**Hospitals Can Amplify Disease**

During the SARS pandemic, modern hospitals and the sophisticated care they provided were double-edged swords. It is certainly true that many victims of SARS were saved in intensive care units around the world. It is reasonable to estimate that the case fatality rate for SARS was cut in half by sophisticated modern health care. (If all patients who required intensive care would have died without it, then the case fatality rate would have been approximately 20% rather than the actual 10%.)

On the other hand, it is likely that SARS would not have become a major epidemic had it not been for the many superspreading events that occurred in hospitals.11 These superspreading events were very often related to certain medical procedures—such as endotracheal intubation, airway suctioning, and noninvasive ventilation—that turn respiratory droplets into aerosols.12,13 Most SARS infections probably occurred in hospitals, and nearly all cases of SARS can be traced back to one or more nosocomial superspreading events starting with relatively small hospital outbreaks in rural Guangdong, then large nosocomial outbreaks in Guangzhou, Hong Kong, Hanoi, Beijing, Singapore, and Toronto.2 That hospitals can function as disease amplifiers is not entirely new: Outbreaks of influenza occur in healthcare facilities every year, and many hospital-related outbreaks of TB have been documented. Hospital-related outbreaks have occurred with other infectious diseases as well, including smallpox14,15 and ebola.16,17

**Hospital Infection Control Measures**

Hospital infection control measures work to stop the spread of pandemics. SARS was brought under control within a matter of months largely due to the fact that the disease was most transmissible when the patients were most sick—that is, when they were in a hospital.2 There was relatively little community transmission of SARS compared to other respiratory infections like influenza.18 For this reason, controlling the transmission in hospitals was key in controlling the outbreak.19 This also explains the large percentage of healthcare workers who became infected and the large percentage of victims who acquired their infections in hospitals. For the most part (with the very important exception of aerosol-generating procedures), transmission in hospitals was brought under control by the use of standard infection control practices, such as isolation of sick patients and wearing of masks, gowns, and gloves by hospital staff.20,21 For those high-risk aerosol-generating procedures, more stringent measures, such as the use of negative pressure isolation and high-efficiency respirators, were effective in reducing transmission.13,22

But an important caveat was also clear: The hospital staff must be properly trained in the correct use of the personal protective equipment (PPE), and the infection control measures must be rigorously applied. When this was done, little transmission occurred; when it was not done, many more healthcare workers were infected.23

**International Scientific Collaboration**

International scientific collaboration is important for controlling the spread of diseases. On March 12, 2003, with similar outbreaks in Hanoi, Hong Kong, and Guangdong, WHO issued its first global alert for the disease that would later become known as SARS. Five days later, WHO set up a virtual network of scientists from around the globe to collaborate on finding a cause of this new disease. Five days after that, on March 22, scientists in Hong Kong and at the CDC identified a novel coronavirus as the likely causative agent.1 Within weeks the virus was fully sequenced and a diagnostic test was developed. That this could be accomplished in such a short time was unprecedented. The WHO network also facilitated real-time collaboration and data-sharing among epidemiologists and clinicians from around the world, which had never before been seen.

**Disease Doesn’t Stop at the Border**

Efforts to contain diseases at national borders provide limited value at great cost. Public health authorities in many locations imposed various forms of quarantine in attempts to quash the outbreaks. Quarantine is the sequestration from the general public of individuals who have potentially been exposed to an infectious disease in an attempt to prevent them from spreading the disease if they turn out to be carriers. It is different from isolation, which is the sequestration of individuals known to have the infection. Isolation was clearly effective in SARS and, in fact, was
the key to its control. Quarantine, although widely employed, was not so clearly effective. In many cases, a large number of people subject to quarantine orders refused to comply. In fact, in some cases the imposition of quarantine orders produced a paradoxical result—people escaped. This may have contributed to the spread of SARS to remote parts of China.24

Various types of travel screening were employed by a number of countries. Despite screening of millions of travelers, only a very few individuals with SARS were discovered. This was especially true of thermal screening. More than 35 million international travelers entering China, Canada, and Singapore had their temperatures measured, but no cases of SARS were found.18

Although the public health benefits of such measures are not clear, the resources required to implement them have been shown to be significant. Canada spent nearly $8 million (Canadian dollars) to implement a passenger screening program at select airports during SARS.25 Given that the program did not ultimately detect a single SARS patient in the 4 months it was in effect, Canadian health authorities have concluded that the costs of the program exceeded the public health benefits.

