

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Certainties and Uncertainties Facing Emerging Respiratory Infectious Diseases: Lessons From SARS

Yee-Chun Chen, 1,2,3 * Shan-Chwen Chang, 1,2,3 Keh-Sung Tsai, 1,2,3,4 Fang-Yue Lin^{5,6}

Every emerging infectious disease is a challenge to the whole of mankind. There are uncertainties regarding whether there will be a pandemic, if it will be caused by the highly pathogenic H5N1 influenza virus, when or where it will occur, how imminent or how severe it will be. No one can accurately predict if and when a given virus will become a pandemic virus. Pandemic prevention strategies must be based on preparing for the unexpected and being capable of reacting accordingly. There is growing evidence that infection control measures were helpful in containment of severe acute respiratory syndrome (SARS) as well as avian influenza. Compliance of standard infection control measures, intensive promotion of hand and respiratory hygiene, vigilance and triage of patients with febrile illness, and specific infection control measures are key components to contain a highly contagious disease in hospital and to protect healthcare workers, patients and visitors. The importance of standard precautions for any patient and cleaning and disinfection for the healthcare environment cannot be overemphasized. SARS illustrated dramatically the potential of air travel and globalization for the dissemination of an emerging infectious disease. To prevent the potential serious consequences of pandemic influenza, timely implementation of pharmaceutical and non-pharmaceutical interventions locally within the outbreak area is the key to minimizing global spread. Herein, we relate our perspective on useful lessons derived from a review of the SARS epidemic that may be useful to physicians, especially when looking ahead to the next epidemic. [J Formos Med Assoc 2008; 107(6):432-442]

Key Words: avian influenza, emerging disease, infection control, pandemic, SARS virus

Every emerging infectious disease is a challenge to the whole of mankind. There is no name, no clearcut clinical diagnosis, no test, no idea of clinical course, no idea of long-term implications, little idea how it is spread, little knowledge of the start and end of infectiousness, and questions regarding short- and long-term immunity. There are uncertainties regarding whether there will be a pandemic, will it be caused by H5N1, when or where it will occur, how imminent it is, or how severe it will be. The uncertainty and destructive potential of disease outbreaks and adult public health emergencies give them a high public and political profile.¹ In the last few decades, new diseases began to emerge at an unprecedented rate of one or more per year. Furthermore, new highly contagious diseases, such as severe acute respiratory syndrome (SARS) and avian influenza, know no borders.

©2008 Elsevier & Formosan Medical Association



Departments of ¹Internal Medicine, ⁴Laboratory Medicine and ⁵Surgery, and ²Center for Infection Control, National Taiwan University Hospital, and Departments of ³Medicine and ⁶Surgery, National Taiwan University College of Medicine, Taipei, Taiwan.

Received: September 19, 2007 **Revised:** February 24, 2008

ELSEVIER Accepted: March 31, 2008

*Correspondence to: Dr Yee-Chun Chen, Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei 100, Taiwan. E-mail: yeechunchen@gmail.com

SARS originated in November 2002 in the Guangdong Province of China, and by February 2003, had spread to Hong Kong and subsequently to 32 other countries or regions, infecting 8096 patients and resulting in 774 deaths.^{2,3} SARS is unique in several aspects. SARS was the first emerging infectious disease for which WHO issued a global alert, on March 12, 2003. It illustrated dramatically the potential of air travel and globalization for the dissemination of an emerging infectious disease. The concentration of cases in previously healthy adults and the proportion of patients requiring intensive care was particularly alarming.4-7 SARS caused morbidity and mortality in healthcare workers (HCWs) and intrahospital transmission amplified regional outbreaks and augmented spread of the illness into the community.^{2,3} All added a tremendous burden to healthcare systems in the absence of natural disaster or war. The cost of SARS was substantial: a 4% drop in GDP in Hong Kong (> 6 billion US dollars) was estimated by the Asian Development Bank.8

From SARS, we know that an infectious disease in one country is a threat to all. An infectious disease outbreak reveals weaknesses in the public health infrastructure. Emerging infectious diseases can be contained with a high level of government commitment and international collaboration. 1,9,10 Multidisciplinary approaches and cooperation from veterinary, medical, public health, epidemiology, microbiology and immunology communities are important for the protection of everyone. In our ever-shrinking world, widespread media coverage of infections-ranging from SARS and influenza in Asia to acute gastroenteritis due to norovirus on cruise ships in Europe and the outbreak due to Escherichia coli 0157 in the United States—has raised public interest in contagious diseases to new heights. 11 Recent experiences with the highly pathogenic avian influenza A/H5N1 have given the world its first advance warning that another influenza pandemic may be imminent.^{1,12,13} To prevent the potential serious consequences of a pandemic, timely implementation of pharmaceutical and non-pharmaceutical interventions locally within the outbreak area is the key to minimizing global spread.^{12,14} As air travel and global trade are now commonplace and have facilitated the international spread of emerging infectious diseases within a very short period of time, a review of the lessons learned from the latest outbreak of SARS is important.

