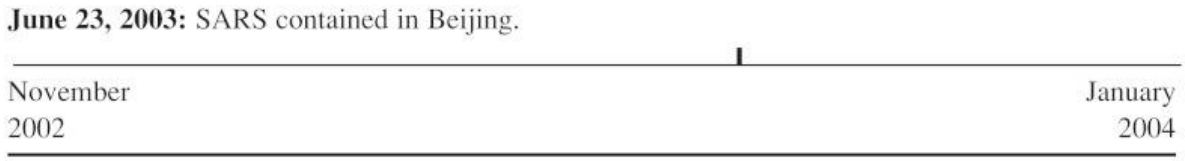
Institute of Medicine (US) Forum on Microbial Threats; Knobler S, Mahmoud A, Lemon S, et al., editors. Learning from SARS: Preparing for the Next Disease Outbreak: Workshop Summary. Washington (DC): National Academies Press (US); 2004.

LESSONS FROM SARS FOR FUTURE OUTBREAKS

Recognizing that it would be impossible to address the vast array of potential microbial threats individually, public health policy makers are formulating general strategies to evaluate and respond to outbreaks of all kinds. At the international level, revisions to the International Health Regulations—rules concerning infectious disease that legally bind WHO member nations—have been underway since 1995, and are expected to be completed in 2005. **Workshop participants concurred that efforts to address microbial threats should encompass and be enriched by existing strategies for defense against bioterrorism. As one participant noted, authorities do not know until well into an outbreak if it is a naturally occurring or manmade threat—in either case a robust and prepared system will be able to respond rapidly and effectively to contain disease spread.**



The importance of collaboration was a common theme among workshop discussions on research. It was discussed in the context of scientists around the globe who identified the causal agent of SARS, of veterinary and biomedical research communities studying zoonotic pathogens, and of private sector companies working in conjunction with government agencies and academia to develop antiviral drugs and vaccines.

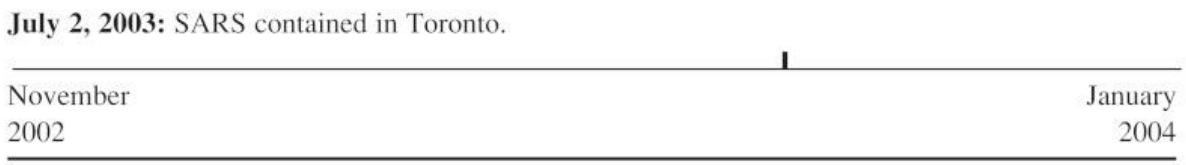
Workshop participants considered what could be learned from the experience of SARS and how that knowledge could improve the public health community's response to future outbreaks of infectious disease. The principal topics discussed include:

- the early detection of outbreaks,
- effective communication to the public in the event of an outbreak,
- the promotion of research and development,
- strategies for containment, and
- multinational collaboration in implementing such strategies.

Importance of Early Detection

The central response to SARS—surveillance and containment, when instituted promptly, rapidly, and effectively—applies to almost any microbial threat. It is clear that the initial

delays in not only detecting the novel SCoV, but also alerting national and global health officials to the disease outbreak significantly increased the spread of SARS and its impact on affected countries. However, soon after the global outbreak alerts were issued, the timely recognition of the emergence of SARS in other countries proved to be an important factor in breaking all chains of transmission. The surveillance networks such as GOARN and GPHIN, supported by personnel and laboratories from 115 other partnerships, made this success ultimately possible. Along with these vital resources, workshop participants identified additional surveillance strategies for microbial threats; these include hospital-based surveillance systems capable of recognizing both known and novel diseases, and occupational clustering, with particular attention paid to illness in health care workers. Behavior-based surveillance could identify such phenomena as drug sales, or even such phenomena as the rapid rise in vinegar sales that occurred in response to SARS in Guangdong in January 2003 (vinegar is commonly used to combat respiratory illness in traditional Chinese medicine).