Other countries experienced similar cost/benefit ratios. In Taiwan, to support a quarantine that placed more than 150,000 people under home quarantine for 10 to 14 days, nurses had to bring the quarantined people 3 meals every day and sometimes helped them with other jobs such as washing clothes or taking care of pets. Such resource requirements are extraordinary, given that most of Taiwan’s 480 SARS cases were unaffected by the quarantine. Only 24 people subjected to quarantine turned out to have SARS.26

Preparing to Respond Can Save Lives

The response to SARS seems to have been largely very successful: In less than 4 months, a novel infectious disease with high rates of morbidity and mortality exploded across Asia and then to many other parts of the world, but within 6 months the pandemic was mostly over. The end of the SARS epidemic has been ascribed to the intervention strategies employed to control it—but those strategies were invented on the fly. After losing patients and staff to nosocomial transmission of SARS, affected hospitals were forced to figure out which infection control measures would halt the spread of infection.

In Canada, where 45% of SARS cases occurred among healthcare workers, a government-sponsored review found that, had the respiratory precautions and isolation policies that were eventually employed in the hospitals been in place at the beginning of the outbreak, many fewer people would have been infected.27 In both hospitals and health departments, advance planning, creation of information and communication systems, education and training, and stockpiling of supplies are necessary to enable an optimal response. Many lives could have been saved, much suffering relieved, and costs avoided if this work had been done before, rather than after, the first case was discovered.

Superspreading and Respiratory Transmission

Controlling the spread of disease requires better understanding of superspreading and the mechanism of respiratory transmission. Probably the most striking epidemiologic feature of SARS was the so-called superspreading phenomenon in which a small number of individuals transmitted their infection to many other people, often causing large outbreaks. Epidemiologists often calculate the reproductive number ($R_0$)* when describing the spread of a contagious disease. The bigger the $R_0$ value is, the faster the disease will spread and the harder it will be to stop. If the $R_0$ of an epidemic is less than 1, the person-to-person transmission will not be sustained. If it is greater than 1, the disease will spread unless something is done to stop it. Influenza is typically said to have an $R_0$ of 1.5 to 2, measles an $R_0$ of 15. Although the $R_0$ for SARS was estimated to be 2 to 4, this number only represents the average number of secondary cases caused by an infected person.28 The reality is that a huge range of transmission rates occurred. While most people with SARS did not infect anyone else, the majority of SARS infections can be traced to a relatively small number of superspreading events in which 1 individual infected many other people.2

Superspreading is not a new phenomenon, having been described with tuberculosis, measles, and smallpox.29 It may well occur more frequently than is recognized in other contagious diseases as well.30 It is important to better understand this phenomenon; if superspreading events can be predicted, they probably can be avoided. In SARS, certain patient factors were identified that were associated with a higher risk of superspreading. These mostly related to conditions that cause some degree of immune-suppression, such as chronic renal disease, diabetes, advanced age, and perhaps corticosteroid therapy. In addition to these host factors, high-risk aerosol-generating procedures were clearly associated with superspreading.

But 3 superspreading events stand out as particularly puzzling: those that occurred at the Metropole Hotel and Amoy Gardens in Hong Kong, and the event in the emergency department (ED) of Scarborough Grace Hospital in Toronto. The event at the Metropole Hotel was the proximate cause of the SARS pandemic, as nearly all cases outside of China can be traced back to it.31 One infected individual stayed 1 night on the ninth floor of the hotel and

\*($R_0$) is the reproductive number in a completely susceptible population—that is, the average number of new people infected by an infected individual.
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infected 16 other people on the same floor who then traveled across the globe before becoming ill. Although several possible explanations have been proposed, there is still no entirely satisfactory explanation for this event.