Transmissibility and Containment Strategies

SARS is a zoonotic disease caused by a new coronavirus (SARS-CoV). 2,9,15,16 SARS-CoV evolved consistently and rapidly within its animal and human hosts, while both the infectivity of the virus and the severity of the disease varied, along with the variation/adaptation of the virus to its hosts. 16 Transmissibility refers to the capacity of an infectious agent to spread from one person to another, and risk of infection depends on the conditions of exposure.¹⁷ Lipsitch et al¹⁸ and Riley et al¹⁹ calculated that the basic case reproduction number (R_0) —the fundamental epidemiologic quantity that determines the potential for disease spread—is of the order of 2-4 (excluding superspreading events). Both studies suggested that an achievable combination of control measures, including hand washing, the use of an appropriate and well-fitted facemask, isolation of SARS cases, enhanced surveillance and effective contact tracing and quarantine of asymptomatic contacts (shortening the time from symptom onset to isolation of patients), can be effective in containing SARS, as mentioned previously.^{7,20} Transmission rates fell during the epidemic: R_0 fell from a mean of 7 in the first week of the Singapore outbreak to a mean of 1.6 in the second week, to a mean below 1 in most weeks thereafter. 18

Molecular epidemiologic studies indicated that viruses from the outbreaks in Hong Kong, Vietnam, Singapore, Toronto, and Taiwan are clonally related. ^{21–24} Compliance with standard precautions, alertness and using inline suction for the undiagnosed SARS patient (first SARS patient in Taiwan) who had respiratory failure and was intubated in the emergency room (ER) were

the reasons that no HCWs became seropositive and no intrahospital spread occurred before implementation of specific infection control strategies at the National Taiwan University Hospital (NTUH).²⁵ Unexpectedly, the good performance of NTUH during the initial phase of the SARS epidemic in Taiwan resulted in underestimation of the continuous risk of transmission from the neighboring affected areas into Taiwan.^{26–28} A similar situation developed in Canada and resulted in a second wave of the epidemic.²⁹

Super-spreading Events

Experts were concerned about the evident heterogeneity in transmission.³⁰ In extreme instances of SARS, there were super-spreading events, where single individuals apparently infected as many as 300 others.^{29,31,32} Understanding and quantifying these super-spreading events is clearly vital for the containment of SARS.³⁰ However, it remains difficult to differentiate such superspreading events that are due to persons secreting an exceptionally high amount of infectious material, from those with an environmental factor working to amplify transmission at some key phase of virus shedding. For example, aerosolgenerating procedures and environmental contamination may have contributed to a large intrahospital spread in the epidemic of SARS. 6,33 A recent study revealed that the independent risk factors associated with nosocomial outbreaks of SARS among hospital wards in Guangzhou and Hong Kong, China, included a distance between beds of ≤ 1 m, lack of availability of washing or changing facilities for staff (protective), resuscitation performed in the ward, staff members working while experiencing symptoms, host patient (index patient or the first patient with SARS admitted to a ward) requiring oxygen therapy, and host patient requiring bi-level positive airway pressure ventilation.³⁴

Two aforementioned phenomena warrant caution when we are facing emerging pandemic influenza: travel and super-spreading events.^{35,36}

It is anticipated that adults undertaking international travel might be infected and spread the disease worldwide, as noted during the SARS epidemic.⁴ Once the elderly and persons with chronic illnesses are infected, the clinical presentation might be atypical and masked by comorbidities. Furthermore, viral load might be high and viral shedding might be prolonged in immunocompromised hosts, resulting in a high chance of spread.³⁷ Thus, super-spreading events should be taken into consideration during preparedness for a pandemic. The community, patients and visitors should be educated in addition to HCWs.

Mode of Transmission and Infection Control Strategies

The major mode of transmission of SARS-CoV is through close contact, in particular, through exposure to droplets of respiratory secretions from an infected person.² Thus, wearing masks is emphasized. However, two overlapping sets of disease signs and symptoms have been reported, with some patients having varying degrees of enteric disease. Diarrhea developed early in the course of disease.^{38,39} Up to seven of the first 10 patients at NTUH38 and five of the first 10 patients in Canada⁴⁰ had diarrhea. Although a review of data from China, Hong Kong, Canada and Singapore showed that only 20.1% of patients had diarrhea,² up to 73.3% of 75 patients treated with ribavirin and steroids had watery diarrhea. 41 Some of these differences may result from the timing and quality of data collection. In our cohort, diarrhea developed before the occurrence of cough⁴²⁻⁴⁴ and became exacerbated in parallel to desaturation in the second week of illness. 38,41

SARS-CoV in feces was identified by RT-PCR in 97% at day 14 and positivity rates were highest in feces, followed by nasopharyngeal aspirates and urine samples.⁴¹ The virus is stable in feces and urine and can survive after drying on surfaces.^{45,46} Thus, contamination of the environment by infectious respiratory secretions or other body fluids (e.g. saliva, tears, urine, feces) may play a role in

disease transmission.^{28,33} Thus, educating HCWs, patients, caregivers and visitors to maintain both hand hygiene and environmental hygiene together are important. SARS-CoV is completely inactivated by ≤ 5 minutes of exposure to 75% ethanol, 500 ppm hypochlorite, and household detergent.^{45,46} Disinfection and disinfestations are important in healthcare settings and households. Disinfection of the sewage system, elimination of rodents and cockroaches, and proper garbage disposal are also important.