Drawing on the SARS experience, a recent WHO global consultation focused on strengthening national capacities for surveillance, response, and control of communicable diseases. After SARS, it was noted, "countries increasingly look at the integration of disease surveillance activities as an effective, efficient and sustainable approach to improving national capacities." Among recommendations issuing from this consultation was the admonition that "member states should review existing legal frameworks to further support strengthening of surveillance including participation of the private sectors and non-governmental organizations" (WHO, 2003k). Several workshop participants observed that more nationally and globally coordinated systems of information-sharing and data analyses among surveillance networks might dramatically improve the world's ability to contain microbial threats.

While discussing the critical role of laboratories for effective surveillance, concerns about laboratory safety were raised. Accidents in a Singapore clinical laboratory (described earlier in this chapter) and a Taiwan research laboratory have been responsible for SARS infections in workers (Center for Disease Control Taiwan, 2003). These incidents highlight the importance of hospital surveillance procedures and appropriate clinical management and infection control measures in preventing an outbreak. They should also raise the awareness of the research community, particularly given the many laboratories now conducting research on SARS, to the risks inherent in handling all communicable agents and the need for strict adherence to well established laboratory procedures.

Overall, workshop participants observed that surveillance must be backed up with action and reinforced by sufficient laboratory capacity, well-trained personnel, and a legal framework consistent with objectives of transparency, global cooperation, and sensitivity to the balance between public protection and the interests of individual countries and persons. Workshop discussants emphasized that investments made toward this end should capitalize on the existing networks and need not be prohibitively extensive or expensive.

Strategies for Containing Future Threats

An estimated 75 percent of emerging human pathogens and 61 percent of all human pathogens are zoonotic (Taylor et al., 2001). Therefore, many predictions about the nature of future novel pathogens anticipate the emergence of zoonoses. Thus, workshop participants considered the strategies for containing known zoonoses—in particular, influenza—as potential models for the containment of SARS and unidentified zoonotic diseases of the future.

July 5, 2003: SARS contained in Taiwan; WHO declares containment of worldwide epidemic.

November 2002 — January 2004

Lessons Learned from Influenza

The same trends that ushered SARS into the human population have been apparent during a century of influenza outbreaks. The exponential increase in avian influenza virus infections among humans over the past decade has been associated with a sharp rise in the size and density of chicken and pig farm populations, their proximity to human settlements, and movement of animals through market channels, which in turn parallels the world's rapidly expanding and mobile population. As with SARS, animal markets provide the breeding ground for recent outbreaks of influenza; laboratory sources also appear to have sparked at least one epidemic. Fortunately, most of the recent influenza outbreaks did not feature the transmission of the virus to humans. However, experts agree that it is only a matter of time until a highly virulent and contagious flu, such as the strain that caused over 20 million and perhaps as many as 40 million deaths during the 1918 influenza epidemic, confronts the world (see Webby and Webster in Chapter 5).[13]

Vaccines and antiviral therapies play a significant role in containing epidemics of influenza. It is advantageous that the timing of annual outbreaks of influenza and the strain or strains of the virus can, to some extent, be anticipated. **However, strategic actions recommended against influenza that could also inform efforts to better prepare for other viral disease outbreaks have yet to be implemented. These strategies include:**[14]

- **stockpiling of broad-spectrum antiviral drugs,**
- **advanced development of pandemic strain vaccines,**
- **the establishment of surge capacity for rapid vaccine production, and**
- **the development of models to determine the most effective means of delivering therapies during an outbreak.**

September 8, 2003: Isolated case of SARS occurs in Singapore due to laboratory accident.