The ED of Scarborough Grace Hospital was the site of a chain of SARS transmission that led to most of the cases in Toronto. In particular, one event there stands out as unusual. The wife of one of the SARS patients sat in the ED waiting room while her husband was being treated. Unbeknownst to the ED staff, she also had SARS, but her symptoms were mild. Despite having mild symptoms, she apparently infected a number of other people in the waiting room and possibly a number of the staff as well. This event contrasts with most other incidents of SARS transmission, which required close contact and occurred only when the patient had severe symptoms. Like the event in the Metropole Hotel, it would be useful to understand what factors contributed to this anomalous event.

The Amoy Gardens event is even more disconcerting. Amoy Gardens is a high-rise apartment complex with 19,000 residents. One infected individual staying there infected 329 others. The best explanation is that a malfunctioning plumbing system allowed the creation of a virus-laden aerosol plume that was blown outdoors, wafted hundreds of yards downwind, and infected people in other buildings through open windows.

If this hypothesis is true, it undermines many assumptions about the transmission of infectious diseases.

This leads to the consideration of how SARS was transmitted—that is, whether it involved droplets or aerosols. Much has been written on this topic, and there are strong opinions on both sides. The distinction is important, because the answer determines the appropriate infection control measures to be used. In fact, there is convincing evidence for both forms of transmission.

In most cases SARS transmission was blocked by simple droplet precautions, but in others it seems clear that aerosol transmission was the only logical explanation; this was especially true in certain hospital outbreaks (eg, Ward 8a of the Prince of Wales Hospital in Hong Kong). Probably both droplets and aerosols were produced as patients coughed, and various host and environmental factors determined which mechanism was predominant at a particular time and place. Better understanding of this phenomenon is important, because if this is also true for other diseases, then the role of aerosol transmission in respiratory infections more generally must be reconsidered.

WHAT REMAINS TO BE DONE

Although some key questions remain unanswered, a great deal was learned from the SARS outbreak. Space does not permit an exhaustive review of all of the lessons, so we have focused on the areas in which we have particular expertise: hospital preparedness and public health. Important lessons were also learned in the area of emergency management at the municipal, provincial/state, and national levels and in the realm of international treaties.

Hospitals

In the first few years following the SARS pandemic, “respiratory etiquette” became the “new normal” in hospitals—anyone with a cough had a surgical mask placed on them at the ED door, and aerosol-generating procedures were done only in closed rooms with staff wearing PPE—and it was said that things would never be the same again. But now when we walk the halls of hospitals, this “new normal” for infection control is hard to detect. If SARS were transmitted easily in hospitals, it seems likely that other respiratory infectious diseases may be, too—perhaps far more than we know.

Given that adhering to basic infection control guidelines and respiratory etiquette appear to have been an effective and inexpensive means of limiting transmission, hospitals should reinvigorate their efforts to adhere to these guidelines. Accrediting and regulatory organizations should make adherence to respiratory infection control guidelines a higher priority when surveying hospitals. Government agencies should fund more research into how respiratory infections spread within hospitals and how the spread can be prevented.

Public Health

Public health agencies in many locations did remarkable work in investigating outbreaks, tracking cases, and coordinating a response during the SARS pandemic. However, U.S. government support for state and local public health preparedness programs has declined steadily since 2005. In the past few years, local health departments have lost 15% of their workforce, and 42% of state health departments have had to cancel entire public health programs. These reductions in federal and state funding jeopardize the many substantial and hard-won gains in readiness that had been made in the aftermath of SARS, and the funds should be restored.

Scientific Community

In the midst of a crisis, the scientific community was able to identify the virus that causes SARS with unprecedented speed—less than 1 month after WHO first recognized the epidemic. However, in the 8 years that have elapsed since the SARS epidemic, many of the gains made in its immediate aftermath seem to be fading. The unprecedented global scientific collaboration that led to the rapid identification of the virus has been replaced by countries being unwilling to share virus samples, and no vaccine candidate has advanced beyond Phase 1 clinical trials.
network for international collaboration that was created during the SARS epidemic should be a foundation and template for ongoing cooperation in scientific research on emerging infectious diseases.

The world has turned its attention to other problems, although the conditions that led to the emergence of SARS and its rapid global spread largely remain unchanged. The lessons of SARS relate to more than that single disease; they relate to many infectious diseases and to public health and hospital infection control more broadly. We forget these lessons at our peril.

References


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