Influenza is transmitted through close contact via large droplets, direct or indirect. Fine droplet inhalational transmission may also occur. 12,13,35,36 Adults infected by seasonal influenza virus are typically infectious at or before the onset of illness. Young children and immunocompromised persons can shed the virus for longer than healthy adults. Contagiousness of influenza varies inversely with the level of immunity in the population. 17,37 Thus, the containment or attenuation of pandemic influenza before the availability of an effective vaccination depends on early detection and before large numbers are involved. 12

Recently, a case report described a human H5N1 infection with fever and diarrhea but no respiratory symptoms.⁴⁷ Avian influenza virus can survive in the environment for days, but it can be inactivated by standard hospital disinfectants.³⁶ Once again, the importance of routine cleaning and disinfection following standard procedures for the healthcare environment cannot be overemphasized.

Implicit Cases and Patients with Dual Diagnosis

Unrecognized cases of SARS are probably the most important factor that led to intrahospital spread and cases among HCWs.^{6,27,28,48} The nonspecific signs and symptoms, long incubation period (mean, 6.4 days), long time between onset of symptoms and hospital admission (from 3–5 days),³² and lack of a reliable diagnostic test in the early phase of the illness can lead to potential

transmission to frontline HCWs and the community. Early diagnosis relies on known history of potential exposure to SARS. High vigilance is needed and clinicians must be familiar with the rapidly changing epidemiology of this infection.

Despite efforts in developing rapid laboratory assays for SARS, the sensitivity of RT-PCR for samples collected during the first 3 days of illness is inadequate for infection control purposes. Yet it is not practical and cost-effective to screen every patient with febrile illness when the incidence of disease is relatively low or when the epidemic becomes overwhelming. Screening tools using easily available symptomatic and laboratory items are highly desirable. A 6-item clinical score was developed for triaging patients with febrile illness in the emergency room. 42-44 The sensitivity reached 92.6% and the specificity 71.2%. 42 In this model, we emphasize the sequential development of symptoms and diarrhea in addition to cough.⁴⁴ As this scoring system was implemented irrespective of the epidemiological link, it was useful when SARS was spreading in the community. However, limitations remained. As this discrimination system was generated during non-influenza seasons and the majority of patients in the deprivation cohort were otherwise healthy adults, the predictive value decreased in the validation cohort when patients with comorbidity acquired SARS.⁴³ The predictive value is anticipated to decrease in those without immunity to seasonal influenza during the influenza season.

Early in the SARS epidemic, a case definition was generated for epidemiological purposes. ⁴⁹ Despite a global alert, several cases remained unrecognized and outbreak investigation found these implicit cases with either atypical presentation or in the early stage of infection, comorbidity or old age. All evidence suggests that heightened vigilance and infection-control measures should be maintained routinely.

The index case causing intrahospital spread in Southern Taiwan was admitted under the diagnosis of acute pyelonephritis. ⁴⁸ A pulmonary consolidation was noted incidentally during a routine chest X-ray. The history of the visit to Hospital A in

Taipei (the first intrahospital spread of SARS in Taiwan) was not obtained until an infectious disease specialist was consulted for persistent fever. The index case causing the NTUH ER outbreak was a 73-year-old man with chronic cardiopulmonary and renal diseases. He had dyspnea and orthopnea. He denied the history of visits to Hospital A for fear of being stigmatized.²⁸ The first patient linked to the second phase of the Ontario outbreak was a 96-year-old man admitted with a fractured pelvis.²⁹ He had no apparent contact with a patient or an HCW with SARS, and aspiration pneumonia and Clostridium difficile-associated diarrhea appeared to be probable explanations for his symptoms. Both elderly patients developed fever and new pulmonary infiltration during hospitalization.

Fisher et al were the first to report four patients with atypical presentations of SARS.50 All had chronic cardiopulmonary diseases and three were elderly patients. According to the updated interim US CDC case definition for SARS on July 16, 2003, the clinical criteria of SARS include asymptomatic or mild respiratory illness, moderate respiratory illness, and severe respiratory illness. 51 This guideline emphasized that clinical judgment should be used when evaluating patients for whom a measured temperature of > 38°C has not been documented. Factors that might be considered include patient self-report of fever, use of antipyretics, presence of immunocompromising conditions or therapies, lack of access to healthcare, or inability to obtain a measured temperature.

Asymptomatic or mild cases, though limited in numbers, were documented. 52-57 The seroprevalence of antibody to SARS-CoV in cohorts of HCWs with subclinical infection in SARS and non-SARS medical wards was 2.3% and 0%, respectively. 57 A seroprevalence survey in Guangzhou identified its presence in 40% of animal traders, 20% of animal slaughterers, 5% of vegetable traders and 0% of controls. 15 Che et al 52 recently reported the first case of asymptomatic SARS with antigenemia and seroconversion who worked in the same restaurant with one of the four community-acquired cases of SARS.