November 2002 — January 2004

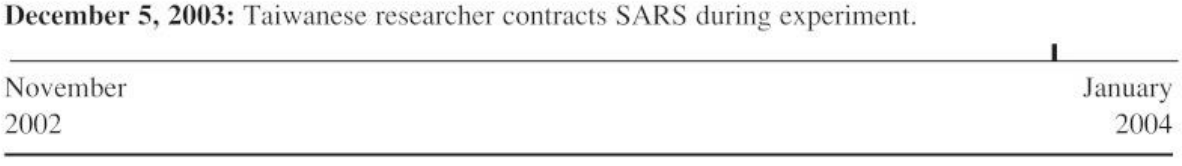
It is evident from the experience of the late 2003 influenza season that our supply and effectiveness of antiviral drugs, capabilities to accurately predict the best viral strain for annual vaccine production, and mechanisms for surge capacity production remain inadequate (Treanor, 2004; WHO, 2003o). Recognition of these vulnerabilities lead numerous workshop participants to call for greater scientific and financial investments to strengthen our defenses against these certain future threats.

Quarantine

Some emerging infections of the future, like SARS, may be truly novel threats for which the world—including its pharmacopoeia—is inadequately prepared. Lacking other forms of effective interventions, the implementation of quarantine or isolation strategies may prove valuable in such instances. Workshop participants discussed several ways that modeling tools might be used to improve and tailor such measures. Models based on detailed observations from previous epidemics can be used to predict demands on hospital capacity during a hypothetical epidemic and to guide the timing and nature of quarantine measures. Models that can estimate the length and severity of an unfolding epidemic will likely increase public acceptance of quarantine by permitting people to form realistic expectations of their sacrifice and its benefit to the community (see Amirfar et al. in Chapter 5).

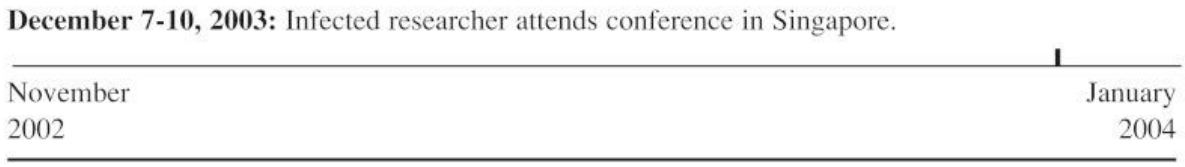
Evidence indicates that a modern approach to quarantine encompassing a range of options designed to reduce the frequency of social contact can significantly reduce the spread of infectious disease. Such options include short-term, voluntary home curfew; suspension or cancellation of public activities (such as events, mass transit, or access to public buildings); and "snow day" or sheltering-in-place measures. These measures could be employed individually or in concert. In addition to or in place of these strategies, a program of contact surveillance—the monitoring of asymptomatic persons exposed to an infectious disease—could be undertaken. Modern quarantine and contact surveillance preserve individual liberties and require far less labor and other community re-sources than would be required to enforce a mandatory quarantine. Voluntary and other forms of scalable quarantine nevertheless reduce productivity and may result in public perceptions that stigmatize groups of individuals and promote irrational behavior. For example, there is evidence that consumers began to avoid Asian restaurants in the United States and other nonaffected countries during the SARS epidemic even though neither quarantine nor public health messages suggested such action. **For any quarantine to be effective, workshop participants noted, a number of needs must be met, including:**

- **education to build public trust in health authorities,**
- **compensation and job security for quarantined workers, and**
- **incentives to health care workers to maintain their morale in the face of increased risk and to pay greater attention to infection control practices.**



In the more difficult case of mandatory quarantine, enforcement requires careful planning and a clear understanding of public health law; this is particularly true in the United States, where quarantine is likely to necessitate the coordination of federal, state, and local jurisdictions and legal authorities. For example, if an infectious disease has the potential to spread across state boundaries but has not yet done so, an action by CDC to limit transmission would require the cooperation of appropriate state and local authorities. The presidential executive order adding SARS to a list of other diseases subject to federal quarantine actions eliminated such jurisdictional uncertainties (Executive Order 13295: Revised List of Quarantinable Communicable Diseases, 2003). Additional legal considerations include planning for due process—proper notice, legal representation, court-reviewed decisions, and remote communications to permit a quarantined person to be heard in court—and for practical contingencies, such as the need for law enforcement officials to serve notice of quarantine (see Matthews in Chapter 5).