What We Know for Certain

Although it is impossible to predict the individual emergence in time and place, we can be confident that new microbial diseases will emerge. Every one of us should work together to build a stronger, more flexible healthcare and public health system that is well-prepared to respond to known disease problems, as well as to address the unexpected, whether it be an influenza pandemic, a disease caused by an unknown organism, or a bioterrorist attack.

SARS and highly pathogenic avian influenza are two important emergent infections with pandemic potential. Both infections have crossed the species barrier to infect humans. As with the outbreak of SARS, the development of sensitive and accurate early diagnostic tests is extremely important for successful control of the outbreak at source. The availability of isolation facilities, the stockpiling of antiviral agents and effective and safe vaccination will be extremely important in minimizing the damage of a new influenza pandemic. However, there are important differences in the dynamics of infection between SARS and influenza A/H5N1 which have had an impact on infection control (Table).⁵⁸⁻⁶⁴

Reinforcement of infection control measures and compliance monitoring on a regular basis Standard precautions should be applied to every patient and education should be given to everyone in healthcare facilities. 25 HCWs, caregivers and even the patient should follow hand hygiene practices (e.g. washing hands before and after touching a patient or the environment, even when no epidemic is apparent). Following the SARS outbreak in a nearby hospital, HCWs at NTUH ER wear N-95 respirators for all patient care. However, masks do not prevent acquisition of SARS from a contaminated environment.^{28,65} Furthermore, it is likely the spread of SARS was facilitated by lack of proper hand washing after taking care of unrecognized SARS patients.34 Compliance monitoring and reinforcement are needed for maximal effectiveness of infection control measures.

	Severe acute respiratory syndrome	Highly pathogenic avian influenza A/H5N1
Etiology	RNA virus of the family Coronaviridae	RNA virus of the family Orthomyxoviridae
National host reservoirs and intermediate hosts	Palm civet, raccoon dogs and horseshoe bats	Wild bird and domestic poultry including chicken, geese, ducks, quail
Mode of transmission	Predominantly human-to-human transmission through droplet transmission, direct and indirect contact of the patients or fomites contaminated by respiratory secretions, feces, urine, and tears of infected individuals, airborne only in unique situation	Predominantly direct avian-to-human transmission through droplet and contact transmission
Human-to-human transmission	Efficient and sustained	Limited and nonsustained, but mutation might occur in the future resulting in improved transmission and possibly a pandemic in humans*
Incubation period	2–14 days	2–8 days
Clinical presentations Transmissibility	 Nonrespiratory prodrome lasting 2–7 days characterized by one or more of the following: fever, headache, malaise, myalgia, diarrhea Respiratory phase beginning 2–7 days after onset, characterized by nonproductive cough and dyspnea Lymphopenia, thrombocytopenia, elevated transaminases, lactate dehydrogenase and creatine phosphokinase levels Physical signs on chest examination are minimal compared with radiographic findings which show abnormalities (ground-glass opacities and focal consolidations, especially in periphery and subpleural regions of the lower zones) in almost all patients by the second week of illness; shifting of radiographic shadows and progressive involvement of both lungs are not uncommon Transmissible on or after the 5th day of onset of fever, in line with rising viral load in 	- High fever with flu-like illness, or diarrhea, vomiting with abdominal and pleuritic pain progress rapidly within the first week to respiratory failure - Lymphopenia, thrombocytopenia and elevated transaminases Most infectious before and in the first 2 days of illness
Courds fetality water	nasopharyngeal secretions that peak at around day 10 - Average number of secondary cases resulting from a single case was 2–4	
Crude fatality rate	9.6% (774/8096)	62.7% (226/360)
Early detection strategy	 Fever surveillance, clinical presentation plus epidemiologic risk factors[†] Direct detection of viral nucleic acids in respiratory secretions by RT-PCR[‡] 	 Clinical presentation plus epidemiologic risk factors[§] Immunologic detection of viral antigen in respiratory secretions, direct detection of viral RNA in respiratory secretions by RT-PCR Repeated collection of multiple specimer types is recommended

Table. Continued		
	Severe acute respiratory syndrome	Highly pathogenic avian influenza A/H5N1
Confirmatory diagnosis	Virus isolation in respiratory, fecal, urine, tissue specimens, immunologic detection of antibody in paired serum samples	Virus isolation in respiratory secretions, immunologic detection of antibody in paired serum samples
Hospital infection control methods	 Early recognition, triage, and prompt isolation of suspected cases Personal protective equipment Droplet and contact precautions, airborne precautions for aerosol-generating procedures Contact tracing and quarantine of contacts, temperature check at entry points 	 Same as for SARS Anticipated performances of triage for early recognition of suspected cases and temperature check to prevent intrahospital spread are poor as compared to those during SARS epidemic
Availability of vaccines	Under development	Under development
Availability of antivirals	No	Oral oseltamivir, inhaled zanamivir

^{*}In Asia, risk of reassortment is particularly high as large populations of domestic poultry and pigs live in close proximity to humans; live birds and poultry are sold in markets, thereby increasing the chance of spread of infection from sick birds to humans. Recent molecular analysis of the complete genome of the 1918 virus revealed that this virus was not a reassortment strain but more likely an avian virus that had adapted to infect humans.

Respiratory hygiene/cough etiquette

Healthcare facilities should promote respiratory hygiene/cough etiquette by educating HCWs, patients, caregivers, and visitors on the importance of containing respiratory spray and secretions to help prevent the transmission of influenza and other respiratory viruses. ^{14,36,66} Healthcare facilities should post signs requesting that patients and family members with acute febrile respiratory illness use respiratory hygiene/cough etiquette and provide resources for hand hygiene in common areas.

It is likely that some aerosol-generating medical procedures (such as endotracheal intubation, open suctioning, nebulizer treatment, bronchoscopy, and positive airway pressure devices) could increase the potential for generation of small aerosols in the immediate vicinity of the patient and may inadvertently spread the disease. Thus, these procedures should be performed with precautions and kept in mind for emerging diseases, tuberculosis and other respiratory infectious diseases. During the epidemic, clear guidelines should be laid out to protect the frontline staff from unnecessary exposure which may jeopardize their

lives. In addition, aerosol-generating procedures should be performed in an airborne isolation environment.³⁶

Recognition of a new disease or a cluster of infection

A repeated theme in reviewing emergent outbreaks is that it is essential that astute clinicians with sufficient experience recognize and distinguish something new.^{25,36} Appropriate history taking when a patient with a fever is seen, to obtain important information, such as recent travel history, occupation, contacts with possibly infected persons, persons with similar symptoms, sick or dead animals, or a cluster of persons with similar symptoms, could help to quickly identify people at risk and reduce spread.

Immediate source and contact tracing, quarantine and isolation

Source and contact tracing should rapidly identify possible early secondary cases and any unrecognized sources of infection for persons without epidemiologic links. Regarding risk of intrahospital

[†]Use of WHO SARS criteria as a clinical screening tool gave a sensitivity of 28%, specificity of 96%, positive predictive value of 11%, and negative predictive value of 99%.

[‡]Only 35–65% of specimens tested positive in the first few days of the disease using the first generation of RT-PCR assays.

[§]Avian influenza was the initial diagnosis in only 10% of patients with confirmed H5N1 virus infection in Indonesian and Thai series.

spread of a highly contagious disease, infectioncontrol teams may additionally institute passive or active surveillance for pneumonia or fever among staff and patients, combined with diagnostic testing for the infectious agent. The intensity of surveillance efforts will need to be tailored to the degree of local transmission within both the community and healthcare facilities.

Specific infection control measures were implemented for patients with SARS, H5N1, or other highly contagious diseases. 14,25,28,36 In non-SARS areas, infection control measures were upgraded stepwise in response to possible healthcare associated transmission and the increasing possibility of community spread of SARS. On the other hand, personal protective equipment in hospital services caring for SARS or avian influenza, and its disposition were stratified based on the risk assessment because resources might be limited. 12,67 In response to inadequate capacity of the negative pressure isolation room within the intensive care facility, intubated patients whose airway secretions, stool and urine become negative for SARS-CoV or H5N1 RNA should be removed from the negative pressure isolation rooms. Droplet and contact precautions and inline suction should be performed in single rooms.

Risk assessment

In facing emerging infectious diseases, WHO emphasizes risk assessment, including burden assessment and needs assessment.¹² Disease pattern, population at risk and factors affecting transmission pattern and control activities will be determined or characterized. The scale of interventions required to control an epidemic depends on the number of infectious cases present at the time the control measures are instituted and on logistical constraints, such as availability of isolation facilities. Furthermore, isolation and quarantine procedures will be less effective as more cases accrue.⁶⁸ Therefore, stringent measures implemented early in the course of the epidemic prevent the need for more stringent measures as the epidemic spreads. 18 Nevertheless, it is practical and most feasible that routine infection control strategies and traditional,

standard interventions used during outbreak control should be applied immediately before laboratory confirmation of the causative agent. Hand and respiratory hygiene should be promoted. Domestic cleaning using household cleaning products, to reduce transmission via fomites and from infectious respiratory secretions on surfaces, is important as well.¹²

Risk communication

Finally, risk communication is essential not only within or between institutions, but also within and between local and national public health authorities.⁶⁹ Disease outbreaks are inevitable, and often unpredictable, events. The environment surrounding an outbreak is unique in public health. Outbreaks are frequently marked by uncertainty, confusion and a sense of urgency. Communication failures delay outbreak control, undermine public trust and compliance, and unnecessarily prolong economic, social and political turmoil. If implemented effectively, guidelines for outbreak communication will result in greater public resilience and guide appropriate public participation to support the rapid containment of an outbreak, thus limiting morbidity and mortality.⁶⁹ In addition, effective outbreak communication will minimize the damage to a nation's international standing, its economy and its public health infrastructure. However, the decisions and actions of public health officials have a greater effect on trust and public risk perception than communication.