Workshop participants also discussed the need to develop strategies by which hospitals—and entire communities, in the event of quarantine—can determine when precautions against infection can be scaled back. Some experts have argued that containment measures should be swiftly imposed in response to a perceived infectious disease threat (as occurred when SARS appeared in Vietnam) and reduced only after surveillance determines the absence of a threat. Clearly, the consequences of false alarms in this case must be weighed against the risks of inaction in the early stages of an epidemic, as demonstrated by China's experience with SARS.



Informing the Public

Although no presentations exclusively addressed the subject of public communication, this topic was identified as important and was widely discussed by workshop participants. Social cohesion and compliance with quarantine in Toronto were attributed in part to a combination of clear communication and practical guidance by public health authorities. The media's sustained and intensive focus on the epidemic, heavy traffic on informational SARS websites operated by WHO and CDC, and a great volume of calls to CDC's SARS hotline reflect the public's hunger for news and information during the public health emergency.

Official travel and health advisories, though deemed necessary, were also linked to consumer avoidance of international travel, international events, and even Asian restaurants. It was suggested that such adverse effects could be mediated in the future by accompanying advisories with educational messages designed to help the public develop a realistic perception of the risks for infection and appropriate responses. **Research designed to identify why societies respond dramatically and irrationally to certain types of public health threats might help communicators to develop messages that positively influence the public's behavior during medical emergencies.**

The media's powerful role in the response to SARS was characterized in both positive and negative terms: as a cause of stigma and discrimination due to sensationalized reporting on the epidemic; as a demystifier of quarantine and other public health measures through exhaustive coverage; and, as a persuasive contributor to China's decision to cooperate with international efforts to control SARS. The Internet, recognized as a key source of early leads to the outbreak of SARS, was also viewed with concern for its potential to propagate false rumors. It is important to guard against such threats in the event of public health emergencies. Likewise, **it will be critical to make use of the media to inform and educate the public on how best to protect themselves and their communities in the event of future outbreaks**

December 17, 2003: Singapore authorities quarantine 70 individuals.

November 2002 — January 2004

Surge Capacity

Health Care Personnel

Workshop participants remarked that the strained capacity of the U.S. and global public health infrastructure—attributed to insufficient funding, labor shortages, and a lack of facilities—impedes preparations for SARS and other threats to public health. As described earlier, even some of the highly developed health care systems of Toronto struggled to cope with inadequate numbers of health care personnel (particularly because of the inevitable toll that moderately to highly contagious diseases take on health care personnel) and were ultimately unable to sustain normal levels of care for both SARS and non-SARS patients.

In moving forward, workshop participants suggested that up-to-date information and skills needed for containing epidemic-prone diseases must be better integrated into the training of ***all*** **health care professionals**, not only those specializing in infectious diseases or infection control. In citing Toronto's call to health care personnel in other regions and countries, a participant recommended **the expansion and establishment of formal networks to rapidly identify, transport, and enlist experienced health care personnel in the event of future outbreaks. Such contingencies would be designed for local, regional, national, and international responses and, in particular, would facilitate the mobilization of human and technical resources that are known to have previously tackled certain disease outbreaks.** The question was asked, if SARS is to reemerge how will we harness the skills and new knowledge of the thousands of individuals involved with finally containing the disease? While some participants lauded the efforts of GOARN and the CDC in this regard, they questioned if that was enough.

Health Care Facilities

The inability to effectively establish isolation areas and procedures within hospitals and other health care facilities contributed to the spread of SARS in several countries. Inadequate facilities not only promoted the spread of the disease, but also forced the suspension of other vital health care procedures. As previously described, one workshop participant suspected

that more patients died during the SARS outbreak in Toronto as a result of the inability to access appropriate care for conditions other than SARS rather than from SARS itself.