Conclusion

The population-dense regions of Southeast Asia are the epicenter of many emerging diseases, as evidenced by the outbreak of SARS, avian influenza A/H5N1, dengue, and enterovirus 71 in this region in the past decade. Rapid identification, epidemiologic surveillance, and prevention of transmission are major challenges in ensuring public health safety. Pandemic prevention strategies must be based on preparing for the unexpected and being capable of reacting accordingly.

Strategies for survival in the face of emerging pathogens include biotechnology (chemoprophylaxis, vaccines, treatment), public health (for foodborne, water-borne and fecal-borne diseases), and behavior modification (for sexually transmitted diseases). However, prevention of airborne transmission of microbes remains a challenge.

The primary role of an infection-control program is to reduce the risk of healthcare-associated infection, thereby protecting patients, HCWs and visitors. Prevention of transmission of a contagious infectious disease is thus an important guard for the whole society. Healthy habits can protect everyone from getting germs or spreading germs at home, school or work. Simple actions, like covering your mouth and nose and washing your hands often, can stop germs and prevent illnesses ⁶⁶

Emerging infectious diseases can be contained with high-level government commitment and international collaboration to strengthen infectious disease surveillance and response, improve methods for gathering and evaluating surveillance data, ensure the use of surveillance data to improve public health practice and medical treatment, strengthen a nation's capacity to monitor and respond to emerging infectious diseases, implement, support, and evaluate programs for the prevention and control of emerging infectious diseases, and to develop, evaluate, and promote strategies to help healthcare providers and other persons change behavior that facilitates disease transmission. The mobilization and coordination of efforts at all levels of government and private sectors are also important. Furthermore, international collaboration and resource and information sharing are also essential for the control of emerging diseases worldwide.

However, challenges remain, including how best to allocate limited medical and public health resources for preparedness planning. Whether avian influenza will become a pandemic or SARS will become a recurring problem is uncertain, but lessons learned while preparing for that eventuality will be important for other global infectious disease outbreaks.

Acknowledgments

We are grateful to all hospital staff and members of the Center for Infection Control for their important contributions during the SARS epidemic. This study was supported by a grant from the Center for Disease Control, Taiwan (DOH96-DC-1010).

References

- World Health Organization. World Health Day 2007: International Health Security—Invest in Health, Build a Safer Future. Available from http://www.who.int/ mediacentre/news/releases/2007/pr11/en/index.html and http://www.who.int/world-health-day/files/2007/ issuespaper_final_lowres_en.pdf [Date accessed: March 31, 2007]
- Peiris JSM, Yuen KY, Osterhaus ADME, et al. The severe acute respiratory syndrome. N Engl J Med 2003;349: 2431–41.
- World Health Organization. Summary of Probable SARS
 Cases with Onset of Illness from 1 November 2002 to 31
 July 2003. Available from http://www.who.int/csr/sars/
 country/table2004_04_21/en/index.html [Date accessed:
 February 14, 2008]
- Tsang T, Lai-Yin T, Pak-Yin L, et al. Update: outbreak of severe acute respiratory syndrome worldwide, 2003. MMWR 2003;52:241–8.
- Tsang KW, Ho PL, Ooi GC, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl | Med 2003;348:1977–85.
- Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Eng J Med 2003;348:1986–94.
- Tomlinson B, Cockram C. SARS: experience at Prince of Wales Hospital, Hong Kong. *Lancet* 2003;361:1486–7.
- Lim W. Presentation at the epidemiology breakout session.
 WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, June 17–18, 2003.
- World Health Organization Multicentre Collaborative Network for Severe Acute Respiratory Syndrome (SARS) Diagnosis. A multicentre collaboration to investigate the cause of severe acute respiratory syndrome. *Lancet* 2003; 361:1730–3.
- 10. Chen YC, Chen MF, Liu SZ, et al. SARS in teaching hospital, Taiwan. *Emerg Infect Dis* 2004;10:1886–7.
- 11. Musher DM, Musher BL. Contagious gastrointestinal infections. *N Engl J Med* 2004;351:2417–27.
- World Health Organization. WHO Pandemic Influenza Draft Protocol for Rapid Response and Containment. Updated draft 30 May 2006. Available from http://www.who.int/csr/resources/publications/influenza/

- WHO_CDS_EPR_GIP_2006_2/en/index.html [Date accessed: March 31, 2007]
- 13. Hsieh YC, Wu TZ, Liu DP, et al. Influenza pandemics: past, present and future. *J Formos Med Assoc* 2006;105:1–6.
- 14. Chen YC, Chang SC. Infection control for influenza and avian influenza. *Formos | Med* 2006;10:79–88. [In Chinese]
- 15. Guan Y, Zheng BJ, He YQ, et al. Isolation and characterization of viruses related to the SARS coronavirus from animal in southern China. *Science* 2003;302:276–8.
- Song HD, Tu CC, Zhang GW, et al. Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. *Proc Natl Acad Sci USA* 2005;102: 2430–5.
- 17. Musher DM. How contagious are common respiratory tract infections? *N Engl | Med* 2003;348:1256–66.
- 18. Lipsitch M, Cohen T, Cooper B, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science* 2003;300:1966–70.
- Riley S, Fraser C, Donnelly CA, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. *Science* 2003;300:1961–6.
- 20. Chan PKS, Ip M, Ng KC, et al. Severe acute respiratory syndrome-associated coronavirus infection. *Emerg Infect Dis* 2003;9:1453–4.
- Ruan Y, Wei CL, Ee LA, et al. Comparative full-length genome sequence analysis of 14 SARS coronavirus isolates and common mutations associated with putative origins of infection. *Lancet* 2003;361:1779–85.
- Tsui SKW, Chim SSC, Lo YMD. Coronavirus genomic sequence variations and the epidemiology of the severe acute respiratory syndrome. *N Engl J Med* 2003;349: 187–8.
- Guan Y, Peiris JSM, Zheng B, et al. Molecular epidemiology of the novel coronavirus that causes severe acute respiratory syndrome. *Lancet* 2004;363:99–104.
- Yeh SH, Wang HI, Tsw CY, et al. Molecular epidemiology and genomic evolution of SARS infection in Taiwan. Proc Natl Acad Sci USA 2004;101:2542–7.
- 25. Chen YC, Chen PJ, Chang SC, et al. Infection control and SARS transmission among healthcare workers, Taiwan. *Emerg Infect Dis* 2004;10:895–8.
- Twu SJ, Chen TJ, Chen CJ, et al. Control measures for severe acute respiratory syndrome (SARS) in Taiwan. *Emerg Infect Dis* 2003;9:718–20.
- 27. Lee ML, Chen CJ, Su IJ, et al. Severe acute respiratory syndrome Taiwan, 2003. *MMWR* 2003;52:461–6.
- 28. Chen YC, Huang LM, Chan CC, et al. SARS in hospital emergency room. *Emerg Infect Dis* 2004;10:782–8.
- Wallington T, Berger L, Henry B, et al. Update: severe acute respiratory syndrome — Toronto, Canada, 2003. MMWR 2003;52:547–50.
- Dye C, Gay N. Modeling the SARS epidemic. Science 2003;300:1884–5.
- 31. Leo YS, Chen M, Heng BH, et al. Severe acute respiratory syndrome Singapore, 2003. *MMWR* 2003;52:405–11.

- Donnelly CA, Ghani AC, Leung GM, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet* 2003;361: 1761–6.
- 33. Dowell SF, Simmerman JM, Erdman DD, et al. Severe acute respiratory syndrome coronavirus on hospital surfaces. *Clin Infect Dis* 2004;39:652–7.
- 34. Yu IT, Xie ZH, Tsoi KK, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not in others? *Clin Infect Dis* 2007;44:1017–25.
- 35. Tellier R. Review of aerosol transmission of influenza A virus. *Emerg Infect Dis* 2006;12:1657–62.
- World Health Organization. Avian Influenza, Including Influenza A (H5N1), in Humans: WHO Interim Infection Control Guideline for Health Care Facilities. Revised 24 April 2006. Available fromhttp://www.who.int/csr/disease/ avian_influenza/guidelines/infectioncontrol1/en/index.html [Date accessed: March 31, 2007]
- Treanor JJ. Influenza virus. In: Mandell G, Bennett J, Dolin R, eds. Principles and Practices and Infectious Diseases, 6th edition. Available from http://www.ppidonline.com/content/default.cfm [Date accessed: March 31, 2007]
- 38. Wang JT, Sheng WH, Fang CT, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. *Emerg Infect Dis* 2004;10:818–24.
- 39. Booth CM, Matukas LM, Tomlinson GA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003;289:2801–9.
- 40. Poutanen SM, Low DE, Henry B, et al. Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003;348:1995–2005.
- 41. Peiris JSM, Chu CM, Cheng VCC, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *Lancet* 2003;361:1767–72.
- 42. Chen SY, Su CP, Ma MHM, et al. Predictive model of diagnosing probable cases of severe acute respiratory syndrome in febrile patients with exposure risk. *Ann Emerg Med* 2004;43:1–5.
- 43. Su CP, Chiang WC, Ma MHM, et al. Validation of a novel severe acute respiratory syndrome scoring system. *Ann Emerg Med* 2004;43:34–42.
- 44. Chen SY, Chiang WC, Ma MHM, et al. Sequential symptomatic analysis in probable severe acute respiratory syndrome cases. *Ann Emerg Med* 2004;43:27–33.
- 45. World Health Organization. First Data on Stability and Resistance of SARS Coronavirus Compiled by Members of WHO Laboratory Network. Available from http:// www.who.int/csr/sars/survival_2003_05_04/en/index. html [Date accessed: March 31, 2007]
- 46. Lai MYY, Cheng PKC, Lim WWL. Survival of severe acute respiratory syndrome coronavirus. *Clin Infect Dis* 2005;41: e67–71.
- 47. World Health Organization. H5N1 Avian Influenza: Timeline of Major Events. Available from http://www.who.int/