January 5, 2004: China and WHO confirm SARS case in Guangdong Province.

November 2002 — January 2004

As such, participants called for **preparedness planning that established procedures for rapid identification and use of facilities designated not only for treatment of suspected and confirmed cases of an epidemic disease, but also facilities that could be isolated for the conduct of other critical procedures such as emergency surgeries, trauma care, and organ transplantation.** In this regard, several participants credited the rapid construction of "SARS hospitals" in China as a key element in ultimately containing the disease.

Supporting the Research Response

Years of investment in basic research on coronaviruses, largely in the veterinary research fields, helped the scientific community to identify the SARS coronavirus within months of its emergence. Consequently, **numerous participants noted that the potential for future outbreaks not only justifies present-day investments in basic research on viruses and microbes, but also argues for greater attention to and investment in research efforts that integrate the direct contributions of zoonotic infectious disease research with biomedical research efforts**. As noted earlier (see Box S-1), a number of basic scientific questions about the biology and epidemiology of SARS need to be answered in order to develop diagnostics and therapeutics for the disease, as well as to construct and implement targeted surveillance strategies. Apart from research that is specific to the SARS coronavirus, however, workshop participants discussed a number of broader areas of basic research that might be pursued in order to counter the threat that would arise from either a recurrence of SARS or the emergence of other new infections.

First, now that the more urgent pace of responding to an ongoing epidemic has subsided, researchers should be encouraged to thoroughly and methodically take stock of data that was accumulated over the course of fighting this epidemic. Workshop participants suggested that the public health community should not be complacent about the eventual success that was had in containing last year's SARS outbreak; **there remains a need to understand exactly what strategies were most effective, what strategies were less successful or even counterproductive, and what steps would be most essential for combating the emergence of a new and possibly more virulent or more infectious pathogen.** As part of this retrospective evaluation, for example, extant patient and hospital records should be assembled, compared, and analyzed in order to provide as exact an assessment as possible of the effectiveness of each of the many control measures that were adopted, as well as the points of greatest weakness that allowed the virus to spread. Some of the lessons to be learned will be specific to the profile of SARS, but many of them will also be readily applicable to other new infections in the crucial early stages of an epidemic when less is known about the biology of the disease than about its manner and rate of spread. On the next occasion when scientists and public health officials are confronted by a novel threat, it is important that they have a battery of well-researched studies to fall back on concerning

measures that have previously been shown to be effective and feasible in controlling even a disease entity that has not yet been well characterized.

Secondly, this evaluative process should expand beyond those areas encompassed by clinical medicine and emergency care. The SARS epidemic illustrated how rapidly the impacts of a new disease can reverberate through the political and economic structures of successive countries and regions, and the decisions that were made in response to the epidemic ultimately reached into the highest levels of government and international bodies. Just as with the measures that were taken within individual hospitals and clinical settings, **the comparative effectiveness of the broader quarantine measures, travel advisories, communications with the general public, and other legal and public health directives that were issued should be gauged relative to their costs and difficulties. Any possible improvements in the measures that were adopted in the case of SARS—or recommendations for flexible options or combinations of options that might be applied in the face of different types of pathogens—may need to be examined within a broad and multidisciplinary discussion framework.**