- csr/disease/avian_influenza/Timeline_2007_03_20.pdf [Date accessed: March 31, 2007]
- 48. Liu JW, Lu SN, Chen SS, et al. Epidemiologic study and containment of a nosocomial outbreak of severe acute respiratory syndrome in a medical center in Kaohsiung, Taiwan. *Infect Control Hosp Epidemiol* 2006;27:466–72.
- World Health Organization. Case Definitions for Surveillance of Severe Acute Respiratory Syndrome (SARS) (revised May 1). Available from http://www.who.int/csr/sars/ casedefinition/en/ [Date accessed: May 4, 2003]
- Fisher DA, Lim TK, Lim YT, et al. Atypical presentations of SARS. Lancet 2003;361:1740.
- Centers for Disease Control and Prevention. Severe Acute Respiratory Syndrome (SARS). Atlanta: 2003. Available from http://www.cdc.gov/ncidod/sars [Date accessed: November 20, 2003]
- 52. Che WY, Di B, Zhao GP, et al. A patient with asymptomatic severe acute respiratory syndrome (SARS) and antigenemia from the 2003–2004 community outbreak of SARS in Guangzhou, China. *Clin Infect Dis* 2006;43:e1–5.
- Wilder-Smith A, Teleman MD, Heng BH, et al. Asymptomatic SARS coronavirus infection among healthcare workers, Singapore. *Emerg Infect Dis* 2005;11:1142–5.
- 54. Ho KY, Singh KS, Habib AG, et al. Mild illness associates with severe acute respiratory syndroem coronavirus infection lessons from a prospective seroepidemiologic study of health-care workers in a teaching hospital in Singapore. *J Infect Dis* 2004;189:642–7.
- Li G, Zhao ZX, Chen LB, et al. Mild severe acute respiratory syndrome. Emerg Infect Dis 2003;9:1182–3.
- Lee HKK, Tso EYK, Chau TN, et al. Asymptomatic severe acute respiratory syndrome-associated coronavirus infection. *Emerg Infect Dis* 2003;11:1491–2.
- 57. Ip M, Chan PKS, Lee N, et al. Seroprevalence of antibody to severe acute respiratory syndrome (SARS)-associated coronavirus among health care workers in SARS and Non-SARS medical wards. Clin Infect Dis 2004;38:e116–8.
- 58. Cheng VCC, Lau SKP, Woo PCY, et al. Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection. *Clin Microbiol Rev* 2007;20: 660–94.
- 59. Ho MS, Su IJ. Preparing to prevent severe acute respiratory syndrome and other respiratory infections. *Lancet Infect Dis* 2004;4:684–9.

- 60. Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza A (H5N1) Virus. Update on avian influenza A (H5N1) virus infection in humans. N Engl J Med 2008;358:261–73.
- 61. World Health Organization. Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO. Available from http://www.who.int/csr/disease/avian_influenza/country/cases_table_20 08_02_12/en/index.html [Date accessed: February 14, 2008]
- Yang Y, Halloran ME, Sugimoto J, et al. Detecting humanto-human transmission of avian influenza A (H5N1). Emerg Infect Dis 2007;13:1348–53. (Also available from http://www.cdc.gov/EID/content/13/9/1348.htm)
- 63. Tambyah PA, Singh KS, Habib AG. SARS, understanding the coronavirus: accuracy of WHO criteria was similar in a "non-SARS" hospital in Singapore. *BMJ* 2003;327:620.
- 64. Taubenberger JK, Reid AH, Lourens RM, et al. Characterization of the 1918 influenza virus polymerase genes. *Nature* 2005;437:889–93.
- Ofner M, Lem M, Sarwal S, et al. Cluster of severe acute respiratory syndrome cases among protected health-care workers—Toronto, Canada, April 2003. MMWR 2003;52: 433–6.
- 66. Centers for Disease Control and Prevention. Respiratory
 Hygiene/Cough Etiquette in Healthcare Settings.
 Available from http://www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm [Date accessed: September 21, 2006]
- World Health Organization. WHO Strategic Action Plans for Pandemic Influenza 2006–2007. Available from http:// www.who.int/csr/resources/publications/influenza/WHO_ CDS_EPR_GIP_2006_2/en/index.html [Date accessed: March 31, 2007]
- Kaplan EH, Craft DL, Wein LM. Emergency response to a smallpox attack: the case for mass vaccination. *Proc Natl Acad Sci USA* 2002;99:10935–40.
- World Health Organization. WHO Outbreak Communication Guidelines. Available from http://www.who.int/infectiousdisease-news/IDdocs/whocds200528/whocds200528en. pdf [Date accessed: February 14, 2008]
- Lederberg J. Paradoxes of the host-parasite relationship. ASM News 1999;65:811.