Finally, basic research needs to be conducted into not only the measures that were most effective in containing the last epidemic but also those steps that would best facilitate research on understanding the next one. The uncertainty and confusion that are likely to be present in an epidemic's early stages may at least be ameliorated if scientists, public health officials, and governmental bodies understand and are well prepared to collect the types of data that have been shown to be most crucial in assessing the nature and magnitude of a novel threat. **A number of workshop participants commented on the need to look into better standards for data capture and coordination during the course of an epidemic, as well as the need to have better models on hand for evaluating the effects of possible intervention strategies as early as possible.** Likewise, while carefully controlled therapeutic trials are often impractical (or at best extremely difficult) during the first stages of a disease outbreak, some workshop participants lamented the fact that relatively little progress was made toward developing a standard treatment algorithm for SARS patients during last year's epidemic, and there remains significant controversy over the effectiveness of certain treatments that were applied. **It was suggested that in the case of any future epidemics, better pooling of data from scattered clinical treatment centers could at least initiate the process of assessing the efficacy of different treatment strategies and provide groundwork for more reliable clinical advisories until the time and means are available for more thorough studies.**

Engaging the Private Sector

Several presentations and considerable discussion concentrated on mechanisms that could potentially engage the private sector—specifically, pharmaceutical and biotechnology companies—in the research and development of products targeted at the greatest threats to public health, including infectious diseases.

For pharmaceutical researchers, streamlining the development process is crucial to productive engagement in strategic research. Means of streamlining this process include the clear identification of patient and physician needs, access to detailed biological studies of the pathogen of interest, and technologies such as computational and combinatorial chemistry that speed target selection and lead generation. Workshop presenters described the need for

technology to improve predictions of the safety of drug candidates so unsafe compounds could be weeded out at an early and less expensive stage of the development process.

Promotion of International Cooperation and Collaboration

If SARS never returns, the 2003 epidemic will nonetheless be remembered as a watershed event in the history of public health because of the degree of multinational cooperation to contain the disease. As the world becomes more conscious of microbial threats to health, countries are increasingly compelled to report infectious outbreaks and join international efforts to contain them. Recognizing that such transparency often comes at a price to a nation's economy, particularly in developing countries, workshop participants attempted to identify incentives to encourage nations and individuals to act for the common good.

Some participants offered specific ideas for incentives, including cooperative grants to support disease-monitoring efforts by academic researchers in developing countries and high-profile awards from bodies such as the Institute of Medicine or World Health Organization to countries or individuals who make important sacrifices for the health of world.

Networking can also play a vital role in local and regional preparedness for infectious disease threats. Tabletop exercises, in which detailed outbreak scenarios are presented to officials who develop a response based on the tools and resources at their disposal, encourage preparedness and provide a forum for building collaborations among the many individuals and sectors essential to an effective, coordinated response. From such exercises, the real-time compilation of epidemiological, clinical, and laboratory data that could be made available to the international community through WHO could also stimulate cooperation and collaboration. When implemented via the Internet or other communication net-works, these exercises can be used to develop systems of communication, as well as working relationships, in advance of an outbreak or other emergency.

Some countries are increasingly cognizant of the fact that the health of the global public affects the individual security of all nations, especially those that are most enmeshed in global networks of trade, tourism, and investment. Nevertheless, many governments continue to allocate inadequate resources to their health care systems and lack the political will to improve the quality of their public health systems and the integration of those systems nationally and internationally. This observation highlights an additional lesson offered by SARS, one that echoes what we have learned from HIV/AIDS, influenza, Ebola, malaria, and a host of other infectious diseases: the desperate state of public health infrastructure in much of the world, and especially in those countries where microbial threats are likeliest to emerge and take hold. If such lessons are to be heeded, global strategies to enhance the prevention and control capabilities of all nations will be important as the world prepares for future outbreaks of infectious disease.

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Footnotes

13

Shortly before the publication of this report in January 2004, the highly pathogenic H5N1 avian influenza virus was implicated in a human outbreak of the disease in Vietnam and Thailand. Sixteen of the 20 individuals so far infected have died. Thousands of birds in eight countries, including Vietnam, The Republic of Korea, Thailand, China, and Japan are suspected to be infected with the virus. See http://www.who.int/en/disease outbreaks for more information.

14

Workshop presentation, Robert Webster, St. Jude's Children's Research Hospital, October 1, 2003.

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